



# Organogermanium compounds anchored on Pt/SiO<sub>2</sub> as chiral catalysts for the enantioselective hydrogenation of 3,4-hexanedione

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## ABSTRACT

This work reports the synthesis of PtGe chiral catalysts using organogermanium compounds containing (–)-menthyl groups as substituents. Chiral inducers were carefully synthesized and characterized in order to obtain optically pure compounds. PtGe catalysts were prepared through a controlled surface reaction between the supported transition metal and the organometallic compound. This technique leads to reproducible and well defined phases. The catalysts were employed in liquid phase enantioselective hydrogenation of 3,4-hexanedione. The obtained systems were active (95% conversion) and enantioselective (enantiomeric excess of 25% for 4-hydroxy-3-hexanone and 10% for 3,4-hexanediol). These results are very encouraging as they are comparable to those obtained previously by our group with similar PtSn catalysts and those reported for classical Pt/cinchonidine systems. The organogermanium compounds presented here have advantages over their tin analogs, mainly due to their greater stability and nontoxicity.

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## 1. Introduction

The work by R. Noyori and T. Ohkuma, who used ruthenium with chiral ligands of the BINAP-Ru type (BINAP = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl), represents a milestone in the enantioselective catalytic hydrogenation of diketones [1]. The advantages of these homogeneous Noyori-type catalysts are their easy utilization and very high activity per volume unit. However, the products have to be eventually separated, and the expensive organometallic complex catalyst is hard to recover. Moreover, the high toxicity of the metal complex has the risk of contaminating the synthesized products. This is the reason why the heterogeneous catalysis of optically active compounds has gained significance, especially for industrial-scale production.

Thus, heterogeneous enantioselective hydrogenation has emerged as a promising route for the synthesis of optically pure compounds. In most of the studies on the enantioselective hydrogenation of carbonyl compounds reported in literature, Pt-based catalysts modified with cinchona alkaloids have been used [2]. These systems have been successful in the hydrogenation of  $\alpha$ -

ketoesters [3]. For example, the enantioselective hydrogenation of ethyl pyruvate over Pt-based catalyst modified with cinchonidine is a classic asymmetric reference system (under appropriate conditions enantiomeric excesses higher than 95% can be obtained). However, high activities and enantioselectivities only are obtained for a specific combination of active metal-chiral modifier-reagent (Pt-cinchona alkaloid- $\alpha$ -ketoester). Therefore, when these catalysts are employed in the reduction of diketones, the enantiomeric excess obtained is much lower than the one obtained for  $\alpha$ -ketoesters [4–8]. Thus, the development of systems that allow the diversification of the hydrogenation reactions of prochiral compounds is a very important topic.

Over the past few years, P. Reyes' group has structurally modified cinchonidine, obtaining a derivative that could be anchored on the SiO<sub>2</sub> surface. Thus, they synthesized a supported metal catalyst that was active in the enantioselective hydrogenation of a diketone, 1-phenyl-propane-1,2-dione [9,10].

The hydrogenation of vicinal diketones is an interesting process since the obtained products are diols and hydroxy ketones with optical activity, of interest in the pharmaceutical industry, because these are widely used in the synthesis of medicines. For instance, the product of the hydrogenation of 1-phenyl-2-propanone, (R)-1-hydroxy-1-phenyl-2-propanone, is an intermediate in ephedrine production [11]. However, the selective reduction of this type of

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compounds is a challenge because these molecules have two groups that can be hydrogenated.

Figure 1 shows the possible hydrogenation products of 3,4-hexanedione. Due to the presence of two conjugated carbonyl groups, the reaction takes place in two consecutive stages [5]. First, the hydrogenation of one of the C=O groups occurs, obtaining two  $\alpha$ -hydroxy ketones: (4S)- and (4R)-hydroxy-3-hexanone. In a second step, (3S,4S)- and (3R,4R)-hexanediol, and meso-hexanediol are produced.

