Tetrahedron 65 (2009) 1140–1146

Contents lists available at ScienceDirect

Tetrahedron

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

$PtCl_2$-catalyzed reactions of *o*-alkynylanilines with ethyl propiolate and dimethyl acetylenedicarboxylate

Xun Li, Jun-Yan Wang, Wei Yu *, Long-Min Wu

State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou, Gansu 730000, PR China

ARTICLE INFO

Article history:
Received 28 May 2008
Received in revised form 10 November 2008
Accepted 26 November 2008
Available online 3 December 2008

Keywords:
Indoles
o-Alkynylanilines
$PtCl_2$
Ethyl propiolate

ABSTRACT

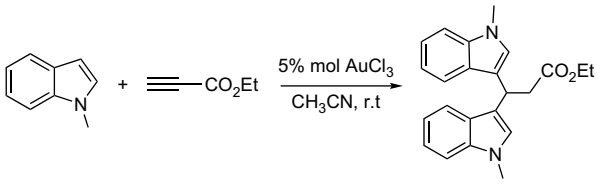
The $PtCl_2$-catalyzed reactions between indoles and ethyl propiolate gave rise to mono and double addition products. The composition of the products was largely influenced by the substituents on the indoles as well as the amount of ethyl propiolate used. *o*-Alkynylanilines reacted with ethyl propiolate and dimethyl acetylenedicarboxylate under the catalysis of $PtCl_2$ to generate the corresponding 2,3-disubstituted indoles. The reaction proceeded by following a sequential cyclization/intermolecular addition pathway.

1. Introduction

The indole ring system exists ubiquitously in nature-occurring products, and many indole-containing compounds exhibit important biological and pharmaceutical activities.[1] The synthesis of indoles has, therefore, been a major area of focus for synthetic organic chemists over the years.[2] Among diverse synthetic strategies toward indoles, the transitional-metal and Lewis acid-catalyzed functionalization of simple indoles constitutes an atom-economical and high efficient approach.[3] As transitional-metal salts could also catalyze the cyclization of *o*-alkynylanilines to indoles,[2,4] it is possible to synthesize muti-substituted indoles through sequential cyclization/alkylation reactions using substituted *o*-alkynylanilines as starting materials. Procedures employing copper, zinc, palladium, platinum, and gold as catalyst have been developed recently to achieve the goal.[5]

The addition of electron-rich arenes and heteroarenes to C–C triple bonds has received much attention recently.[6] Gold and platinum are particularly effective to promote these transformations due to their pronounced alkynophilicity.[7] The use of gold and platinum salts enables these reactions to proceed under mild conditions with high selectivity.[6b,c,8,9] Echavarren et al. recently reported a systematic investigation on the gold-catalyzed intra and intermolecular addition of indoles to alkynes.[10] Cheng et al.[11] investigated the reactions of indoles with alkynyl alcohols employing platinum as catalyst. These studies demonstrate that a variety of substituted indoles could be accessed though the reactions of indoles with alkynes.

The gold and platinum-catalyzed reactions of indoles with electron-poor alkynes such as ethyl propiolate, on the other hand, are far less explored. One research concerning this issue was conducted by He et al.[9b] The authors found that the reaction of *N*-methyl indole with ethyl propiolate in the presence of $AuCl_3$ led only to the formation of double addition product (Scheme 1).



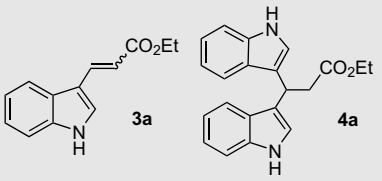
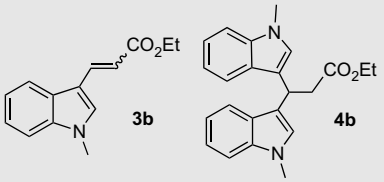
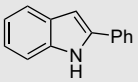
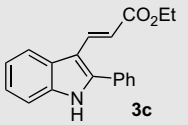
Scheme 1.

Similar results were reported by Fujiwara et al., who employed $Pd(OAc)_2$ in acetic acid to catalyze the similar transformations.[12] Recently, we reexamined the reactions of indoles with ethyl propiolate using $PtCl_2$ as catalyst. We found that the composition of the products was largely influenced by the substituents on the indoles. Furthermore, we extended the reactions to using *o*-alkynylanilines as starting materials, which reacted with ethyl priopiolate and dimethyl acetylenedicarboxylate to give the corresponding 2,3-disubstituted indoles. Herein we wish to report our results.

* Corresponding author. Tel.: +86 931 8912500; fax: +86 931 8915557.
E-mail address: yuwei@lzu.edu.cn (W. Yu).

