

## Synthesis of Amines and Enamines by Hydroaminomethylation of Alkenes Catalyzed by Rhodium (I) or Rhodium (III) Complexes

BASSAM EL ALI

*King Fahd University of Petroleum and Minerals, Chemistry Department*

*Dhahran - Saudi Arabia*

E-mail: belali@kfupm.edu.sa

**ABSTRACT** As an efficient one-pot synthesis of amines, hydroaminomethylation of olefins has attracted great attention to the chemists due to the recent developments for preparative applications. Hydroaminomethylation of olefins as a one-pot synthesis of amines has reached its synthetic applications in recent years.  $[\text{Rh}(\text{CO})\text{Cl}]_2$  and  $[\text{Rh}(\text{COD})\text{Cl}]_2$  are the most common rhodium catalysts employed in the hydroaminomethylation reactions. The hydroaminomethylation of alkenes to give amines under relatively mild conditions by using zwitterionic rhodium complex  $[\text{Rh}^+(\text{COD})(\eta^5\text{-PhBPh}_3)]$  as catalyst. Also, the reactions of vinyl sulfones under hydroaminomethylation conditions led to discovery of a new type of one-pot reaction toward the formation of sulfonated enamines by rhodium complex.

The hydroaminomethylation of alkenes has been also studied in the presence of rhodium (III) catalyst and phosphine ligands. Rhodium (III) - bidentate phosphine ligands favors the formation of enamines as major products.

### Introduction

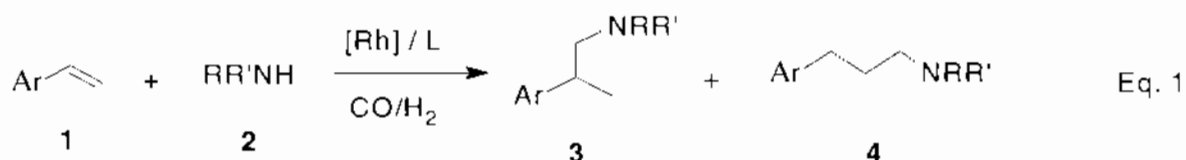
The catalytic carbonylation reactions of olefins, alkynes and other  $\pi$ -bonded compounds have industrial potential because they lead to valuable products (Hartley & Patai, 1982; Tsuji, 1995; Beller & Bolm, 1998). These reactions are usually catalyzed by various transition-metal complexes, such as palladium, rhodium, ruthenium, or nickel complexes in combination with phosphines, phosphites and other types of ligand (Colquhoun *et al.*, 1991; Masters, 1993; Parshall & Iitell, 1993). The reactions of alkenes with carbon monoxide (CO) or  $\text{CO}/\text{H}_2$  in the presence of group VIII metals and a suitable nucleophile affords aldehydes, alcohols, amines, carboxylic acid derivatives and other carbonyl compounds (Colquhoun *et al.*, 1991; Masters, 1993; Parshall & Iitell, 1993). While many metals have been successfully employed as catalysts in the carbonylation reactions, they often lead to mixtures of products under drastic experimental conditions.

The hydroaminomethylation of olefins is among the carbonylation reactions that has attracted great attention to the chemists as an atom-economic efficient one-pot synthesis of amines (Eilbracht *et al.*, 1999). This reaction was originally discovered by Reppe and coworkers (Reppe & Vetter, 1953). In general, hydroaminomethylation is consisting of a

reaction sequence of hydroformylation of olefins, which usually leads to aldehydes, followed by condensation of amine forming enamines as intermediates, and a subsequent hydrogenation lead to new amine compounds as final products. This process was originally catalyzed by iron and cobalt carbonyl complexes, which have been replaced by more efficient rhodium and ruthenium complexes in the last two decades (Iqbal, 1971). Rhodium (I) complexes such as  $[\text{Rh}(\text{CO})\text{Cl}]_2$  and  $[\text{Rh}(\text{COD})\text{Cl}]_2$  were among the most active catalysis employed in the hydroaminomethylation reactions (Eilbracht *et al.*, 1999). Hydroaminomethylation of long chain alkenes with dimethylamine was also investigated. The reaction was catalyzed by a water-soluble rhodium-phosphine complex,  $\text{RhCl}(\text{CO})(\text{TPPTS})_2$  [TPPTS:  $\text{P}(\text{m-C}_6\text{H}_4\text{SO}_3\text{Na})_3$ ], in an aqueous-organic two-phase system in the presence of the cationic surfactant cetyltrimethylammonium bromide (CTAB) (Wang *et al.*, 2004). A highly chemoselective and regioselective hydroaminomethylation of simple as well as functionalized  $\alpha$ -olefins using a cationic rhodium pre-catalyst together with Xantphos as ligand was reported (Beller *et al.*, 2003).

