



# Rh<sub>6</sub>(CO)<sub>16</sub>-H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>-catalyzed one pot hydroformylation–cyclotrimerization of cyclohexene and cyclopentene into 2,4,6-trisubstituted-1,3,5-trioxanes

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## Abstract

A new one pot reaction of hydroformylation–cyclotrimerization of cyclopentene **1a** and cyclohexene **1b** was selectively catalyzed by Rh<sub>6</sub>(CO)<sub>16</sub> and H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O (HPA-W<sub>12</sub>) in THF as a solvent at 40 atm (CO/H<sub>2</sub> = 1/1) to give 2,4,6-trisubstituted-1,3,5-trioxanes **3a** and **3b** as major products along with the corresponding aldehydes **2a** and **2b**.

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**Keywords:** Rhodium; Heteropolyacid; Hydroformylation; Cyclotrimerization; Cyclohexene; Trioxane

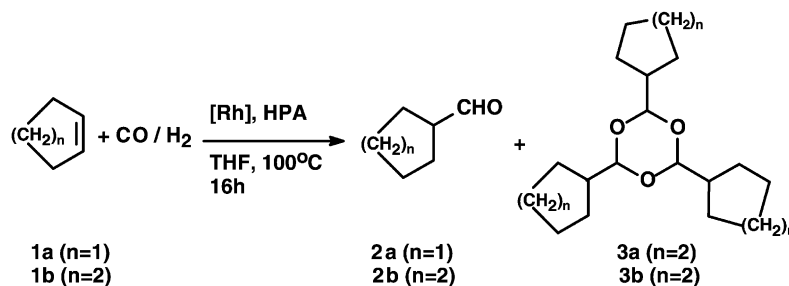
## 1. Introduction

The metal-catalyzed hydroformylation reaction, which uses carbon monoxide and hydrogen, is one of the most extensively investigated methods for the conversion of olefins to aldehydes [1–4]. Among transition metal complexes, rhodium and cobalt show the highest catalytic activity for the hydroformylation reaction, with rhodium being 10<sup>3</sup>–10<sup>4</sup> times more active than cobalt [1]. The acetalization–hydroformylation reactions represent a one pot simple and important route for the production of acetals via aldehydes in the presence of alcohols or ethyl orthoformate [3,4]. Also, the hydroaminomethylation of olefins as a one pot synthesis of variety of amines via aldehydes in the presence of amine has reached its synthetic applications in recent years [5].

The copolymerization of trioxane and cyclic ethers, such as ethylene oxide, produced acetal resins used as engineering thermoplastics [6]. Trioxane was commonly produced by the liquid- and vapor-phase catalytic trimerization of aqueous formaldehyde in the presence of an acid, such as H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O or H<sub>3</sub>PMo<sub>11</sub>VO<sub>40</sub>·xH<sub>2</sub>O [7]. Other substituted trioxanes were also synthesized by the cyclotrimerization of the corresponding aldehydes using zirconium catalyst, CpZr(Otf)<sub>2</sub> [8] and solvent-free liquid-phase cyclotrimerization of aliphatic aldehydes to 2,4,6-trialkyl-1,3,5-trioxanes [9,10], or Lewis acid catalyst, Me<sub>3</sub>SiNtf<sub>2</sub> [11], or acetonyltriphenylphosphonium bromide as a catalyst [12]. Other reactions have been also described but they required drastic conditions of pressure or gave poor yields of products [13]. To best of our knowledge, the one pot hydroformylation–polymerization reaction, which may produce trimers, tetramers, or polymers, is not yet well known in literature. We would like to report in this communication our important discovery of a new one pot reaction that

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Scheme 1.

includes hydroformylation–trimerization of cyclopentene **1a** and cyclohexene **1b** producing the corresponding carboxyaldehydes **2a** and **2b** and the new 2,4,6-trisubstituted-1,3,5-trioxanes **3a** and **3b** (Scheme 1).

