Short communication

Platinum-catalyzed intermolecular hydroamination of terminal alkynes

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Abstract

The hydroamination of terminal alkyl- and arylacetylenes with aniline is catalyzed by platinum(II) bromide, yielding the corresponding imines. Contrary to what has been previously demonstrated for the platinum(II)-catalyzed hydroamination of α-olefins, the presence of n-Bu$_4$PBr has a detrimental effect on the course of the reaction. The hydroamination of 1-hexyne is highly regioselective (Markovnikov) at 60 °C, but the regioselectivity decreases upon increasing the temperature. The hydroamination of phenylacetylene is fully regioselective (Markovnikov) at 100 °C. TON up to 146 were obtained in the presence of a catalytic source of protons.
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1. Introduction

The direct addition of an N−H bond across unsaturated C−C multiple bonds (hydroamination) offers a promising, atom economic route to a variety of amines, enamines and imines [1–8]. Thermodynamic considerations suggest that the hydroamination of alkynes should be easier to perform than that of alkenes [6–8]. Thus, the intermolecular hydroamination of alkynes has met with success using different group IV metal, lanthanide and actinide complexes as catalysts [6–8]. However, it is well recognized that a great advantage of using late transition metal catalysts is their lower sensitivity to oxygen and moisture, relative to early transition metals, lanthanides or actinides. Since the first report by Uchimaru in 1999 [9] only a few systems based on late transition metals have been reported [7,9–11], the most efficient one being that reported by Wakatsuki et al. and consisting of Ru$_3$(CO)$_{12}$ and an acidic additive (NH$_4$PF$_6$) [10]. Recent advances in this area have pointed out the interest of Au(I) [12] and aquapalladium catalysts [13].

We have recently reported what we believe is the most efficient transition metal-based catalytic system reported so far for the intermolecular hydroamination of aliphatic olefins [14–17]. The hydroamination of ethylene with anilines is catalyzed by PtBr$_2$ (0.3%) in ionic solvents (n-Bu$_4$PBr or imidazolium bromide), yielding the N-alkylated aniline with TON up to 240 and yields up to 67% [15]. Remarkably, the same catalytic activity was obtained for the hydroamination of 1-hexene (TON up to 240 and yields up to 70%), the reaction occurring with 95% Markovnikov regioselectivity [17]. Moreover, it has been demonstrated that this remarkable catalytic activity is due to the presence of the bromide ions associated with the ionic solvent.

Therefore, we were interested in testing our platinum(II) system for the catalytic hydroamination of alkynes. We report below our first experiments conducted with two terminal alkynes, 1-hexyne and phenylacetylene.

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2. Experimental

2.1. Methods and materials

n-Tetrabutylphosphonium bromide (Janssen), 1-hexyne (Acros), phenylacetylene (Acros), anilinium sulfate (Acros), *N,N*-dibutylaniline (Aldrich), and platinum bromide (Strem) were use as received. Aniline (Fluka) was distilled before use.

2.2. Instrumentation

GC analyses were performed on a Hewlett-Packard HP 4890 (FID) chromatograph (HP 3395 integrator) equipped with a 30 m HP1 capillary column and GC–MS analyses were performed on a Hewlett-Packard HP 6890 apparatus equipped with an HP 5973 M ion detector. NMR analyses were performed on a Bruker AM 250 apparatus.

Catalytic experiments were conducted in a 100 mL stainless steel autoclave with a glass liner and a magnetic stirring bar.

2.3. Reactions

The general procedure is exemplified in the case of phenylacetylene (run 16, Table 2). The autoclave was charged with PtBr$_2$ (47 mg, 0.129 mmol) and anilinium sulfate (110 mg, 0.4 mmol), then closed and submitted to argon-vacuum cycles. A degassed solution of phenylacetylene (5 mL, 45 mmol) in aniline (4.1 mL, 45 mmol), prepared independently, was then syringed into the autoclave and the temperature was adjusted to 100 °C. After 48 h, the autoclave was allowed to cool to room temperature. The reaction mixture was dropped into 50 mL of diethylether. The external standard (*N,N*-dibutylaniline) was added to the etheral phase and the solution analyzed by GC and GC–MS.

Characterization of 2-pentyl-3-butylquinoline (**5**): **5** was isolated by liquid chromatography from the reaction mixture of run 9 (Table 1).

