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LETTERS

Zwitterionic rhodium complex catalyzed hydroaminomethylation of arylethylenes

Yong-Shou Lin, Bassam El Ali[†] and Howard Alper*

Center for Catalysis Research and Innovation, Department of Chemistry, University of Ottawa, 10 Marie Curie, Ottawa, Ont., Canada K1N 6N5

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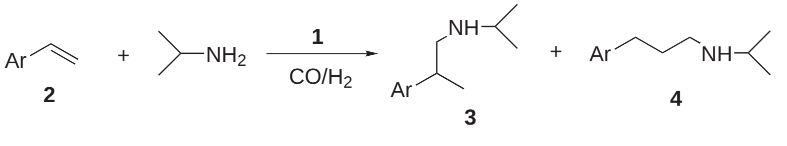
Abstract—The hydroaminomethylation of arylethylenes can be achieved in high regioselectivity using the zwitterionic rhodium complex $[\mathrm{Rh}^+(\mathrm{cod})(\eta^6\text{-}\mathrm{PhBPh}_3)^-]$ (**1**) as the catalyst under relatively mild conditions. © 2001 Elsevier Science Ltd. All rights reserved.

The hydroaminomethylation of olefins has attracted attention as an atom-economical efficient, one-pot synthesis of amines.[1,2] Originally discovered by Reppe and co-workers,[3] hydroaminomethylation consists of a reaction sequence of hydroformylation of an olefin followed by condensation with an amine and hydrogenation. Catalysts used initially were iron and cobalt carbonyl complexes, with more efficient rhodium and ruthenium complexes developed in the last two decades.[4] $[\mathrm{Rh(CO)_2Cl}]_2$ and $[\mathrm{Rh(cod)Cl}]_2$ are the most common rhodium catalysts employed in hydroaminomethylation reactions.[1a]

The zwitterionic rhodium complex $[\mathrm{Rh}^+(\mathrm{cod})(\eta^6\text{-}\mathrm{PhBPh}_3)^-]$ (**1**) is an excellent catalyst for the hydroformylation of olefins with high regioselectivity.[5] Complex **1**-catalyzed hydroformylation of aryl olefins gives aldehydes in a high branched/linear ratio.[5a] Relatively few studies on the hydroaminomethylation of styrenes have been reported in the literature.[6] We have found that the hydroaminomethylation of various aryl olefins using complex **1** as the catalyst, under relatively mild conditions, affords the corresponding branched methylated amines in high regioselectivity.

Hydroaminomethylation of styrene (**2a**, $\mathrm{CO/H_2} = 1{:}1$, 200 psi) in the presence of isopropylamine and a catalytic amount of complex **1** in THF afforded *N*-isopropyl-2-phenylpropylamine (**3a**) in 85% isolated yield, with the linear isomer as a by-product (**4a**, entry 1 of Table 1 and Eq. (1)). The branched/linear ratio (11.5:1.0) is higher than that previously reported.[6c,7] In general, hydroaminomethylation has been carried out at relatively higher pressures of syngas (≥100 bar), except when one uses the dinuclear rhodium complex $[\mathrm{Rh_2(\mu\text{-}SBu^t)_2(CO)_2(PPh_3)_2}]$ as the catalyst for the aminomethylation of oct-1-ene.[8] However, the latter gave linear amine as the major product. If the $\mathrm{CO/H_2}$ pressure was increased to 1000 psi in the present reaction, a much higher branched/linear ratio was obtained (15.3:1, entry 2). A decrease or increase of the reaction temperature resulted in a lower conversion of styrene (entry 3), or a lower ratio of **3a** to **4a** together with the formation of other by-products (entry 4).