Zwitterionic rhodium complex  $[\text{Rh}^+(\text{cod})(\eta^6\text{-PhBPh}_3)^-]$   $[\text{Rh}]^+$  has been widely used as a catalyst for the hydroformylation of olefins giving high regioselectivity for the branched or linear product depending on the substrates (Amer & Alper, 1990; Alper & Zhou, 1992; Totland & Alper, 1993; Lee & Alper, 1995).

We would like to report now a review of the results in the hydroaminomethylation of various aryl olefins catalyzed by the cationic rhodium complex  $[\text{Rh}^+]$ , and the new results on the use of rhodium (III) complex,  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ , with and without the addition of a phosphine ligand **L**, forming amines or enamines in high yields (eq. 1).



## Materials and Methods

### General procedure

Rhodium complexes, phosphine and phosphite ligands, Alkenes, amines and all solvents were purchased from commercial sources. Dry solvents have been used in all experiments.

$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on 500 MHz Joel 1500 NMR machine. Chemical shifts were reported in ppm ( $\delta$ ) relative to tetramethyl silane (TMS) using  $\text{CDCl}_3$ . Gas chromatography analyses were realized on HP (6890-plus) chromatography equipped with 30 m capillary column HP-5.

### General procedure for the hydroaminomethylation of alkenes

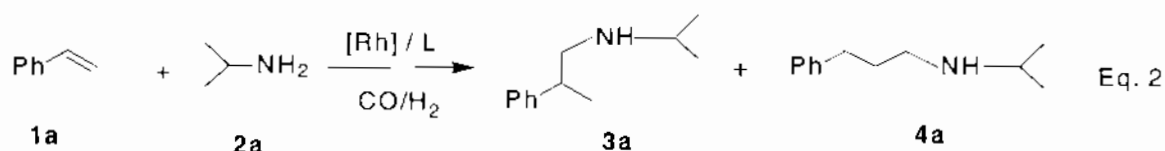
A mixture of styrene (5.0 mmol), amine (5 mmol), rhodium catalyst (1%) dissolved in 5.0 ml of dry solvent was placed in the liner of a 45 ml high-pressure Parr autoclave. The autoclave was purged three times with carbon monoxide, subsequently pressurized with carbon monoxide followed by hydrogen. The autoclaves were placed in oil baths heated on hotplates controlled by temperature sensor to maintain the temperature constant ( $\pm 0.5^\circ\text{C}$ ). After the reaction time elapsed, the autoclave was cooled down to room

temperature and the gas was carefully released and the autoclave was open. The reaction mixture was filtered on Celite to remove the catalyst. The products were identified using GC, GC-MS,  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR techniques. The ratio of branched to linear amines or enamines was determined by GC and  $^1\text{H}$  NMR.

## Results and Discussion

### Hydroaminomethylation of alkenes with rhodium (I) cationic complex $[\text{Rh}]^+$

The hydroaminomethylation of styrene (**1a**) with isopropylamine (**2a**) was studied as a model reaction to optimize of the experimental conditions with the rhodium (I) cationic complex  $[\text{Rh}^+(\text{cod})(\eta^6\text{-PhBPh}_3)^-] [\text{Rh}]^+$  (eq. 2).