## 2. Experimental

### 2.1. General

RhCl<sub>3</sub>·3H<sub>2</sub>O, [Rh(COD)Cl]<sub>2</sub>, [Rh(CO)<sub>2</sub>Cl]<sub>2</sub>, RhH(CO)(PPh<sub>3</sub>)<sub>3</sub>, RhCl(PPh<sub>3</sub>)<sub>3</sub>, Rh<sub>6</sub>(CO)<sub>16</sub>, Rh/C (5% Rh) were purchased from Strem Company and used without purification. The heteropolyacids H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>·25H<sub>2</sub>O, H<sub>3</sub>PMo<sub>12</sub>O<sub>40</sub>·25H<sub>2</sub>O and H<sub>3</sub>SiMo<sub>12</sub>O<sub>40</sub>·20H<sub>2</sub>O, and the other acids, such as CH<sub>3</sub>SO<sub>3</sub>H, HCOOH and 3-pyridine sulfonic acid, and cyclohexene and cyclopentene were purchased from Sigma–Aldrich. Dry solvents have been used in all experiments. H<sub>5</sub>PMo<sub>10</sub>V<sub>2</sub>O<sub>40</sub> was prepared according to the literature method [14].

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on 500 MHz Joel 1500 NMR machine. Chemical shifts were reported in ppm (δ) relative to tetramethyl silane (TMS) using CDCl<sub>3</sub>. Gas chromatography analyses were realized on HP 6890 plus chromatography equipped with capillary column HP-5.

### 2.2. General procedure for the carbonylation of cyclohexene (**1b**)

A mixture of cyclohexene (**1b**) (5 mmol), Rh<sub>6</sub>(CO)<sub>16</sub> (0.0010 mmol), H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>·25H<sub>2</sub>O (0.010 mmol) in THF (5 ml) was placed in a 45 ml stainless steel autoclave equipped with a glass liner and a magnetic stirrer. The autoclave was purged three times with carbon

monoxide and then pressurized by CO and H<sub>2</sub> to a total pressure of 40 atm. The reaction was carried out in an oil bath equipped with temperature controller to maintain the reaction temperature constant. After reaction, the autoclave was cooled slowly to room temperature and the gas was released. The product **3** was precipitated and recrystallized from THF or acetone solution. The aldehyde **2b** and the unreacted cyclohexene were determined by gas chromatography using 50 ml of anisole as internal standard. The product **3b** was fully characterized by <sup>1</sup>H and <sup>13</sup>C NMR, MS, elemental analysis, and X-ray technique (Fig. 1) [9,10].

#### 2.2.1. 2,4,6-Tricyclopentyl-1,3,5-trioxane (**3a**)

White crystal, mp = 94.2 °C. <sup>1</sup>H NMR δ (ppm) CDCl<sub>3</sub>: 1.43–1.72 (m, 27H, cyclopentyl), 4.60 (d, 3H, *J* = 5.85 Hz, O–CH–O of trioxane). <sup>13</sup>C NMR δ (ppm) CDCl<sub>3</sub>: 25.71, 25.78, 26.52, 27.21, 43.25, 104.41. *m/z*: 294 (*M*<sup>+</sup>). Anal. calcd. for C<sub>18</sub>H<sub>30</sub>O<sub>3</sub>: C, 73.43; H, 10.27. Found: C, 73.85; H, 10.42.

#### 2.2.2. 2,4,6-Tricyclohexyl-1,3,5-trioxane (**3b**)

White crystal, mp = 91.6 °C. <sup>1</sup>H NMR δ (ppm) CDCl<sub>3</sub>: 1.01–1.26 (m, 15H, cyclohexyl), 1.56–1.83 (m, 18H, cyclohexyl), 4.50 (d, 3H, *J* = 6.20 Hz, O–CH–O). <sup>13</sup>C NMR δ (ppm) CDCl<sub>3</sub>: 25.67, 26.47, 27.04, 41.88 104.29. *m/z* 336 (*M*<sup>+</sup>). Anal. calcd. for C<sub>21</sub>H<sub>36</sub>O<sub>3</sub>: C, 74.94; H, 10.78. Found: C, 74.65; H, 10.63.