(1)

Various *para*-substituted styrenes (**2**) have been aminomethylated to the corresponding branched amine (**3**) as the major product, together with the linear isomer (**4**, Table 1, entries 5–10, and Eq. (1)). Both electron-withdrawing and electron-donating substituents in the *para* position gave the branched amine as the major product. Somewhat lower yields of

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* Corresponding author. Tel.: +1-613-562-5189; fax: +1-613-562-5871; e-mail: halper@uottawa.ca

[†] Present address: KFUPM, Chemistry Department, Dhahran 31261, Saudi Arabia.

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Table 1. Hydroaminomethylation of arylethylenes in the presence of isopropylamine[a]

Entry	Ar	Yield (mol%)[b]		Ratio
		3	**4**	**3/4**
1	C_6H_5- (**2a**)	92 (85, **3a**)	8 (**4a**)	11.5
2[c]	C_6H_5- (**2a**)	92 (**3a**)	6 (**4a**)	15.3
3[d]	C_6H_5- (**2a**)	25 (**3a**)	0 (**4a**)	–
4[e]	C_6H_5- (**2a**)	34 (**3a**)	29 (**4a**)	1.2
5	p-$CH_3C_6H_4$- (**2b**)	85 (65, **3b**)	15 (8, **4b**)	5.7
6	p-$CH_3OC_6H_4$- (**2c**)	90 (74, **3c**)	10 (7, **4c**)	9.0
7[f,g]	p-$(CH_3)_3CC_6H_4$- (**2d**)	70 (62, **3d**)	19 (14, **4d**)	3.7
8[f,h]	p-ClC_6H_4- (**2e**)	77 (57, **3e**)	14 (**4e**)	5.5
9	p-FC_6H_4- (**2f**)	86 (67, **3f**)	14 (10, **4f**)	6.1
10	p-PhC_6H_4- (**2g**)	87 (76, **3g**)	13 (**4g**)	6.7

[a] Reaction conditions: arylethylene (2 mmol), isopropylamine (2.2 mmol), catalyst (0.01 mmol), CO/H_2 (1:1, 200 psi), THF (5 mL), 80°C, 24 h, unless otherwise described.

[b] The yields were determined by ^1H NMR and GC (the isolated yield is in parenthesis).

[c] The reaction was carried out under CO/H_2 (1:1, 1000 psi).

[d] The reaction was run at 50°C, and 75% of styrene was recovered.

[e] The reaction was run at 110°C, and *N*,*N*-bis(2-phenylpropyl)-isopropylamine and its isomers were detected as by-products.

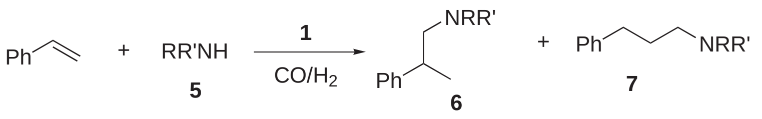
[f] A trace amount of $ArCOCH_3$ was detected.

[g] 8 mol% of olefin was recovered.

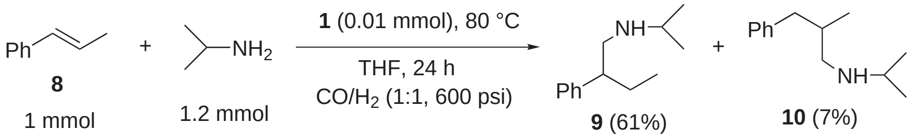
[h] 9 mol% of by-products were unidentified.

branched amines resulted using *para*-*tert*-butylstyrene and *para*-chlorostyrene as substrates (entries 4 and 5, respectively).