0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.11.095

Table 1
$PtCl_2$-catalyzed reactions of indoles with ethyl propiolate (**2a**)[a]

Entry	Indole	2a	Reaction time (h)	Products	Yield[b] (%)
1	 **1a**	1.2 equiv	40	 **3a** **4a**	57 (**1a**) 6 (*Z*-**3a**) 7 (*E*-**3a**) 22 (**4a**)
2		3 equiv	40		11 (*Z*-**3a**) 46 (*E*-**3a**) 42 (**4a**)
3	 **1b**	1.2 equiv	40	 **3b** **4b**	53 (**4b**)
4		3 equiv	20		9 (*Z*-**3b**) 40 (*E*-**3b**) 20 (**4b**)
5	 **1c**	1.2 equiv	63	 **3c**	28 (**3c**)
6		3 equiv	50		65 (**1c**) 71 (**3c**)

[a] The reactions were carried out in THF at refluxing temperature. $PtCl_2$ (10 mol %) was used as catalyst.
[b] Isolated yields.

2. Results and discussion

The reactions of indoles (**1**) with ethyl propiolate (**2a**) were carried out in the presence of 10 mol % $PtCl_2$. The best results were obtained when THF was used as solvent at refluxing temperature (Table 1). Unsubstituted indole (**1a**) reacted with ethyl propiolate, forming both the mono addition product **3a** and the double addition product **4a** (Table 1, entries 1 and 2). The conversion was low when only 1.2 equiv of ethyl propiolate was used, with the majority of **1a** recovered. Using 3 equiv of ethyl propiolate raised the yields of both **4a** and **3a**. The yields of the products were much lower when the reactions were performed in other solvents (Table 2). The reaction did not proceed when $AuCl_3$ was used as catalyst. In the case of *N*-methyl indole (**1b**), only double addition product (**4b**) was obtained when 1.2 equiv of ethyl propiolate was used (Table 1, entry 3). This result was consistent with those observed by He et al.[9b] When the usage of ethyl propiolate was raised to 3 equiv, the mono addition products **3b** were also obtained beside **4b** (Table 1, entry 4). On the other hand, the reaction of 2-phenyl indole (**1c**) with ethyl propiolate only gave rise to mono addition product **3c** whatever the amount of ethyl propiolate used (Table 1, entries 5 and 6). These results indicate that the substituents on indoles have profound effect on the consequence of the reactions between indoles and electron-deficient alkynes.

Table 2
The reactions of **1a** with ethyl propiolate (**2a**) in other solvents[a]

Entry	Solvent	2a	Reaction time (h)	Products and yields[b] (%)
1	$ClCH_2CH_2Cl$[c]	1.2 equiv	40	40 (**1a**), 6 (*Z*-**3a**), 5 (*E*-**3a**), 36 (**4a**)
2	$ClCH_2CH_2Cl$[c]	3 equiv	40	2 (**1a**), 15 (*Z*-**3a**), 23 (*E*-**3a**), 45 (**4a**)
3	CH_3CN[c]	1.2 equiv	40	48 (**1a**), 1 (*Z*-**3a**), 3 (*E*-**3a**), 22 (**4a**)
4	CH_3CN[c]	3 equiv	40	4 (**1a**), 4 (*Z*-**3a**), 14 (*E*-**3a**), 40 (**4a**)
5	$PhCH_3$[d]	1.2 equiv	40	37 (**1a**), trace (*Z*-**3a**), 3 (*E*-**3a**) 38 (**4a**)
6	$PhCH_3$[d]	3 equiv	40	6 (*Z*-**3a**), 14 (*E*-**3a**), 55 (**4a**)

[a] The reactions were performed on a 0.2 mmol scale with 10 mol % of $PtCl_2$ as catalyst.
[b] The yields were determined by GC and GC–MS.
[c] The reaction was performed at refluxing temperature.
[d] The reaction was performed at 80 °C.

It is noteworthy that in all the cases summarized in Table 1, the mono addition products were obtained with the preference for *E*-configuration. In the case of **1c**, the only isomer that could be isolated from the reaction mixture was *E*-**3c**. This result is in contrast to those observed previously for the reactions of electron-rich arenes with ethyl propiolate, in which *Z*-selectivity was generally observed.[6a,8,9] We speculated that this *E*-stereoselectivity might be caused by the ready isomerization of *Z*-**3** to *E*-**3** under our reaction conditions. To support this hypothesis, *Z*-**3a** was subjected to the reaction conditions mentioned above to see if the isomerization could take place. As expected, after 30 h, *Z*-**3a** was converted nearly completely to *E*-**3a**. This process must have been very fast in the case of *Z*-**3c**, where the presence of a phenyl group at the 2-position of the indole ring would cause a strong steric repulsion, and therefore, only the thermodynamically favored *E*-**3c** was obtained. Similar preference for *E*-configuration was observed in the $Pd(OAc)_2$/TFA-catalyzed reactions of mesitylene with 3-butyn-2-one,[6a] and the gold-catalyzed hydroarylation of 3-butyne-2-one.[8]

The cyclization of *o*-alkynylanilines to indoles can be readily catalyzed by platinum and gold salts.[7d,e] Recently, Arcadi et al. reported that $NaAuCl_4 \cdot 2H_2O$ could effect the reactions of *o*-alkynylanilines with α,β-enones, and the reactions took place by following a sequential cyclization/Michael type addition pathway.[5d] On the other hand, Li et al. found that $AuCl_3$/AgOTf-catalyzed reactions between *o*-alkynylanilines and arylacetylenes under neat conditions led to the formation of *N*-vinylindoles via a different mechanism, in which the hydroamination of anilines with arylacetylenes took place prior to the cyclization.[5g] It was of our interest to see, which type of products might form if *o*-alkynylanilines were allowed to react with ethyl propiolate.

