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# RhCl<sub>3</sub>-catalyzed hydroboration of alkenyl nitriles

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Abstract—RhCl<sub>3</sub>-promoted hydroboration–oxidation reactions of representative alkenyl nitriles have been carried out. Carbanion of acetonitrile is formed from the carbon–carbon heterolytic bond breaking in allyl cyanide during hydroboration. An unexpected process-trimerization of carbanion of acetonitrile has lead to the formation of 4-amino-2,6-dimethylpyrimidine. © 2003 Elsevier Ltd. All rights reserved.

## 1. Introduction

Hydroboration reactions of alkenes containing functional groups such as alkenyl amines,<sup>1</sup> alkenyl chlorides,<sup>2</sup> alkenyl alcohols,<sup>3</sup> and their ethers,<sup>4</sup> and alkenyl amino-acids<sup>5</sup> have been extensively studied since the functional groups can serve as chiral auxiliaries in the asymmetric induction and they have wide applications in the enantio-selective synthesis of natural products.<sup>6,7</sup> Hydroboration of aliphatic and aromatic nitriles yield borazine derivatives which can be hydrolyzed to the amines.<sup>8–11</sup> Transition metal-catalyzed hydroboration reactions are widely applicable to the synthetic procedures.<sup>12–14</sup> Therefore, catalyzed hydroborations of alkenes have been studied extensively,<sup>15–17</sup> but catalyzed hydroborations of alkenyl nitriles have never been studied in detail.<sup>18</sup> Our previous studies on the hydroboration of 1-octene in the presence of rhodium trichloride (RhCl<sub>3</sub>) showed unusual regioselectivity.<sup>19</sup> Therefore, it seems appropriate to study the hydroboration reactions of alkenyl nitriles in the presence of rhodium trichloride, since they have two reactive centers for hydroboration reactions: the carbon–carbon double bond and carbon-nitrogen triple bond. We have chosen the following alkenyl nitriles for hydroboration reactions: allyl cyanide, acrylonitrile and 5-hexenenitrile.



#### Scheme 1.

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# 2. Hydroboration of allyl cyanide

The hydroboration of allyl cyanide in the presence of  $RhCl_3$  and further oxidation lead to the following transformations (Scheme 1).

(a) Heterolytic cleavage of C–C bond and the trimerization of acetonitrile carbanion;

- (b) Isomerization;
- (c) Hydrogenation.

Three compounds can be formed in the result of hydroboration-oxidation reaction of allyl cyanide in the presence of RhCl<sub>3</sub>: 4-amino-2,6-dimethylpyrimidine 1, methacrylamide 2 and butyramide 3. These compounds are the results of different chemical processes. For example: 4-amino-2,6-dimethylpyrimidine is formed during the trimerization of acetonitrile carbanion obtained in the result of the carbon–carbon bond cleavage of allyl cyanide. Butyramide can be obtained as the result of the hydrogenation of the double bond in the allyl cyanide and methacrylamide via the isomerization of allyl cyanide. The nitrile group in the allyl cyanide is hydrolyzed to an amide group.

These compounds can be selectively synthesized by changing the ratio of starting materials (Table 1).

The ratio of starting compounds is an important factor for the reaction control. The selective synthesis of one compound can be achieved by changing the ratio of starting materials. Table 1 shows that the optimal ratio of reactants for the selective synthesis of the corresponding compounds.

The hydroboration of allyl cyanide has been carried out varying the hydroboration period (Table 2).

Initially butyramide and methacrylamide are formed and then the formation of 4-amino-2,6-dimethylpyrimidine, ethanol, and acetonitrile occurs. The cleavage of allyl cvanide and the trimerization of the newly formed acetonitrile give rise to the formation of 4-amino-2,6dimethylpyrimidine. However, the hydroboration of acetonitrile under the same conditions did not yield 4-amino-2,6-dimethylpyrimidine.<sup>8-11</sup> This fact allowed us to conclude that the carbon-carbon bond cleavage occurs heterolytically and the acetonitrile carbanion and ethyl cation are formed. The highly reactive and unstable carbanions of acetonitrile undergoes trimerization process by forming 4-amino-2,6-dimethylpyrimidine (Scheme 2). The relatively high yield (10.5%) for the 4-amino-2,6-dimethylpyrimidine was achieved when the reaction kept going for 1.5 h (exp. 4). Longer reaction times favored butyramide. We propose the following possible mechanism for the formation of 4-amino-2,6-dimethylpyrimidine from the carbanion of acetonitrile (Scheme 2).