The effect of the total pressure of  $\text{CO} + \text{H}_2$  ( $\text{CO}/\text{H}_2 = 1/1$ ) was investigated in the presence of isopropylamine and a catalytic amount of complex **1** (1 mol%) in THF at  $80^\circ\text{C}$  for 24 h (Fig. 1). The branched amine N-isopropyl-2-phenylpropylamine (**3a**) was formed in excellent yield (92 %) at 600 psi of a total pressure. Lower yield and selectivity toward the branched amine were observed at lower total pressure.

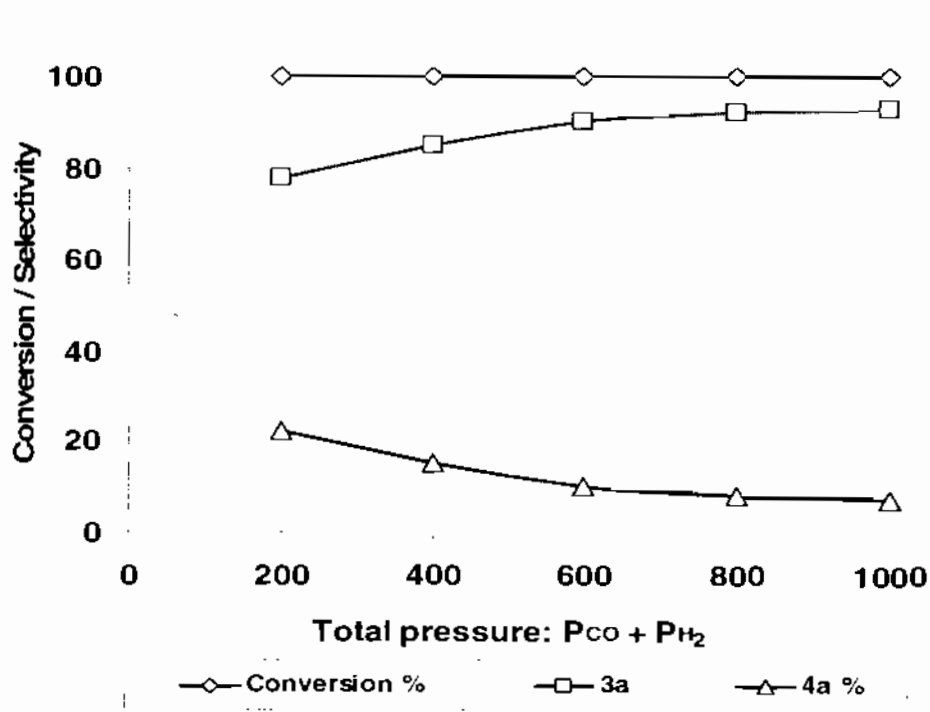


Fig. 1. Hydroaminomethylation of styrene by  $[\text{Rh}]^+$ . Effect of the total pressure. Reaction conditions: catalyst  $[\text{Rh}]^+$  (1 mol%), styrene (2.0 mmol), isopropylamine (2.4 mmol),  $\text{CO}/\text{H}_2$  (1:1), THF (5 ml),  $80^\circ\text{C}$ , 24 h.

The temperature showed a significant effect on the selectivity of the reaction (Fig. 2). The maximum yield in **3a** was obtained at 80°C. At temperatures >80°C, the ratio of **3a/4a** decreases significantly and the formation of the by-products such as ethyl benzene and other unidentified products has increased.