The hydroaminomethylation reaction of styrene can be applied to both primary and secondary amines. The results using different amines (**5**), to form branched and linear arylamines (**6** and **7**, respectively), are summarized in Table 2 (Eq. (2)). Cyclohexylamine (**5a**) gave higher conversion with the corresponding branched amine (**6a**) as the predominant product (entry 1). A substantially higher ratio of branched/linear amines was again obtained by increasing the CO/H_2 pressure (entry 2). *n*-Butylamine gave a higher branched/linear ratio than *tert*-butylamine (entries 4 and 5). Benzylamine as well as secondary amines including diethylamine and piperidine also afforded higher yields of the corresponding branched amines, with linear amines as minor products (entries 6, 9, and 10). Higher CO/H_2 pressures led to higher regioselectivity for branched amines in the case of benzylamine (entry 7). However, aniline formed the corresponding branched and linear amines in a ratio of only 1.9:1 (entry 8). It is also noteworthy that hydroaminomethylation of an internal olefin, 1-phenyl-1-propene (**8**), in the presence of isopropylamine, gave isopropyl-(2-phenylbutyl)amine (**9**) as the principal product (61%), together with isopropyl-(2-methyl-3-phenylpropyl)amine (**10**, 7%, Eq. (3)).



(2)



(3)

Table 2. Hydroaminomethylation of styrene with various amines[a]

Entry	RR′NH	CO/H_2	Yield (mol%)[b]		Ratio
	5	(1:1, psi)	**6**	**7**	**6/7**
1	Cyclohexylamine (**5a**)	200	78 (68, **6a**)	22 (**7a**)	3.5
2	Cyclohexylamine (**5a**)	1000	91 (**6a**)	7 (**7a**)	13.0
3[c]	*n*-Butylamine (**5b**)	200	45 (**6b**)	10 (**7b**)	4.5
4[d]	*n*-Butylamine (**5b**)	600	89 (68, **6b**)	6 (**7b**)	14.8
5[e]	*tert*-Butylamine (**5c**)	600	58 (40, **6c**)	14 (7, **7c**)	4.1
6	Benzylamine (**5d**)	600	84 (**6d**)	14 (**7d**)	6.0
7[f]	Benzylamine (**5d**)	1000	84 (78, **6d**)	6 (**7d**)	14.0
8[g]	Aniline (**5e**)	600	58 (41, **6e**)	30 (**7e**)	1.9
9	Diethylamine (**5f**)	200	81 (60, **6f**)	18 (11, **7f**)	4.5
10	Piperidine (**5g**)	200	88 (74, **6g**)	12 (10, **7g**)	7.3

[a] Reaction conditions: styrene (2 mmol), amine (2.2 mmol), catalyst (0.01 mmol), CO/H_2, THF (5 mL), 80°C, 24 h.

[b] The yields were determined by ^1H NMR and GC GC (the isolated yield is in parenthesis).

[c] 23 mol% of the imine, $PhCH(CH_3)CH{=}NRR'$, was found, and 22% of styrene was recovered.

[d] 5 mol% of styrene was recovered.

[e] 19 mol% of imine was formed together with a small amount of unidentified products.

[f] 9% of ethylbenzene was formed.

[g] Small amounts of acetophenone (6%) and unidentified products (<6%) were detected.

In conclusion, the zwitterionic rhodium complex **1** is an efficient catalyst for the hydroaminomethylation of arylethylenes under relatively mild conditions, to give branched chain amines in high regioselectivity.

General experimental procedure: A mixture of olefin (2 mmol), amine (2.2 mmol), zwitterionic rhodium complex **1** (0.01 mmol), and THF (5 mL) was placed in a 45 mL stainless steel autoclave equipped with a glass liner and magnetic stirrer. The autoclave was purged three times with carbon monoxide and then pressurized to the desired level by CO and then H_2. The reaction was carried out in an oil bath, and once complete, the autoclave was cooled to room temperature and the gas was released. After evaporation of volatile components, $CDCl_3$ (1 mL) and $Cl_2CHCHCl_2$ (0.5 mmol, as an internal reference) were added, and the products were analyzed by ^1H NMR and GC–MS. Purification of the branched amines was attained by column chromatography (alumina), preparative TLC or by HPLC. The branched amines **3**, **6**, and **9** obtained were fully characterized by ^1H and ^{13}C NMR, MS, and HRMS.

Acknowledgements

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