^{1}H NMR (CDCl$_3$, 250 MHz): δ(ppm) = 8.02 (d, 1H), 7.83 (s, 1H), 7.70 (td, 1H), 7.43 (td, 1H), 2.96 (t, 2H), 2.78 (t, 2H), 1.6–1.8 (m, 4H), 1.3–1.5 (m, 6H), 0.8–1.0 (m, 6H). This spectrum is identical to that of an authentic sample prepared according to Kharasch et al. [21].

GC–MS (EI, 70 eV) *m/z*: 255 (M$^+$); 226; 199; 184; 157 (base peak).

3. Results and discussion

3.1. Hydroamination of 1-hexyne (Table 1)

The first experiments were conducted by reacting aniline, **1**, with 1-hexyne, **2**, in the presence of *n*-Bu$_4$PBr-PtBr$_2$ (**1**/**2**/*n*-Bu$_4$PBr/PtBr$_2$ ratio: 350/100/65/1) for 10 h at 60 °C. GC–MS analysis of the reaction products indicated the formation of *N*-(2-hexenylidene)aniline, **3** and *N*-(2-hexyl)aniline, **4**, together with traces of **5** (later isolated and characterized as 2-pentyl-3-, see Section 2) and traces of an unidentified compound, **6** (*m/z* = 189). Compounds **3** and **4** were identified by comparison (GC–MS) with authentic samples prepared according to literature procedures [18,19]. Quantitative GC analysis with an external standard (*N,N*-dibutylaniline) indicated that **3** and **4** were formed with TON = 27 and 1, respectively.

As previously proposed by several authors, **5** is believed to be formed through dimerization of the linear imine PhN=CH–C$_5$H$_{11}$ (followed by in situ heterocyclisation, deamination and dehydrogenation) [21]. The amine **4** is likely formed from **3**, by transfer hydrogenation from 2-pentyl-3-butyl-1,2,3,4-tetrahydroquinoline (last step of the formation of **5**). It has been previously shown that PtBr$_2$ catalyzes the transfer hydrogenations from 1,2,3,4-tetrahydroquinoline [15].

When the same reaction was performed in the absence of *n*-Bu$_4$PBr (run 2), a higher catalytic activity was observed, affording **3** and **4** with TON = 44 and 2, respectively (i.e. a 44% yield of **3** versus 1-hexyne). The same observation was made when the amount of 1-hexyne was increased to 350 equiv./PtBr$_2$ (runs 3 and 4) or 700 equiv./PtBr$_2$ (runs 5 and 6). This observation was rather unexpected since, for the hydroamination of alkenes (ethylene, 1-hexene) catalyzed by PtBr$_2$, the presence of *n*-Bu$_4$PBr induces a remarkable increase of the catalytic activity. Increasing the reaction time

Table 1
PtBr$_2$-catalyzed reaction of aniline with 1-hexyne[a]

Run	**2** (equiv./Pt)	*n*-Bu$_4$PBr (equiv./Pt)	Reaction temperature (°C)	Reaction time (h)	**3** (TON)[b]	**4** (TON)[b]	**5** (TON)[b]
1	100	65	60	10	27	1	t
2	100	–	60	10	44	2	t
3	350	65	60	10	37	1	t
4	350	–	60	10	46	1	3
5	700	65	60	10	41	1	t
6	700	–	60	10	46	1	2
7	700	–	60	96	93	5	2
8	100	65	100	10	41	4	9
9	100	–	100	10	42	4	8

[a] PtBr$_2$: 0.13 mmol; aniline/PtBr$_2$ = 350/1.
[b] TON = turnover number.

Table 2
PtBr$_2$-catalyzed reaction of aniline with phenylacetylene[a]

Run	1 (equiv./Pt)	7 (equiv./Pt)	n-Bu$_4$PBr (equiv./Pt)	Reaction time (h)	8 (TON)[b]
10	350	350	65	10	61
11	350	350	–	10	95
12	350	100	–	10	41
13	100	350	–	10	51
14	350	350	–	20	116
15	350	350	–	48	128
16[c]	350	350	–	48	146

[a] Reactions conducted at 100 °C with 0.13 mmol PtBr$_2$.

[b] TON = turnover number.