## 3. Results and discussion

In order to determine the optimum conditions of the reaction and to achieve the highest yields of the product **3**, the hydroformylation–cyclotrimerization of

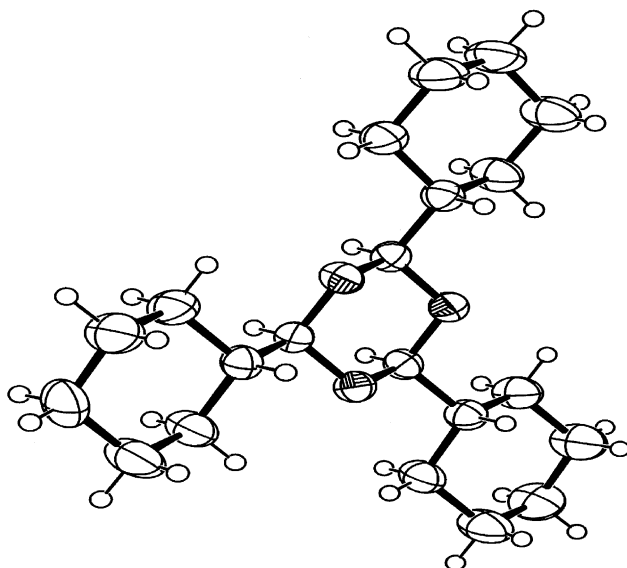
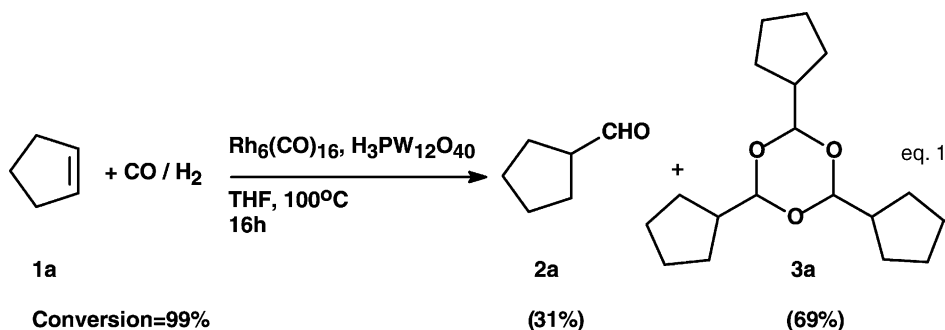


Fig. 1. X-ray structure of 1,3,5-tricyclohexyltrioxane **3b**.

cyclohexene **1b** was carefully examined using different rhodium catalysts and various co-catalysts in different solvents. The results of the study on the effect of the type of rhodium catalyst are summarized in Table 1. The rhodium cluster,  $\text{Rh}_6(\text{CO})_{16}$ , known as an active catalyst for the hydroformylation of internal alkenes, gave the highest isolated yield (81%) of the substituted trioxane **3b** in the presence of  $\text{H}_3\text{PW}_{12}\text{O}_{40} \cdot x\text{H}_2\text{O}$  as a co-catalyst in THF as a solvent at  $100^\circ\text{C}$  and 40 atm of syngas ( $\text{CO}/\text{H}_2 = 1/1$ ) (Table 1, entry 1).  $\text{Rh}/\text{C}$  (5% Rh), and the rhodium dimer  $[\text{Rh}(\text{COD})\text{Cl}]_2$  gave also excellent conversion (90–98%) of cyclohexene and high yields of **3b** under the same experimental conditions