Subsequently, several different substituted *o*-alkynylanilines (**5**) were treated with 3 equiv of ethyl propiolate (**2a**) in the presence of 10 mol % of $PtCl_2$ in THF at refluxing temperature, and the results are listed in Table 3. Under the reaction conditions, 2-ethynylbenzenamine (**5a**) was transformed to indole **1a** in good yield (entry 1), while the intermolecular addition products **3a** and **4a** formed in only trace amount. Using 20 mol % of $PtCl_2$ did not improve the yields of **3a** and **4a** significantly. When **5b** was used as the substrate, the products were complex mixtures (entry 2). On the

Table 3
Reactions of 2-*o*-alkynylanilines (**5**) with electron-deficient alkynes (**2**)

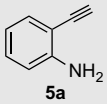
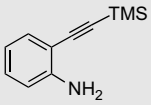
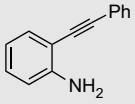
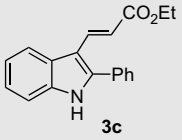
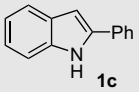
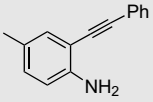
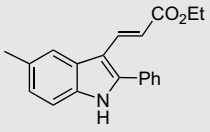
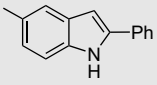
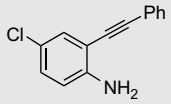
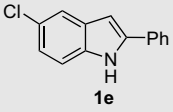
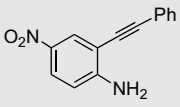
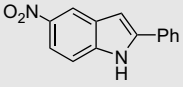
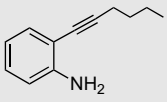
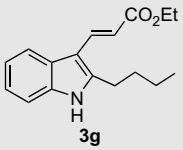
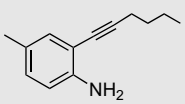
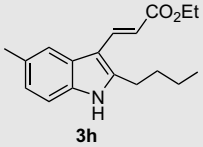
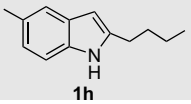
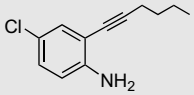
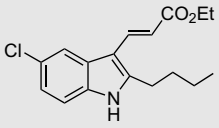
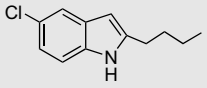
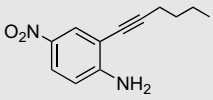
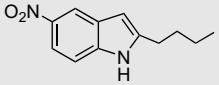
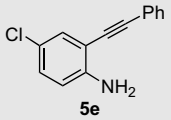
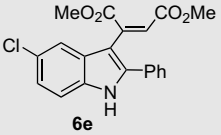
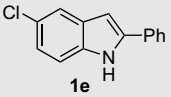
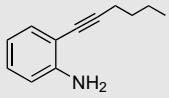
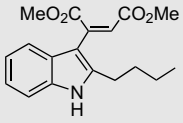
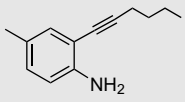
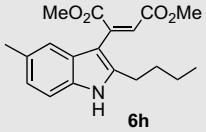
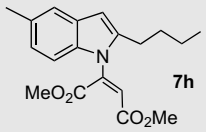
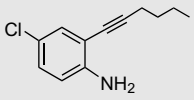
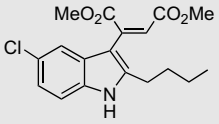
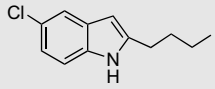
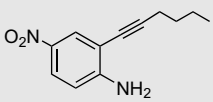
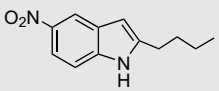
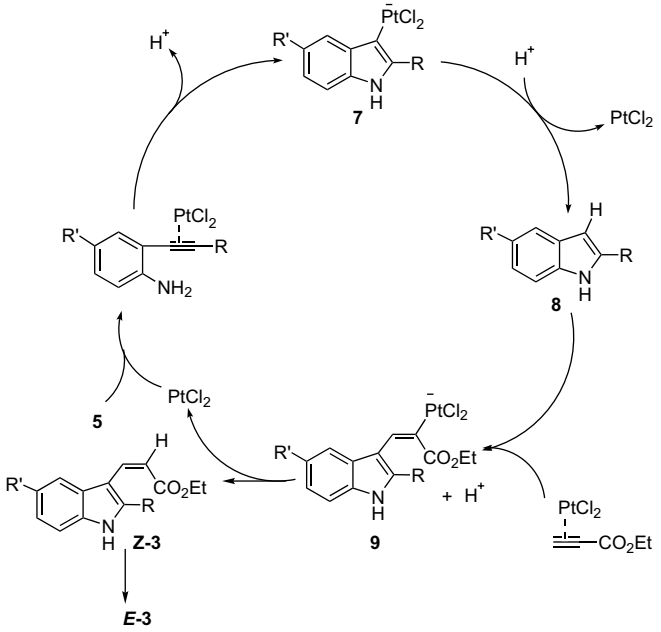
Entry	5	2	Reaction time (h)	Products[a]	Yield[b] (%)
1	 **5a**	**2a**	40	 **1a**	78
2	 **5b**	**2a**	40	Complex mixtures	
3	 **5c**	**2a**	24	 **3c**  **1c**	69 (**3c**) 14 (**1c**)
4	 **5d**	**2a**	36	 **3d**  **1d**	53 (**3d**) 34 (**1d**)
5	 **5e**	**2a**	36	 **1e**	85
6	 **5f**	**2a**	30	 **1f**	75
7	 **5g**	**2a**	14	 **3g**	78
8	 **5h**	**2a**	20	 **3h**  **1h**	56 (**3h**) 27 (**1h**)