In previous work, our research group demonstrated that systems modified with chiral organotin inductors, derived from the (–)-menthyl group [(–)-Men], were active and enantioselective in the hydrogenation of 3,4-hexanedione, especially in the first step of the reaction [12,13]. The enantiomeric excess reached was higher than the one obtained with the Pt/cinchonidine system [5]. However, these catalysts showed a low enantiodifferentiating capacity for the corresponding diols.

Taking into account that toxic wastes are hard to separate, the use of organotin derivatives would be disadvantageous in a synthetic industrial process, especially in the case of pharmaceutical products. Therefore, it is important to obtain new organometallic compounds with the versatility of organotin, but without its toxicity problems. Considering that organotin and organo-germanium compounds have similar chemical properties, chiral germanium organic compounds containing (–)-menthyl groups were synthesized. These compounds have advantages over their analogous tin-containing ones, mainly due to their greater stability and nontoxicity.

In a previous work, Pt-based catalysts modified with (–)-Men<sub>3</sub>GeMe were prepared, in order to use them in enantioselective hydrogenation of acetophenone. Many interesting and encouraging results were obtained [14]. In such work, we had demonstrated that it is possible to obtain PtGe bimetallic catalysts by a selective reaction between an organo-germanium compound and the transition metal. In such way, a system with (–)-menthyl groups (potential inductors of chirality) anchored on the surface was synthesized. This system was used in the enantioselective hydrogenation of acetophenone in liquid phase. The catalyst was active and chemo/enantioselective to obtain 1-phenylethanol.

Based on this preliminary experience, in the present work is proposed the synthesis of organo-germanium compounds, derived from the (–)-menthyl group, to prepare new supported chiral Pt-based catalysts. Chiral inducers were carefully synthesized and characterized in order to obtain optically pure compounds. PtGe

catalysts were prepared through a controlled surface reaction between the supported transition metal and the organometallic compound, derived from Surface Organometallic Chemistry on Metals (SOMC/M) techniques. These techniques lead to reproducible and well-defined phases. The catalytic activity and enantioselectivity of the catalysts obtained in the liquid-phase enantioselective hydrogenation reaction of 3,4-hexanedione were studied. Tests were performed to evaluate the catalytic activity and the enantioselectivity reached after four reuses.

## 2. Experimental

### 2.1. Synthesis and characterization of (–)-menthylgermanium compounds

#### 2.1.1. Synthesis of (1R,2S,5R)-(–)-dimethylgermanium dichloride (2) and (1R,2S,5R)-(–)-trimethylgermanium chloride (3)

A (1R,2S,5R)-menthylmagnesium chloride (**1**) solution in dry THF (98.7 mL, 1.58 M) was added dropwise over a GeCl<sub>4</sub> solution in dry benzene (5.64 g, 26 mmol), at room temperature and under N<sub>2</sub> atmosphere. The **1** compound was prepared by techniques reported in literature [15]. The mixture was heated under reflux for 20 h and stirred at room temperature for 15 h. An HCl solution (20 mL 10%) was added and the mixture was transferred to a separatory funnel. After addition of Et<sub>2</sub>O (150 mL), the organic phase was allowed to decant, it was washed three times with water and dried over MgSO<sub>4</sub>. The solvent was removed under reduced pressure. By chromatographic analysis was determined that the mixture consisted of two compounds: (1R,2S,5R)-(–)-dimethylgermanium dichloride (**2**) and (1R,2S,5R)-(–)-trimethylgermanium chloride (**3**), in a molar ratio 30:70. These compounds were separated by column chromatography (silica gel 60) with diethyl ether/hexane mixture as eluent.

#### 2.1.2. Synthesis of (1R,2S,5R)-(–)-trimethylmethylgermanium (4)

A MeMgI in Et<sub>2</sub>O solution (3.7 mL, 1.53 M) was added dropwise and stirring over a solution of **3** in dry benzene (3.0 g in 12 mL), under N<sub>2</sub> atmosphere, at 0 °C. The mixture was heated under reflux for 3 h, cooled to 0 °C and an HCl solution was added (5 mL, 10%). The organic phase was separated and the aqueous phase was extracted three times with Et<sub>2</sub>O (2 mL each one). The extracts were dried over MgSO<sub>4</sub> and the solvent was evaporated under reduced pressure. The reaction product was purified by column chromatography obtaining **4** as a white solid.