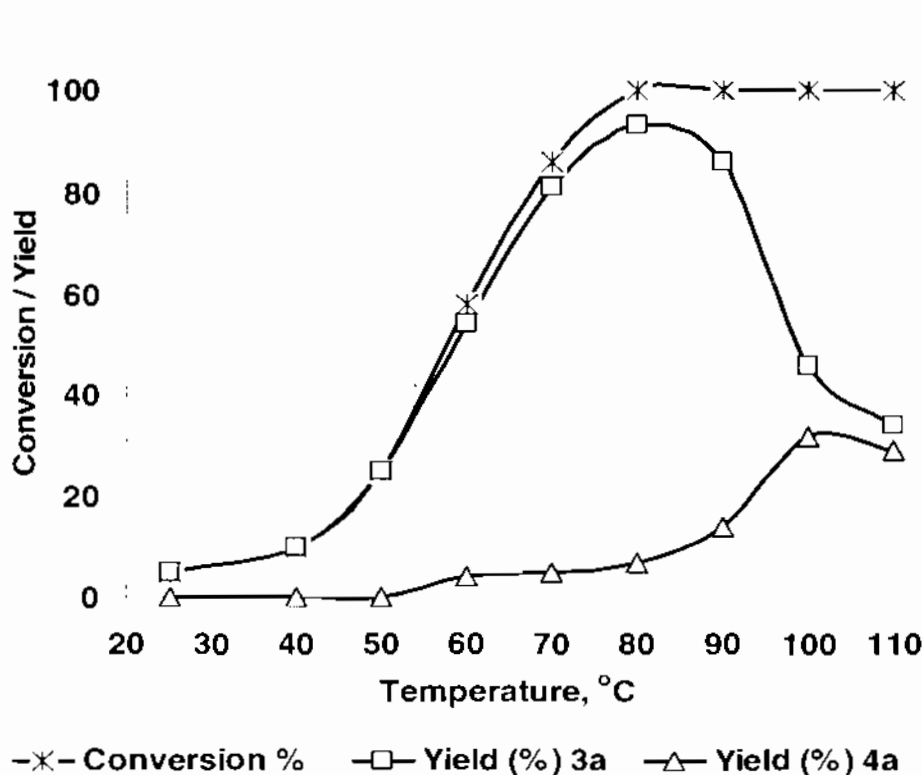


Fig. 2. Hydroaminomethylation of styrene by  $[\text{Rh}]^+$ . Effect of the temperature. Reaction conditions: catalyst  $[\text{Rh}]^+$  (1% mol), styrene (2.0 mmol), isopropylamine (2.4 mmol),  $\text{CO}/\text{H}_2$  (1:1, 600psi), THF (5 ml), 24 h

Various primary and secondary amines have used in the hydroaminomethylation reactions of styrene catalyzed by  $[\text{Rh}]^+$ . The results obtained from the use of different amines (**2**) are shown on Fig. 3. For example, cyclohexylamine gave high conversion with the formation of the corresponding branched amine as a predominant product. The yield depends strongly on the total pressure where the ratio of branched/linear amines increased with the increase of  $\text{CO}/\text{H}_2$  total pressure. Also, *n*-Butylamine gave higher branched/linear ratio than *tert*-butylamine. Benzylamine as well as secondary amines, such as piperidine, also gave higher yields of the corresponding branched amines together with linear amines as minor products. Again, higher  $\text{CO}/\text{H}_2$  total pressure led to higher regioselectivity toward the branched amine in the case of benzylamine. However, aniline formed the corresponding branched and linear amines in a ratio of only 1.9 to 1.