Table 3 (*continued*)

Entry	5	2	Reaction time (h)	Products[a]	Yield[b] (%)
9	 **5i**	**2a**	40	 **3i**	59 (**3i**)
				 **1i**	31 (**1i**)
10	 **5j**	**2a**	40	 **1j**	75
11	 **5e**	**2b**	40	 **6e**	56 (**6e**)
				 **1e**	36 (**1e**)
12	 **5g**	**2b**	20	 **6g**	85
13	 **5h**	**2b**	36	 **6h**	40 (**6h**)
				 **7h**	57 (**7h**)
14	 **5i**	**2b**	36	 **6i**	45 (**6i**)
				 **1i**	49 (**1i**)
15	 **5j**	**2b**	40	 **1j**	76

[a] The products were identified by ^{1}H NMR, ^{13}C NMR, EIMS, and HRMS.
[b] Isolated yields.

other hand, when **5c** and **5d** were subject to the condition, **3c** and **3d** were generated, respectively, as the major products (entries 3 and 4), along with the cyclization product **1c** and **1d**. Similarly, 2-hex-1-nyl benzenamines **5g**–**5i** were transformed to the corresponding **3g**–**3i** by reacting with ethyl propiolate. These results suggest that the reactions between *o*-alkynylanilines and ethyl propiolate follow a cyclization/addition reaction pathway, similar to the reactions of *o*-alkynylanilines with α,β-enones.[5d] As indicated in Table 3, the reactions proceeded with high stereoselectivity, with only the *E*-isomers obtained after reaction finished. Based on the previously reported mechanistic studies dealing with the gold and platinum-catalyzed hydroarylation of alkynes and alkenes, a reaction mechanism as depicted in Scheme 2 was proposed to rationalize the formation of products **3**. The first step should involve the intramolecular attack of the amino group on the $PtCl_2$-activated carbon–carbon triple bond in **5**, leading to the formation of intermediate **7**. Compound **7** was converted to **8** by a rapid proton–platinum exchange, and the latter then attacked platinum-complexed ethyl propiolate to give **9**. Finally, **9** was protonated to generate **3**. It is generally believed that in the hydroarylation of alkynes under gold catalysis, the arenes attack the triple bond from the opposite side of the coordinated gold, leading to the formation of *Z*-olefins. The *E*-selectivity observed under certain circumstances is due to the isomerization of the initially produced *Z*-isomer.[7h,8] Considering the similarities on the catalytic behavior between platinum and gold, we think that the same pattern also works in $PtCl_2$-catalzyed reactions, and it is probable that the protonation of **9** would first give rise to sterically demanding *Z*-**3**, which then rapidly isomerized to the thermodynamically more stable *E*-**3**. As mentioned above, our experiments showed that the isomerization from *Z*-**3a** to *E*-**3a** could proceed under the reaction conditions, lending support to the assumption. However, it is also possible that *E*-**3** could be generated directly from **9**. Further theoretical work needs to be done to elucidate this issue.

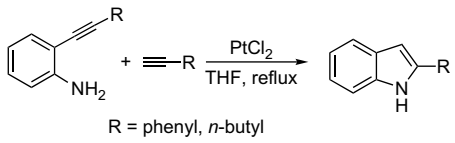


Scheme 2.

For the intermolecular addition to take place, an attachment of alkyl group or aryl group to the carbon–carbon triple bond would be necessary, probably by enhancing the nucleophilicity at the 3-position of indoles. The sensitivity to substituents in the addition step was further demonstrated in the results with **5e**, **5f**, and **5j** (entries 5, 6, and 10). In these cases, only the cyclization products were obtained, indicating that the electron-withdrawing groups at the phenyl ring would hinder the addition to ethyl propiolate, but wouldn't affect the cyclization to indoles.

To further explore the scope of the protocols, the reactions of **5** with dimethyl acetylenedicarboxylate (**2b**) were examined. The results were also summarized in Table 3. As expected, the substrates were transformed to the corresponding 2,3-disubstituted indoles in moderate to good yields except for **5j**. In the case of **5h** (entry 13), beside the normal product **6h**, *N*-substituted product **7h** was also generated.