(Table 1, entries 2 and 3). The isolated yields of 2,4,6-tricyclohexyl-1,3,5-trioxane **3b** obtained with these rhodium catalysts were also very high (74–81%). It was also observed that rhodium catalysts including  $\text{Rh}_6(\text{CO})_{16}$ ,  $\text{Rh}/\text{C}$  and  $[\text{Rh}(\text{COD})\text{Cl}]_2$  were very active towards the hydroformylation of cyclohexene in the absence of HPA- $\text{W}_{12}$  but the only product was the aldehyde **2b**. However, the rhodium(I) complexes  $\text{RhH}(\text{CO})(\text{PPh}_3)_3$  and  $\text{RhCl}(\text{PPh}_3)_3$  gave either low conversion (50%) and yield of **3b** (40%) (Table 1, entry 4), or showed no catalytic activity in this reaction due probably to its high sensitivity toward the acidity of the heteropolyacid (Table 1, entry 5). Also the rhodium(III),  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ , did not give

Table 1

Hydroformylation–trimerization of cyclohexene **1b**: effect of the type of rhodium catalyst<sup>a</sup>

Entry	Catalyst (mmol)	Conversion (%) <sup>b</sup>	Yield <b>2b</b> (%) <sup>b</sup>	Yield <b>3b</b> (%) <sup>c,d</sup>
1	Rh <sub>6</sub> (CO) <sub>16</sub> (0.0010)	98	14	81
2	Rh/C (5% Rh) (0.0050)	94	13	76
3	[Rh(COD)Cl] <sub>2</sub> (0.0050)	90	13	74
4	RhH(CO)(PPh <sub>3</sub> ) <sub>3</sub> (0.0050)	50	6	40
5	RhCl(PPh <sub>3</sub> ) <sub>3</sub> (0.0050)	0	–	–
6	RhCl <sub>3</sub> ·3H <sub>2</sub> O (0.0100)	0	–	–

<sup>a</sup> Reaction conditions: H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O (0.010 mmol), cyclohexene (5.0 mmol), THF (10 ml), 40 atm (CO/H<sub>2</sub> = 1/1), 100 °C, 16 h.<sup>b</sup> Determined by GC using anisole as internal standard.<sup>c</sup> Isolated yield.<sup>d</sup> Identified by <sup>1</sup>H and <sup>13</sup>C NMR and X-ray technique.

any traces of product and the starting material was recovered (Table 1, entry 6). Therefore, Rh<sub>6</sub>(CO)<sub>16</sub>, the most active rhodium complex, was adopted as the catalyst of choice for further study. The role of the heteropolyacid in the hydroformylation step was not obvious but it is definitely the real catalyst of the cyclotrimerization of the aldehyde.

The type of the co-catalyst was very important for the occurrence of the reaction. Table 2 summarizes the results of the hydroformylation–cyclotrimerization of cyclohexene with different heteropolyacids and other acids. Although the conversions in most cases were extremely high, however, no substituted trioxane **3b** was detected in the absence of the heteropolyacid or other additives (Table 2, entries 1, 5 and 6). Among the heteropolyacids of Keggin structure of general formula H<sub>3+n</sub>XM<sub>12-n</sub>V<sub>n</sub>O<sub>40</sub>·xH<sub>2</sub>O (X = P, Si; M =

Mo, W), the following complexes have been used: H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O (HPA-W<sub>12</sub>), H<sub>3</sub>PMo<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O (HPA-Mo<sub>12</sub>), H<sub>4</sub>SiMo<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O (HSiA-Mo<sub>12</sub>), H<sub>5</sub>PMo<sub>10</sub>V<sub>2</sub>O<sub>40</sub>·xH<sub>2</sub>O (HPA-Mo<sub>10</sub>V<sub>2</sub>) (Table 2, entries 1–5). Surprisingly, only HPA-W<sub>12</sub> (0.010 mmol) exhibited excellent conversion (98%) of cyclohexene and high yield (81%) of the substituted trioxane **3b** (Table 2, entry 2). The increase of the concentration of HPA-W<sub>12</sub> (0.030 mmol in place of 0.010 mmol in 10 ml THF) led to the increase of the yield of aldehyde **2b** due probably to acid decomposition of the substituted trioxane **3b** (Table 2, entry 3). In general, the conversions were excellent but the main product was the aldehyde **2b** in addition to low yield of **3b** obtained with HPA-Mo<sub>10</sub>V<sub>2</sub> (Table 2, entries 4–6). We believe that the product **3b** was formed in situ by the catalytic polymerization of cyclohexanecar-