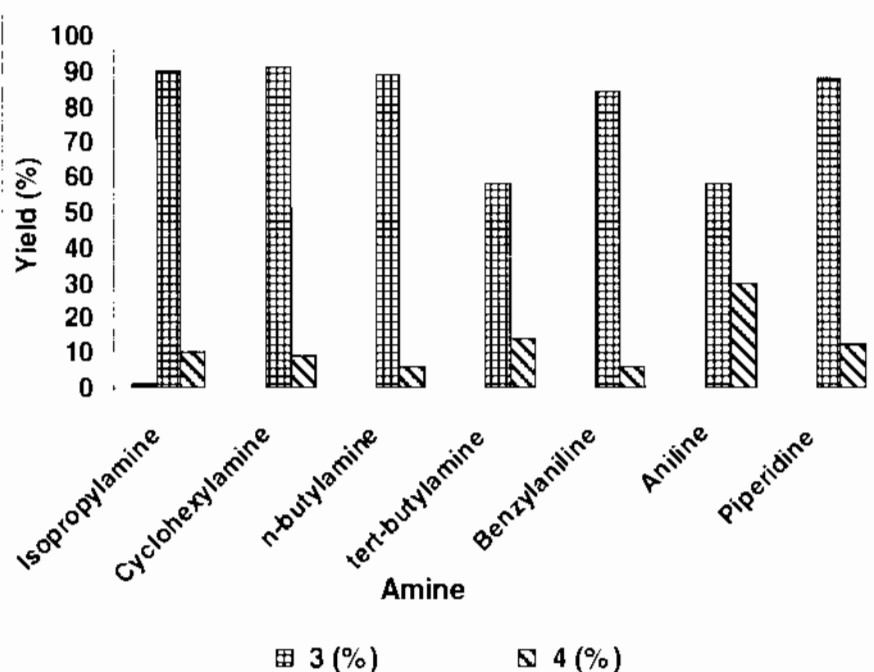


Fig. 3. Hydroaminomethylation of styrene by  $[\text{Rh}]^+$ . Effect of the type of amine. Reaction conditions: catalyst  $[\text{Rh}]^+$  (1% mol), styrene (2.0 mmol), CO/H<sub>2</sub> (1:1, 600 psi), THF (5 ml), 80 °C, 24 h – (Lin *et al.*, 2001).

Various *para*-substituted styrenes (**2**) have been converted into the amines. The branched amine (**3**) was formed as a major product along with linear isomer amine (**4**) as shown in Entries 2-7 of Table 1 (eq. 1) (Lin *et al.*, 2001). Both electron-withdrawing and electron-donating substituent in the *para* position predominantly gave the branched amine (**3**). Relatively lower yields of branched amines were obtained in the cases of *para*-*tert*-butylstyrene and *para*-chlorostyrene as substrates (Table 1, entries 4 and 5, respectively).

Table 1. Hydroaminomethylation of Arylalkenes **1** in the presence of isopropylamine **2a** (Lin *et al.*, 2001).<sup>a</sup>

Entry	Ar	Yield (mol%) <sup>b</sup>		Ratio <sup>b</sup>
		3	4	
1	C <sub>6</sub> H <sub>5</sub> - (1a)	92 (3a)	8 (4a)	11.5
2	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> - (1b)	85 (3b)	15 (4b)	5.7
3	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> - (1c)	90 (3c)	10 (4c)	9.0
4	<i>p</i> -(CH <sub>3</sub> ) <sub>2</sub> CC <sub>6</sub> H <sub>4</sub> - (1d)	70 (3d)	19 (4d)	3.7
5	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> - (1e)	77 (3e)	14 (4e)	5.5
6	<i>p</i> -FC <sub>6</sub> H <sub>4</sub> - (1f)	86 (3f)	14 (4f)	6.1
7	<i>p</i> -PhC <sub>6</sub> H <sub>4</sub> - (1g)	87 (3g)	13 (4g)	6.7

a) Reaction conditions: alkene (2 mmol), isopropylamine (2.4 mmol), catalyst (1% mol), CO/H<sub>2</sub> (1:1, 200 psi), THF (5 ml), 80 °C, 24 h.

b) The yields were determined by <sup>1</sup>H NMR and GC.

Methyl vinyl sulfone **5** was converted to **6a** in the presence of  $[\text{Rh}]^+$  complex together with phosphine ligand and isopropylamine under syngas in one-pot manner (eq. 3 and Table 2) (Lin *et al.*, 2001). **7a**, a product of Michael-type reaction involving the hydroamination of the alkenes without carbonylation, was formed as a by-product. This process represents the first example for one-pot formation of sulfonated enamine from the corresponding vinyl sulfone catalyzed by rhodium complex, which is different from the

hydroaminomethylation that gave saturated amine as major product. The new process, named as *hydroaminovinilation*, takes place probably *via* a sequence of hydroformylation and amine condensation followed by double bond isomerization of imine. Various reaction conditions were examined (Table 2). The use of chelating ligands, such as dppb and dppe afforded **6a** in good yields (Table 2, entries 1 and 5), PPh<sub>3</sub> gave moderate yield of **6a** (Table 2, entry 7), whereas the yield of **6a** was lower when PCy<sub>3</sub> or dppm was used (Table 2, entries 6 and 8). In the absence of phosphine ligand, **7a** was formed exclusively as the Michael-type reaction product (Table 2, entry 1). A decrease of the reaction temperature to 50°C resulted in lowering the yield of **6a** (Table 2, entry 3) due to the low reactivity of the substrate and also to the formation of more of **7** compared to higher temperature conditions. The reduction of the double bond in **6a** did not occur even though the hydrogen pressure was increased to 500 psi (Table 2, entry 4).