Attempts were also made to realize the tandem reactions between *o*-alkynylanilines and electron-rich alkynes such as phenylacetylene and 1-hexyne. However, only cyclization products were produced (Scheme 3). The intermolecular addition did not took place, despite that the reactions of indoles with terminal alkynes could be effected by the action of $PtCl_2$.[11]



Scheme 3.

3. Conclusion

In summary, we found that the $PtCl_2$-catalyzed addition of indoles to ethyl propiolate led to the formation of both mono addition and double addition products. The composition of the products was largely affected by the substituents on the indoles as well as the amount of ethyl propiolate used. $PtCl_2$ could effectively catalyze the tandem cyclization/intermolecular addition reactions of *o*-alkynylanilines with electron-poor alkynes such as ethyl propiolate and dimethyl acetylenedicarboxylate, and the protocol provides a convenient approach for the synthesis of 2,3-disubstituted indoles.

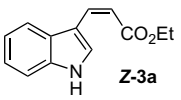
4. Experimental

4.1. General

^1H and ^{13}C NMR spectra (300 and 75.5 MHz, respectively) were recorded on a Varian Mercury Plus-300 spectrometer with TMS as the internal standard in $CDCl_3$. EIMS spectra were measured on an HP 5988A spectrometer by direct inlet at 70 eV. The high resolution mass spectra (HRMS) were measured on a Bruker Daltonics APEX II 47e spectrometer by ESI.

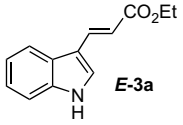
General procedure for the reactions between **5** and ethyl propiolate (or dimethyl but-2-yne dioate): 0.2 mmol of **5**, 0.6 mmol of ethyl propiolate (or dimethyl but-2-yne dioate), and 5 mg $PtCl_2$ (10 mol%) were added into 1 mL anhydrous THF. The mixture was stirred at refluxing temperature under argon atmosphere. After the reaction finished as indicated by TLC analysis, the solvent was removed at reduced temperature. The residual was treated with silica gel chromatography to give the products.

4.2. Spectroscopic data of the products



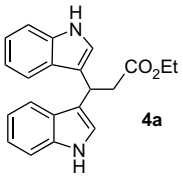
^1H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.91 (s, 1H), 8.61 (br s, 1H), 7.75 (d, 1H, J=6.0 Hz), 7.43–7.40 (m, 1H), 7.32–7.23 (m, 3H), 5.83 (d,

1H, *J*=12.3 Hz), 4.24 (q, 2H, *J*=7.2 Hz), 1.35 (t, 3H, *J*=7.2 Hz). EIMS *m*/*z* (rel int., %): 215 (M^+, 100), 170 (90), 143 (71), 115 (43).[13]



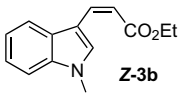
***E*-3a**

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.47 (br s, 1H), 7.95–7.80 (m, 2H), 7.50 (d, 1H, *J*=3.0 Hz), 7.42 (m, 1H), 7.31–7.27 (m, 2H), 6.47 (d, 1H, *J*=15.9 Hz), 4.28 (q, 2H, *J*=7.2 Hz), 1.33 (t, 3H, *J*=6.9 Hz). EIMS *m*/*z* (rel int., %): 215 (M^+, 90), 170 (100), 143 (81), 115 (59).[13]



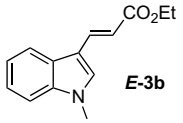
4a

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 7.94 (br s, 2H), 7.59 (d, 2H, *J*=8.4 Hz), 7.34 (d, 2H, *J*=8.4 Hz), 7.16 (t, 2H, *J*=7.5 Hz), 7.07–7.01 (m, 4H), 5.12 (d, 1H, *J*=7.5 Hz), 4.03 (q, 2H, *J*=6.9 Hz), 3.19 (d, 2H, *J*=7.5 Hz), 1.10 (t, 3H, *J*=6.9 Hz). EIMS *m*/*z* (rel int., %): 332 (M^+, 3), 245 (15), 215 (34), 170 (39), 115 (41).[14]



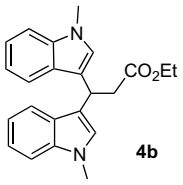
***Z*-3b**

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.80 (br s, 1H), 7.74 (d, 1H, *J*=7.5 Hz), 7.34–7.23 (m, 4H), 5.76 (d, 1H, *J*=12.3 Hz), 4.22 (q, 2H, *J*=6.9 Hz), 3.86 (s, 3H), 1.34 (t, 3H, *J*=6.9 Hz). EIMS *m*/*z* (rel int., %): 229 (M^+, 93), 184 (86), 157 (100), 115 (37).