#### 2.1.3. Synthesis of (1R,2S,5R)-(–)-trimethylgermanium hydride (5)

A LiAlH<sub>4</sub> (0.14 g) suspension in dry Et<sub>2</sub>O (8 mL) was added to a solution of compound **3** (1.9 g) in dry Et<sub>2</sub>O (20 mL), at room temperature, under N<sub>2</sub> atmosphere. The mixture was heated under reflux for 7 h and then was added an NH<sub>4</sub>Cl saturated solution (10 mL). The organic phase was discarded and the aqueous phase was extracted three times with Et<sub>2</sub>O. The extracts were dried over MgSO<sub>4</sub> and the solvent was eliminated under reduced pressure. Compound **5** was obtained as a white solid.

The obtained compounds were characterized by elemental analysis (C,H), GC/MS (HP5-MS capillary column, 30 m × 0.25 mm × 0.25 mm), <sup>1</sup>H NMR and <sup>13</sup>C NMR (Bruker ARX 300 MHz). Melting points were determined in a Kofler hot stage and are uncorrected. Specific rotations were determined with a Polar L- $\mu$ P, IBZ messtechnik.

### 2.2. Catalyst preparation and characterization

A Pt monometallic catalyst was prepared by ionic exchange,

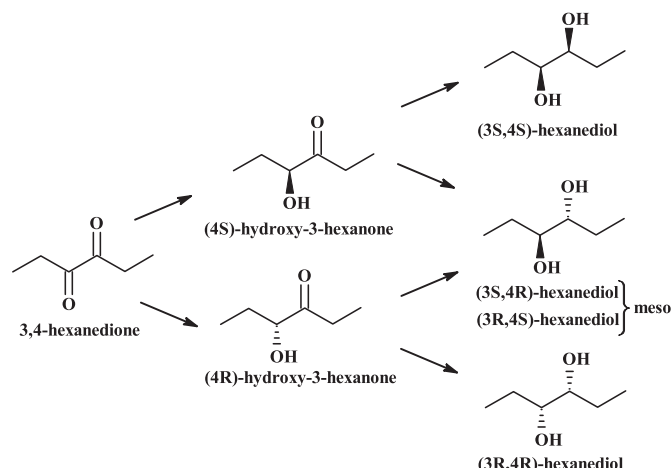


Figure 1. Hydrogenation of 3,4-hexanedione.

employing SiO<sub>2</sub> as support (Evonik, 200 m<sup>2</sup>/g), previously treated in ammonia solution. The functionalized solid was contacted with an aqueous solution of [Pt(NH<sub>3</sub>)<sub>4</sub>]Cl<sub>2</sub>, in an appropriate concentration, to obtain 1% w/w Pt in the resulting catalyst. The solid was exchanged for 24 h at room temperature, washed and dried at 105 °C. Later, the catalyst was calcined at 500 °C and reduced in H<sub>2</sub> flow for 2 h at 500 °C.

Chiral organogermanium catalysts were prepared through techniques derived from Surface Organometallic Chemistry on Metals. After reduction, the monometallic catalyst (0.25 g) was contacted with a solution of (–)-Men<sub>3</sub>GeMe or (–)-Men<sub>3</sub>GeH in *n*-decane. The reaction was carried out at 120 °C for 4 h under H<sub>2</sub> atmosphere. Once the reaction was complete, the catalyst was repeatedly washed with *n*-heptane under Ar atmosphere. These catalysts have a molar ratio Ge/Pt = 0.8 and correspond to solids containing organic groups anchored to a metal surface. These solids are denominated Pt-Men<sub>3</sub>GeMe and Pt-Men<sub>3</sub>GeH.