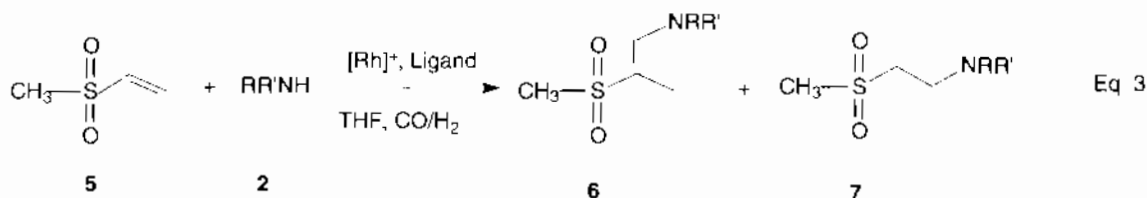


Table 2. Hydroaminovinilation of methyl vinyl sulfone **5** in the presence of syngas and isopropylamine **2a** [R=(CH<sub>3</sub>)<sub>2</sub>CH; R'=H] Lin *et al.*, 2001.<sup>a</sup>

Entry	L (mol%)	T (°C)	CO/H <sub>2</sub> (psi)	Yield (mol%) <sup>b</sup>	
				6a	7a
1	none	80	100/100	0	100
2	dppb (3)	80	100/100	92	3
3	dppb (3)	50	100/100	64	36
4	dppb (3)	80	100/500	95	5
5	dppe (3)	80	100/100	93	7
6	dppm (3)	80	100/100	17	49
7	PPh <sub>3</sub> (6)	80	100/100	61	25
8	PCy <sub>3</sub> (6)	80	100/100	10	61

a) Reaction conditions: methyl vinyl sulfone (1 mmol), isopropylamine (1.2 mmol), rhodium (0.01 mmol), THF (5 ml), 24 h

b) The yields were determined by <sup>1</sup>H NMR and GC.

Different primary and secondary amines have been considered in the reaction of the hydroaminovinilation of methyl vinyl sulfone to afford the corresponding unsaturated amines **6** together with Michael-type reaction product **7** as by-product (eq. 3 and Table 3). Surprisingly, bulkier amines, such as *tert*-butylamine, and less basic amines, such as aniline, underwent hydroaminovinilation exclusively to afford **6** (Table 3, entries 2 and 5). Cyclohexylamine and benzylamine gave the corresponding vinylated amines in high yields together with a small amount of **7** (Table 3, entries 3-4). In the case of butylamine, moderate yield of **6b** was formed by increasing the amount of **7b** (Table 3, entry 1). Diethylamine gave hydroaminovinylated amine **6g** in 84% together with 16% of Michael-type reaction product **7g** (Table 3, entry 6).

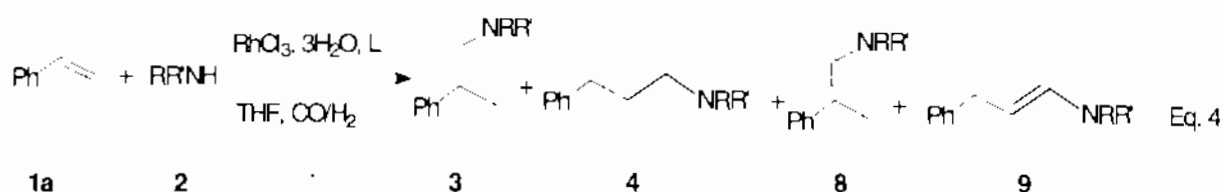
Table 3. Hydroaminovinylation of methyl vinyl sulfone **5** in the presence of various amines (Lin *et al.*, 2001).<sup>a</sup>