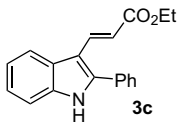
***E*-3b**

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 7.90 (m, 2H), 7.35–7.28 (m, 4H), 6.41 (d, 1H, *J*=16.5 Hz), 4.27 (q, 2H, *J*=6.9 Hz), 3.82 (s, 3H), 1.35 (t, 3H, *J*=6.9 Hz). EIMS *m*/*z* (rel int., %): 229 (M^+, 95), 184 (77), 157 (100), 115 (37).[15]



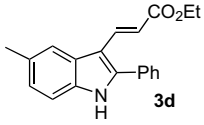
4b

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 7.62 (d, 2H, *J*=8.1 Hz), 7.29 (d, 2H, *J*=8.1 Hz), 7.21 (t, 2H, *J*=7.2 Hz), 7.06 (t, 2H, *J*=7.2 Hz), 6.88 (s, 2H), 5.13 (t, 1H, *J*=7.5 Hz), 4.04 (q, 2H, *J*=6.9 Hz), 3.71 (s, 6H), 3.18 (d, 2H, *J*=7.5 Hz), 1.12 (t, 3H, *J*=7.2 Hz). EIMS *m*/*z* (rel int., %): 360 (M^+, 5), 273 (35), 229 (87), 184 (80), 157 (100).[9b]



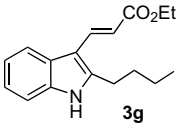
3c

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.58 (br s, 1H), 8.03–7.98 (m, 2H), 7.56–7.41 (m, 6H), 7.32–7.27 (m, 2H), 6.59 (d, 1H, *J*=15.9 Hz), 4.24 (q, 2H, *J*=7.2 Hz), 1.32 (t, 3H, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 14.4, 60.1, 109.7, 111.5, 114.0, 120.8, 121.6, 123.3, 126.5, 128.3, 128.9, 129.1, 131.2, 136.4, 138.7, 142.4, 168.6. EIMS *m*/*z* (rel int., %): 291 (M^+, 17), 218 (44), 143 (48), 84 (100). HRMS (ESI): calcd for $C_{19}H_{17}O_2N$+H: 292.1332; found: 292.1328.



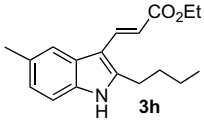
3d

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.35 (br s, 1H), 7.99 (d, 1H, *J*=16.5 Hz), 7.79 (s, 1H), 7.58–7.46 (m, 5H), 7.32 (d, 1H, *J*=8.1 Hz), 7.12 (d, 1H, *J*=8.1 Hz), 6.58 (d, 1H, *J*=15.9 Hz), 4.26 (q, 2H, *J*=7.2 Hz), 2.52 (s, 3H), 1.34 (t, 3H, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 14.4, 21.7, 60.0, 109.5, 111.0, 113.9, 120.7, 124.9, 126.8, 128.9, 129.0, 129.1, 131.2, 131.4, 134.6, 138.8, 142.4, 168.5. EIMS *m*/*z* (rel int., %): 305 (M^+, 45), 260 (17), 232 (100), 217 (58), 115 (21). HRMS (ESI): calcd for $C_{29}H_{19}O_2N$+H: 306.1489; found: 306.1496.



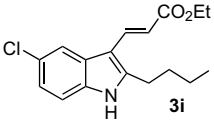
3g

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.50 (br s, 1H), 7.96 (d, 1H, *J*=15.9 Hz), 7.88 (m, 1H), 7.32 (m, 1H), 7.23–7.19 (m, 2H), 6.45 (d, 1H, *J*=15.9 Hz), 4.28 (q, 2H, *J*=7.2 Hz), 2.87 (t, 2H, *J*=7.5 Hz), 1.684–1.635 (m, 2H), 1.43–1.30 (m, 5H), 0.92 (t, 3H, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 13.8, 14.5, 22.4, 26.1, 31.8, 60.0, 109.2, 110.9, 112.0, 120.2, 121.3, 122.4, 126.2, 135.7, 137.5, 144.8, 168.8. EIMS *m*/*z* (rel int., %): 271 (M^+, 38), 196 (20), 183 (44), 168 (45), 154 (100). HRMS (ESI): calcd for $C_{17}H_{21}O_2N$+H: 272.1645; found: 272.1646.



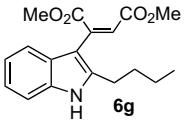
3h

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.3 (br s, 1H), 7.9 (d, 1H, *J*=15.9 Hz), 7.7 (s, 1H), 7.2 (d, 1H, *J*=8.1 Hz), 7.02 (d, 1H, *J*=7.9 Hz), 6.43 (d, 1H, *J*=15.9 Hz), 4.29 (q, 2H, *J*=6.9 Hz), 2.87 (t, 2H, *J*=7.8 Hz), 2.48 (s, 3H), 1.66 (m, 2H), 1.43–1.30 (m, 5H), 0.93 (t, 3H, *J*=6.9 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 13.8, 14.5, 21.6, 22.4, 26.1, 31.9, 60.0, 108.8, 110.5, 111.6, 120.2, 123.8, 126.5, 130.8, 133.9, 137.7, 144.9, 168.8. EIMS *m*/*z* (rel int., %): 285 (M^+, 71), 240 (24), 198 (42), 182 (52), 168 (100). HRMS (ESI): calcd for $C_{18}H_{23}O_2N$+H: 286.1802; found: 286.1798.