[c] In the presence of anilinium sulfate: 3 equiv./PtBr$_2$.

from 10 to 96 h (runs 6 and 7) allowed to improve the TON from 41 to 93 (Eq. (1)), thus indicating that, under these experimental conditions, PtBr$_2$ is not a strong polymerization catalyst (no trace of the possible tributylbenzenes could be detected (GC–MS analysis) [20].

$$\tag{1}$$
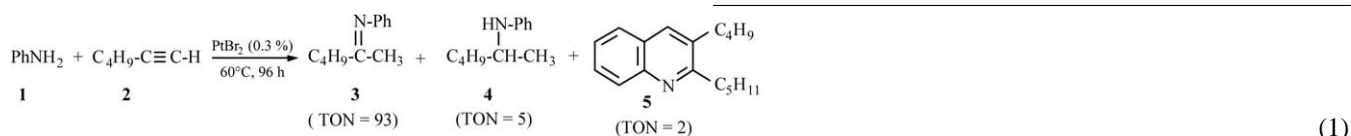
Increasing the reaction temperature to 100 °C suppressed the detrimental effect of n-Bu$_4$PBr. In both cases, the TON for **3** is similar and slightly lower than that obtained at 60 °C (compare runs 8 and 9 with run 2), but the TON for **4** is increased to 4. In fact, the main temperature effect is the increased formation of **5**, which is there formed with TON = 8–9. Thus, it seems that increasing the reaction temperature changes the regioselectivity of the hydroamination step. Indeed, for run 2, conducted at 60 °C, the regioselectivity may be estimated to be 98/4 Markovnikov/anti-Markovnikov (M/a-M) whereas at 100 °C (runs 8 and 9), the regioselectivity corresponds to a 45/18 M/a-M ratio. At higher temperature (150 °C) (1-hexyne/aniline/PtBr$_2$ = 700/350/1) the phosphonium salt has a beneficial effect, affording **3**, **4** and **5** with TON of 135, 12 and 27, respectively. However, under these conditions, the reaction is unworkable because of the formation of more than 10 unidentified secondary products (GC–MS detected, $m/z < 350$). Control experiments showed that none of the above side-products was formed when the reaction was carried out in the absence of aniline for 10 h at 150 °C.
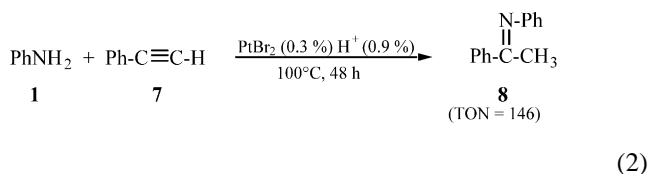
3.2. Hydroamination of phenylacetylene (Table 2)

The reaction of aniline with phenylacetylene, **7**, was first conducted in the presence of n-Bu$_4$PBr (**1**/**7**/n-Bu$_4$PBr/PtBr$_2$ = 350/350/65/1). After 10 h at 100 °C, the reaction cleanly afforded the branched imine **8** as the sole reaction product, with TON = 61 (run 10). As in the case of 1-hexyne, in the absence of the phosphonium salt, the reaction afforded **8** with a higher TON (95, run 11), although with traces of an unidentified side-product **9** ($m/z = 209$). Increasing the reaction temperature to 150 °C (with or with-

out n-Bu$_4$PBr) had a detrimental effect on the TON for **8** and promoted the formation of a few side-products, especially **9** (Table 2).

Thus PtBr$_2$ catalyzes the hydroamination of phenylacetylene with aniline. At 100 °C, the reaction is fully regioselective, affording the branched imine (Markovnikov type) as the sole reaction product with TON = 95 after 10 h reaction (run 11). Variation of the relative aniline/alkyne ratio (runs 12 and 13) did not increase the reaction rate. Increasing the reaction time to 20 or 48 h (runs 14 and 15) indicated that after ca. 100 cycles, the reaction becomes very slow, suggesting possible catalyst poisoning. Last, as for the platinum-catalyzed hydroamination of alkenes, the presence of a catalytic source of protons (anilinium sulfate) slightly improves the TON up to 146 (i.e. 42% yield, Eq. (2)).

$$\tag{2}$$

4. Conclusions

It has been found for the first time that PtBr$_2$ catalyzes the hydroamination of terminal alkynes with aniline. The reaction is fully regioselective in the case of phenylacetylene, affording the branched imine (Markovnikov). Although TON up to ca. 150 have been obtained, this Pt(II) catalyst affords lower yields, at least in the present form, than the late transition metal catalysts cited in the Introduction [7,9–11]. An important piece of information which emerges from this preliminary study is that, contrary to what has been demonstrated and developed for the platinum-catalyzed hydroamination of α-olefins [14,15,17], n-Bu$_4$PBr has no beneficial effect for the platinum-catalyzed hydroamination of terminal alkynes. In contrast, the presence of this compound seems to have a

detrimental effect, especially at reaction temperatures below 100 °C. Work is in progress to develop more active platinum(II) catalysts.

Acknowledgements

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