Entry	Amine	Yield (mol%) <sup>b</sup>	
		6	7
1	butylamine ( <b>2b</b> )	66 ( <b>6b</b> )	34 ( <b>7b</b> )
2	<i>tert</i> -butylamine ( <b>2c</b> )	100 ( <b>6c</b> )	0
3	cyclohexylamine ( <b>2d</b> )	90 ( <b>6d</b> )	10 ( <b>7d</b> )
4	benzylamine ( <b>2e</b> )	87 ( <b>6e</b> )	13 ( <b>7e</b> )
5	aniline ( <b>2f</b> )	100 ( <b>6f</b> )	0
6	HNEt <sub>3</sub> ( <b>2g</b> )	84 ( <b>6g</b> )	16 ( <b>7g</b> )

a) Reaction conditions: methyl vinyl sulfone (1 mmol), amine (1.2 mmol), rhodium (0.01 mmol), dppb (0.04 mmol), THF (5 mL), 80°C, 24 h.

b) The yields were determined by <sup>1</sup>H NMR and GC.






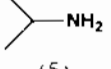
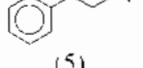
The hydroaminomethylation of styrene **1a** with piperidine **2h** was chosen as a model reaction (eq. 4, Table 3). Other primary amines such as isopropylamine **2a** and 2-phenylethylamine **2i** were used in the reaction. The effects of the temperature, the type of ligands, and the amount of amine have been studied. The hydroaminomethylation of styrene **1a** with piperidine **2h** occurred smoothly at relatively mild conditions (100°C, 800 psi, 20h) with RhCl<sub>3</sub>·3H<sub>2</sub>O used as a catalyst precursor in THF as a solvent and produced the branched amine **3** as a major product (Table 3, entry 2). The reaction at a lower temperature (80°C) led to lower conversion with the formation of the enamine **8** as a major product (Table 3, entry 1). The enamine **8** was also formed as a major product in the presence of an excess of piperidine **2h** or when a chelating phosphine ligands such as dppp and dppb were used (Table 3, entries 3-5). These results can be simply explained by the formation of **N-Rh-N** or **P-Rh-P** that have little hydrogenating power of the enamines into amines. The hydroaminomethylation of styrene with primary amines led to the formation of amines in the presence or in the absence of phosphine ligand.



## Conclusion

In conclusion, active and selective catalyst systems have been introduced in the hydroaminomethylation reactions. Zwitterionic rhodium complex **[Rh]<sup>+</sup>** showed high catalytic activity in the hydroaminomethylation of aryl alkenes. Also a new one-pot hydroaminovinylation reaction has been achieved for the selective synthesis of sulfonated enamines using the Zwitterionic rhodium complex **[Rh]<sup>+</sup>** together with a chelating phosphine ligand as the catalyst. In addition, a simple rhodium (III) catalyst RhCl<sub>3</sub>·3H<sub>2</sub>O in THF as a solvent catalyzes efficiently the hydroaminomethylation of styrene. Excellent selectivity toward the branched enamines was obtained when excess of amine was used or when dppp or dppb was added as a ligand. The conversion of styrene into branched amines was also controlled.

Table 4. Hydroaminomethylation of styrene **1a** by  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ .<sup>a</sup>

Entry	Amine (mmol)	Ligand (mmol)	T °C	Yield Amines (%) <sup>b</sup>	Selectivity Amines (%) <sup>b</sup>		Yield Enamines (%) <sup>b</sup>	Selectivity Enamines (%) <sup>b</sup>	
					3	4		8	9
1	 (5)	-	80	5	60	40	30	100	0
2	 (5)	-	100	99	88	12	0	-	-
3	 (25)	-	100	4	43	57	55	98	2
4	 (5)	dppp (0.02)	100	10	100	0	90	97	3
5	 (5)	dppb (0.02)	100	0	-	-	90	93	7
6	 (5)	-	100	94	86	14	0	-	-
7	 (5)	-	100	99	90	10	0	-	-

a) Reaction conditions: styrene (5 mmol),  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  (1% mmol),  $\text{CO}/\text{H}_2$  (100/700 psi), THF (5 ml), 20 h

b) The yields were determined by  $^1\text{H}$  NMR and GC.