3i

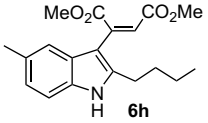
^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.4 (br s, 1H), 7.89 (d, 1H, *J*=15.9 Hz), 7.84 (s, 1H), 7.25 (d, 1H, *J*=9.0 Hz), 7.16 (d, 1H, *J*=9.0 Hz), 6.38 (d, 1H, *J*=15.9 Hz), 4.29 (q, 2H, *J*=7.2 Hz), 2.87 (t, 2H, *J*=7.5 Hz), 1.67 (m, 2H), 1.42–1.32 (m, 5H), 0.93 (t, 3H, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 13.8, 14.4, 22.4, 26.1, 31.7, 60.2, 108.9, 111.8, 112.6, 119.8, 122.6, 127.1, 127.3, 134.0, 136.8, 145.8, 168.6. EIMS *m*/*z* (rel int., %): 305 (M^+, 73), 260 (33), 188 (70), 167 (63), 154 (100). HRMS (ESI): calcd for $C_{17}H_{20}O_2NCl$+H: 306.1255; found: 306.1248.



6g

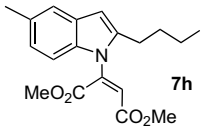
^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.21 (br s, 1H), 7.25–7.21 (m, 2H), 7.11–7.04 (m, 3H), 3.77 (s, 3H), 3.57 (s, 3H), 2.54 (t, 2H,

J=7.5 Hz), 1.55 (m, 2H), 1.30 (m, 2H), 0.87 (t, 3H, J=7.5 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 13.7, 22.3, 26.7, 30.9, 51.7, 52.7, 106.2, 110.6, 118.5, 119.9, 121.4, 127.8, 128.2, 134.9, 138.4, 139.1, 165.8, 167.8. EIMS m/z (rel int., %): 315 (M^+, 100), 256 (38), 241 (33), 154 (92). HRMS (ESI): calcd for $C_{18}H_{21}O_4N$+H: 316.1543; found: 316.1546.



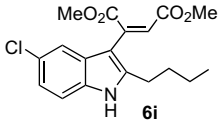
6h

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 7.99 (br s, 1H), 7.17 (d, 1H, J=8.4 Hz), 7.10 (s, 1H), 7.00 (s, 1H), 6.94 (d, 1H, J=8.1 Hz), 3.78 (s, 3H), 3.57 (s, 3H), 2.60 (t, 2H, J=7.5 Hz), 2.39 (s, 3H), 1.60 (m, 2H), 1.33 (m, 2H), 0.89 (t, 3H, J=7.5 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 13.8, 21.5, 22.3, 26.7, 30.9, 51.7, 52.8, 105.9, 110.2, 118.3, 122.9, 128.0, 128.1, 129.2, 133.2, 138.5, 139.0, 165.8, 167.9. EIMS m/z (rel int., %): 329 (M^+, 45), 287 (48), 228 (50), 168 (65). HRMS (ESI): calcd for $C_{19}H_{23}O_4N$+H: 330.1700; found: 330.1702.



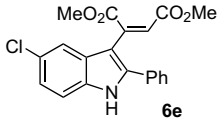
7h

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 7.30 (s, 1H), 7.28 (s, 1H), 6.92 (d, 1H, J=8.4 Hz), 6.84 (d, 1H, J=8.1 Hz), 6.31 (s, 1H), 3.78 (s, 3H), 3.52 (s, 3H), 2.50 (t, 2H, J=7.5 Hz), 2.40 (s, 3H), 1.66 (m, 2H), 1.38 (m, 2H), 0.91 (t, 3H, J=7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 13.8, 21.4, 22.2, 26.5, 30.2, 52.3, 53.3, 101.2, 108.8, 119.9, 122.9, 128.2, 128.9, 129.6, 135.6, 136.7, 141.6, 163.5, 164.3. EIMS m/z (rel int., %): 329 (M^+, 45), 287 (48), 228 (50), 168 (65). HRMS (ESI): calcd for $C_{19}H_{23}O_4N$+H: 330.1700; found: 330.1702.



6i

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.19 (br s, 1H), 7.15 (m, 3H), 7.04 (d, 1H, J=8.1 Hz), 3.80 (s, 3H), 3.62 (s, 3H), 2.56 (t, 2H, J=7.5 Hz), 1.59 (m, 2H), 1.31 (m, 2H), 0.88 (t, 3H, J=7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 13.8, 22.3, 26.7, 30.8, 51.9, 53.0, 106.0, 111.6, 118.1, 121.7, 125.7, 128.8, 129.2, 133.3, 137.8, 140.4, 165.5, 167.4. EIMS m/z (rel int., %): 349 (M^+, 35), 290 (21), 275 (29), 188 (64), 59 (100). HRMS (ESI): calcd for $C_{18}H_{20}O_4NCl$+H: 350.1154; found 350.1153.



6e

^{1}H NMR ($CDCl_3$, 300 MHz, δ ppm): 8.55 (br s, 1H), 7.41–7.32 (m, 5H), 7.24 (d, 1H, J=1.8 Hz), 7.18 (d, 1H, J=8.7 Hz), 7.11 (s, 1H), 7.07 (dd, 1H, J_1=1.8 Hz, J_2=8.7 Hz), 3.58 (s, 3H), 3.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, δ ppm): 51.9, 52.7, 106.8, 112.3, 118.5, 122.9, 126.2, 127.2, 128.4, 128.9, 129.0, 129.4, 131.9, 134.1, 138.1, 138.5, 165.7, 167.2. EIMS m/z (rel int., %): 369 (M^+, 20), 309 (29), 278 (47), 59 (100). HRMS (ESI): calcd for $C_{20}H_{16}O_4NCl$+Na: 392.0660; found: 392.0651.