The reactive Rh–B–H species first proposed by Mannig and Noth<sup>20</sup> are likely involved in our proposed mechanism. The availability of two reactive centers in the allyl cyanide molecule, the carbon–carbon double bond and carbon–nitrogen triple bond, allows the addition of Rh–B–H species at both centers. These additions cause the carbon–carbon bond in allyl cyanide break (Scheme 3) heterolytically because of the torsional strain between hydroborated carbon–carbon double bond and carbon–nitrogen triple bond and as a result two reactive species such as hydroborated carbanion of acetonitrile and ethyl carbocation are formed. The carbanion of acetonitrile is bonded to the Rh–B–H species on the nitrogen end of the carbon–nitrogen triple bond and to the nucleophilic carbon of this carbanion. The Rh–B–H

Table 1. Hydroboration of allyl cyanide with borane in the presence of RhCl<sub>3</sub>

Exp. #	Allyl cyanide (ml)	Borane (ml)	Volume ratio	Mole ratio	Total yield (%)	Yield of ethanol (%)	Yield of products $3/2/1$ (%)
1	1.00	15.00	1:15	1:1.5	60	15	13.6/0.0/71.3
2	1.00	10.00	1:10	1:1	60	16	31.3/0.0/52.3
3	1.00	5.00	1:5	1:0.5	55	10	68.2/0.0/22.0
4	1.00	3.00	1:3	1:0.3	40	3.4	58.7/33.4/4.4
5	1.00	2.00	1:2	1:0.2	40	12	71.4/16.3/0.0
6	1.00	1.00	1:1	1:0.1	61	4.6	0.0/95.4/0.0
7	1.00	0.50	2:1	1:0.05	50	2.4	0.0/97.6/0.0
8	1.00	0.25	4:1	1:0.025	60	2.4	0.0/97.6/0.0
9	1.00	0.00	1:0	1:0.00	20	1.9	0.0/98.1/0.0

Table 2. Hydroboration of allyl cyanide for different reaction period (in %) (mole ratio of allyl cyanide:borane 1:0.3)

Exp. #	Time (h)	Butyramide	Methacrylamide	Uncoupled acetonitrile	Ethanol	4-Amino-2,6-dimethylpyrimidine
1	0.25	68.00	32.00	0.00	0.00	0.00
2	0.50	54.68	30.32	2.00	11.00	3.00
3	1.00	51.20	17.30	2.00	22.6	6.80
4	1.50	33.34	13.34	5.70	37.00	10.50
5	2.00	45.00	25.50	8.00	18.00	3.34
6	3.00	68.40	10.30	10.60	10.60	2.54
7	5.00	80.60	14.50	2.50	2.50	3.00



Scheme 2.



## Scheme 3.

intermediate migrates reversibly via these tautomeric forms (Scheme 4).



## Scheme 4.

These two reactive species undergo trimerization to form the organoborane adduct of 4-amino-2,6dimethylpyrimidine. Further hydrolysis of this adduct affords 4-amino-2,6-dimethylpyrimidine. The hydrolysis of ethyl carbocation results in ethanol.

## 3. Hydroboration of acrylonitrile

Hydroboration of acrylonitrile 4 yields propionamide 6, the hydrogenation product of the carbon–carbon dou-

ble bond of acrylonitrile. In this reaction the carbon-carbon double bond gets reduced but carbon-nitrogen triple bond remains unchanged. Hydrolysis converts nitrile group into amide group. Both room temperature and reflux conditions also afforded the same product (Scheme 5).

The unsaturated centers in acrylonitrile that are close to each other afford only one hydrogenated product. The competition between carbon–carbon double bond and carbon–nitrogen triple bond results in the hydrogenation of the former. The absence of carbon–carbon bond breaking can be explained by this competition and steric hindrance within acrylonitrile.

## 4. Hydroboration of 5-hexenenitrile

Hydroboration of 5-hexenenitrile 7 gave net hydration product 8 on the carbon–carbon double bond. This reaction is an example of the hydroboration preference



#### Scheme 6.

Scheme 5.

between carbon-carbon double bond and carbon-nitrogen triple bond. Hydroboration favored to net hydration of carbon-carbon double bond in accord with *anti*-Markovnikov addition (Scheme 6). The carbon-carbon bond breaking is not observed in this because of the lack of torsional strain between hydroborated double and triple bonds.

**General hydroboration procedure**: In the flask equipped with a condenser, under nitrogen 10 mg of RhCl<sub>3</sub> was dissolved in 10 ml of freshly distilled tetrahydrofuran and 1.0 ml (0.0125 mol) of allyl cyanide was added. After 10 min of stirring, 15 ml (0.15 mol) or required amount of 0.1 M BH<sub>3</sub> in THF was added to the solution using a syringe. The reaction mixture was stirred at room temperature for 2 h. Then 10 ml of 30% H<sub>2</sub>O<sub>2</sub> was added followed by 10 ml of 3 M NaOH at 0°C. After 4 h the solution was filtered and extracted with 40 ml of diethyl ether three times. Solvent was removed with rotator evaporator to obtain the final product. The structures were confirmed with GC/MS and NMR.

**4-Amino-2,6-dimethylpyrimidine.** <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  (ppm) = 6.63 (2H, d, J = 2.5 Hz, NH), 6.086 (1H, s, J = 2.3 Hz, arom. H), 2.272 (3H, d, J = 2.6 Hz), 2.152 (3H, s); MS m/z (%): 123 (M<sup>+</sup>, 100); 68 (30); 56 (50).

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