### Acknowledgment

We are grateful to Professor Howard Alper from Chemistry department at the Ottawa University (Canada) for his support of the good part of the project. We also thank King Fahd University of Petroleum & Minerals (KFUPM-Saudi Arabia) for providing the facility and for financial support.

### References

- Ahmed, M., Seayad, A.M., Jackstell, R. and Beller, M. (2003) *J. Am. Chem. Soc.*, **125**: 10311.
- Alper, H. and Zhou, J.Q. (1992) *J. Org. Chem.*, **57**: 3729.
- Amer, I. and Alper, H. (1990) *J. Am. Chem. Soc.*, **112**: 3674.
- Beller, M. and Bolm, C. (1998) "Transition Metals for Organic Synthesis", V. 1 & 2, Wiley-VCH, New York.
- Colquhoun, H.M., Thompson, D.J. and Twigg, M.V. (1991) "Carbonylation", Plenum Press, New York.
- Eilbracht, P., Bäracker, L., Buss, C., Hollmann, C., Kitsos-Rzychon, B.E., Kranemann, C.L., Risché, T., Roggenbuck, R. and Schmidt, A. (1999) *Chem. Rev.*, **99**: 3329.
- Hartley, R. and Patai, S. (1982) "The Chemistry of Metal-Carbon", V. 3, Wiley, New



York.

**Iqbal, A.F.M.** (1971) *Helv. Chim. Acta*, **45**: 1440.

**Lee, C.W. and Alper, H.** (1995) *J. Org. Chem.*, **60**: 499.

**Lin, Y.S., El Ali, B. and Alper, H.** (2001) *Tetrahedron Lett.*, **42**: 2423.

**Lin, Y.S., El Ali, B. and Alper, H.**, *J. Am. Chem. Soc.*, **123**: 7719. (2001).

**Masters, C.** (1993) "*Homogeneous Transition-Metal Catalysis*". Wiley, New York.

**Parshall, G.W. and Ittel, S.D.** (1993) "*Homogeneous Catalysis*". Wiley-Interscience, New York.

**Reppe, W. and Vetter, H.** (1953) *Liebigs Ann. Chem.*, **582**: 133.

**Totland, K. and Alper, H.** (1993) *J. Org. Chem.*, **58**: 3326.

**Tsuji, J.** (1995) "*Palladium Reagents and Catalysts*". Wiley, New York.

**Wang, Y.Y., Luo, M.M., Li, Y.Z., Chen, H. and Li, X.J.** (2004) *Applied Catalysis*, **272**: 151.

## اصطناع الأمينات والاينامينات بواسطة الهيدروأمينوميثلة الألكينات باستخدام عوامل محفزة من مترابطات الروديوم (I) والروديوم (III)

بسام العلي

قسم الكيمياء ، جامعة الملك فهد للبترول والمعادن

الظهران - المملكة العربية السعودية

المستخلص. إن تكوين الأمينات بتفاعل أحادي فعال يتم بتفاعل الهيدروأمينوميثلايش للألكينات. إن هذا التفاعل يجذب الكثير من الباحثين الكيميائيين بسبب التطور العلمي في هذا المجال وخاصة خلال السنين العشر الأخيرة. إن مركبات  $[\text{Rh}(\text{CO})\text{Cl}]_2$  and  $[\text{Rh}(\text{COD})\text{Cl}]_2$  هي من أكثر المركبات استخداما في تفاعلات الهيدروأمينوميثلايش للألكينات. إن الاكتشافات التي قمنا بها حديثا في مجال الهيدروأمينوميثلايش للألكينات وذلك لتكوين الأمينات باستخدام مركب الروديوم (1)  $[\text{Rh}^+(\text{COD})(\eta^6\text{-PhBPh}_3)]$  كحفاز فعال تمت تحت حالات تفاعلية معتدلة. إن تفاعلات فيلات السلفونات تمت أيضا باستخدام الحالات التفاعلية المستخدمة في الهيدروأمينوميثلايش للألكينات بتفاعل أحادي يؤدي إلى تكوين الأمينات. إن هيدروأمينوميثلايش الألكينات تمت دراستها بوجود الروديوم (III) والفوسفونات حيث وجد أن الإينامينات تتكون بشكل كمي.