Acknowledgements

We thank the National Natural Science Foundation of China (No. 20772053) and Natural Science Foundation of Gansu Province (No. 3ZS061-A25-004) for financial support.

References and notes

1. Sundberg, R. J. *Indoles*; Academic: London, 1996.
2. For reviews on synthesis of indoles, see: (a) Gribble, G. W. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, UK, 1996; Vol. 2, p 207; (b) Bandini, M.; Melloni, A.; Tommasi, S.; Umani-Ronchi, A. *Synlett* **2005**, 1199; (c) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875.
3. For recent examples, see: (a) Lane, B. S.; Sames, D. *Org. Lett.* **2004**, *6*, 2897; (b) Reddy, A. V.; Ravinder, T.; Goud, T. V.; Krishnaiah, P.; Raju, T. V.; Venkateswarlu, Y. *Tetrahedron Lett.* **2003**, *44*, 6257; (c) Wang, Y.-Q.; Song, J.; Hong, R.; Li, H.; Deng, L. *J. Am. Chem. Soc.* **2006**, *128*, 8156; (d) Sakai, N.; Annaka, K.; Konakahara, T. *Tetrahedron Lett.* **2006**, *47*, 631; (e) Liu, C.; Bender, C. F.; Han, X.; Widenhoefer, R. A. *Chem. Commun.* **2007**, 3607.
4. (a) Arcadi, A.; Bianchi, G.; Marinelli, F. *Synthesis* **2004**, *4*, 610; (b) Kamijo, S.; Sasaki, Y.; Yamamoto, Y. *Tetrahedron Lett.* **2004**, *45*, 35; (c) Hiroya, K.; Itoh, S.; Sakamoto, T. *J. Org. Chem.* **2004**, *69*, 1126.
5. (a) Takeda, A.; Kamijo, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 5662; (b) Cacchi, S.; Fabrizi, G.; Parisi, L. M. *Synthesis* **2004**, 1889; (c) Shimada, T.; Nakamura, I.; Yamamoto, Y. *J. Am. Chem. Soc.* **2004**, *126*, 10546; (d) Alfonsi, M.; Arcadi, A.; Aschi, M.; Bianchi, G.; Marinelli, F. *J. Org. Chem.* **2005**, *70*, 2265; (e) Nakamura, M.; Ilies, L.; Otsubo, S.; Nakamura, E. *Org. Lett.* **2006**, *8*, 2803; (f) Nakamura, M.; Ilies, L.; Otsubo, S.; Nakamura, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 944; (g) Zhang, Y.; Donahue, J. P.; Li, C.-J. *Org. Lett.* **2007**, *9*, 627; (h) Yin, Y.; Ma, W.; Chai, Z.; Zhao, G. *J. Org. Chem.* **2007**, *72*, 5731; (i) Cariou, K.; Ronan, B.; Mignani, S.; Fensterbank, L.; Malacria, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1881; (j) Li, G.; Huang, X.; Zhang, L. *Angew. Chem., Int. Ed.* **2008**, *47*, 346.
6. For reviews, see: (a) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633; (b) Nevado, C.; Echavarren, A. M. *Synthesis* **2005**, 157; (c) Bandini, M.; Emer, E.; Tommasi, S.; Umani-Ronchi, A. *Eur. J. Org. Chem.* **2006**, 3527.
7. For recent reviews on platinum and gold catalysis, see: (a) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200; (b) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271; (c) Jiménez-Núñez, E.; Echaverren, A. M. *Chem. Commun.* **2007**, 333; (d) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410; (e) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180; (f) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395; (g) Shen, H. *Tetrahedron* **2008**, *64*, 3885; (h) Skouta, R.; Li, C.-J. *Tetrahedron* **2008**, *64*, 4917.
8. Reetz, M.; Sommer, K. *Eur. J. Org. Chem.* **2003**, 3485.
9. (a) Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669; (b) Li, Z.; Shi, Z.; He, C. *J. Organomet. Chem.* **2005**, *690*, 5049.
10. Ferrer, C.; Amijs, C. H. M.; Echavarren, A. M. *Chem.—Eur. J.* **2007**, 1358.
11. Bhuvaneswari, S.; Jeganmohan, M.; Cheng, C.-H. *Chem.—Eur. J.* **2007**, *13*, 8285.
12. Lu, W.; Jia, C.; Kitamura, T.; Fujiwara, Y. *Org. Lett.* **2000**, *2*, 2927.
13. Kusurkar, R. S.; Patil, U. G. *Indian J. Chem., Sect B* **1986**, *25*, 1038.
14. Singh, H.; Singh, K. *Tetrahedron* **1988**, *44*, 5897.
15. Sala, G. D.; Izzo, I.; Spinalla, A. *Synlett* **2006**, 1319.