Table 2

Hydroformylation–trimerization of cyclohexene **1b**: effect of the amount of and the type of co-catalyst<sup>a</sup>

Entry	Co-catalyst (additive, mmol) <sup>b</sup>	Conversion (%) <sup>c</sup>	Yield <b>2b</b> (%) <sup>c</sup>	Yield <b>3b</b> (%) <sup>d,e</sup>
1	–	99	99	0
2	HPA-W <sub>12</sub> (0.010)	98	14	81
3	HPA-Mo <sub>12</sub> (0.010)	92	85	4
4	HSiA-Mo <sub>12</sub> (0.010)	60	60	0
5	HPA-Mo <sub>10</sub> V <sub>2</sub> (0.010)	99	70	25
6	CH <sub>3</sub> SO <sub>3</sub> H (0.050)	96	40	56
7	3-Pyridine sulfonic acid (0.050)	98	98	0
8	HCOOH (0.050)	90	90	0

<sup>a</sup> Reaction conditions: Rh<sub>6</sub>(CO)<sub>16</sub> (0.0010 mmol), cyclohexene (5.0 mmol), THF (10 ml), 40 atm (CO/H<sub>2</sub> = 1/1), 100 °C, 16 h.<sup>b</sup> HPA-W<sub>12</sub> (H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O); HPA-Mo<sub>12</sub> (H<sub>3</sub>PMo<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O); HSiA-Mo<sub>12</sub> (H<sub>4</sub>SiMo<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O); HPA-Mo<sub>10</sub>V<sub>2</sub> (H<sub>5</sub>PMo<sub>10</sub>V<sub>2</sub>O<sub>40</sub>·xH<sub>2</sub>O).<sup>c</sup> Determined by GC using anisole as internal standard.<sup>d</sup> Isolated yield.<sup>e</sup> Identified by <sup>1</sup>H and <sup>13</sup>C NMR and X-ray technique.

Table 3

Hydroformylation–trimerization of cyclohexene **1b**: effect of the temperature and the type of solvent<sup>a</sup>

Entry	Solvent	<i>T</i> (°C)	Conversion (%) <sup>b</sup>	Yield <b>2b</b> (%) <sup>b</sup>	Yield <b>3b</b> (%) <sup>c,d</sup>
1	THF	60	65	22	40
2	THF	80	85	14	66
3	THF	100	98	14	81
4	CH <sub>2</sub> Cl <sub>2</sub>	100	75	75	0
5	Toluene	100	87	87	0
6	Hexane	100	84	84	0

<sup>a</sup> Reaction conditions: Rh<sub>6</sub>(CO)<sub>16</sub> (0.0010 mmol), HPA-W<sub>12</sub> (0.010 mmol), cyclohexene (5.0 mmol), solvent (10 ml), 40 atm (CO/H<sub>2</sub> = 1/1), 16 h.

<sup>b</sup> Determined by GC using anisole as internal standard.

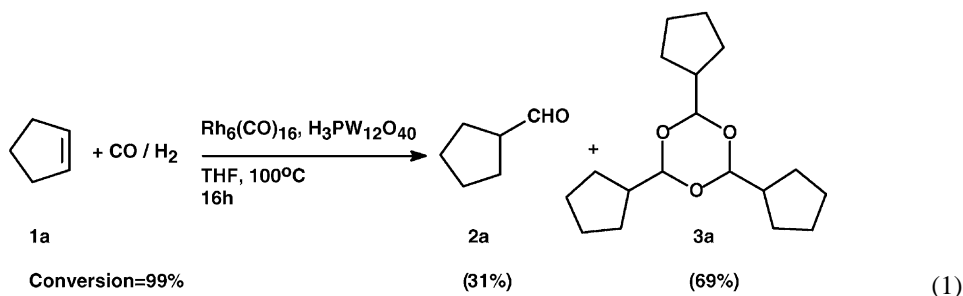
<sup>c</sup> Isolated yield.

<sup>d</sup> Identified by <sup>1</sup>H and <sup>13</sup>C NMR.

boxyaldehyde **2b** in the presence of H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> [9,10]. However, H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> may also participate in the stabilization of the active intermediate species formed from Rh<sub>6</sub>(CO)<sub>16</sub> and syngas in THF.

The effects of the temperature and the type of solvent were also carefully studied (Table 3). Interestingly, the reaction in THF at 100 °C gave the best

identified in the reaction mixture by GC and NMR. Unfortunately, the reaction of hydroformylation of cyclooctene occurred with acceptable conversion (60%) but the major product of the reaction was the corresponding carboxyaldehyde; only traces of 2,4,6-tricyclopentyl-1,3,5-trioxane were detected in the mixture.



conversion of cyclohexene and the highest isolated yield of **3b**. At lower temperature (<80 °C) the conversions of cyclohexene dropped seriously and subsequently the isolated yields of **3b** also decreased (Table 3, entries 1 and 2). It is important to note that the use of other solvents, such as CH<sub>2</sub>Cl<sub>2</sub>, toluene, or hexane gave only the aldehyde **2** as the sole product with no formation of 2,4,6-tricyclohexyl-1,3,5-trioxane **3b** (Table 3, entries 4–6).

The catalytic system consisting of Rh<sub>6</sub>(CO)<sub>16</sub>/H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>/CO/H<sub>2</sub> in THF was applied to cyclopentene **1a** as a reactant (Eq. (1)). The conversion of the reaction reached 99% after 16 h leading to good isolated yield (69%) of 2,4,6-tricyclopentyl-1,3,5-trioxane **3a**; the carboxyaldehyde **2a** was the only other product

The mechanism of the hydroformylation of alkenes by rhodium catalysts is now well elaborated in numerous books and reviews [1–5]. However, the mechanism of the catalytic cyclotrimerization of aldehydes into substituted trioxanes by the heteropolyacids as catalysts is still not yet very clear and obvious for us. Further study is needed to clarify this mechanism.

#### 4. Conclusion

In conclusion, we have developed a new one pot process that involves the hydroformylation and trimerization reactions of cyclopentene and cyclohexene toward the selective formation of 2,4,6-trisubsti-

tuted-1,3,5-trioxanes in high yields. The reaction was simply catalyzed by  $\text{Rh}_6(\text{CO})_{16}$  and  $\text{H}_3\text{PW}_{12}\text{O}_{40}$ . Other rhodium catalysts, such as  $[\text{RhCl}(\text{COD})]_2$  and Rh/C have shown also high catalytic activity in this process. However, the use of other heteropolyacids such  $\text{H}_3\text{PMo}_{12}\text{O}_{40} \cdot x\text{H}_2\text{O}$ ,  $\text{H}_4\text{SiMo}_{12}\text{O}_{40} \cdot x\text{H}_2\text{O}$ ,  $\text{H}_5\text{PMo}_{10}\text{V}_2\text{O}_{40} \cdot x\text{H}_2\text{O}$  gave either no 2,4,6-trisubstituted-1,3,5-trioxanes or only low yield of product. The process could be extended to other alkenes and aldehydes that may lead selectively to substituted trioxanes, which may have potential industrial applications.

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