The monometallic catalyst was characterized by atomic absorption (Varian Spectra AA55), temperature-programmed reduction (TPR) (Quantachrome, 25 cm<sup>3</sup> min<sup>-1</sup>, 5% H<sub>2</sub> in N<sub>2</sub>, 10 °C min<sup>-1</sup>), H<sub>2</sub> and CO chemisorption (RXM-100 Advanced Scientific Designs Inc., USA) and specific surface (Micromeritics ASAP 2020). The particle size distribution was determined by transmission electron microscopy (TEM) in a JOL 100Cx microscope.

The Ge/Pt ratio in the organobimetallic catalyst was measured by gas chromatography (GC Varian CP-3800, capillary column FactorFour 15 m × 0.25 mm × 0.25 mm), through the difference between the initial and final concentrations of solutions of the organometallic compounds used in their preparation.

### 2.3. Hydrogenation of 3,4-hexanedione

The hydrogenation of 3,4-hexanedione was carried out in an autoclave-type reactor at 1 MPa H<sub>2</sub> pressure, 40 °C, 800 rpm, using 0.25 g of catalyst and 2-propanol as solvent. In each test, 0.4 mL of 3,4-hexanedione and 60 mL of 2-propanol (0.06 M) were used. The experimental conditions were selected to avoid mass transfer effects. In agreement with others authors, we had verified experimentally that the stirring rate and the size of catalyst particles employed assure the kinetic control of reaction and, as a consequence, the diffusional control is negligible [12,13,16]. The reaction progress was monitored by taking microsamples that were analyzed in a Varian CP-3800 gas chromatograph provided of a CP wax 52 CB (30 m, i.d. 0.53 mm) capillary column and FID detector. The reaction products were identified by GC/MS Shimadzu QP5050 with a SUPELCO SPB TM-5 (30 m, 0.25 mm i.d.) capillary column. The enantiomeric excess was calculated according to: ee% = 100(S - R)/(S + R), taking into account the data obtained by gas chromatography with a BETA DEXTM 120 (30 m, 0.25 mm i.d.) chiral capillary column.

As a model, we selected the Pt-Men<sub>3</sub>GeH catalyst to study the stability of these systems. This catalyst allowed obtaining a slightly higher enantiomeric excess to hydroxy ketones. In each test, the catalyst was washed and reused in four hydrogenation cycles.

## 3. Results and discussion

### 3.1. Synthesis and characterization of (–)-menthylgermanium compounds

The synthesis of optically pure organogermanium compounds, used as chiral inducers, is a key step in the preparation of the proposed chiral catalysts, in this work.

From our experience in organotin compounds synthesis and its utilization in the preparation of enantioselective catalysts [13,17],

we proposed to prepare the tri-(–)-menthylgermanium derived by direct synthesis between the Grignard reagent (1) and GeCl<sub>4</sub>. The products obtained were 2 and 3 in a ratio 30:70. Based on 3 it was possible to prepare 4 and 5, according to the scheme shown in Figure 2.

Below are reported the results of characterization by melting point measure, specific rotation measure, <sup>1</sup>H NMR spectroscopy, mass spectrometry and elemental analysis (C,H):

Compound 2: mp 83–84 °C; [α]<sub>D</sub><sup>22</sup> = –82.3° (c 1, C<sub>6</sub>H<sub>6</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, Me<sub>4</sub>Si) δ ppm: 0.80 [d, 6H, <sup>3</sup>J(H,H) 6.9]; 0.87 [d, 6H, <sup>3</sup>J(H,H) 6.5]; 0.93 [d, 6H, <sup>3</sup>J(H,H) 7.0]; 0.99–2.00 (m, 20H). MS (*m/z*, relative intensity): 388 [79, (M – Cl)<sup>+</sup>], 352 [17, (M – 2Cl)<sup>+</sup>], 249 [15, (M – Cl – C<sub>10</sub>H<sub>19</sub>)<sup>+</sup>], 213 [9, (M – 2Cl – C<sub>10</sub>H<sub>19</sub>)<sup>+</sup>], 137 (5), 55 (100). Anal. Calcd. for C<sub>20</sub>H<sub>38</sub>GeCl<sub>2</sub>: C 56.91; H 9.08. Found: C 57.03; H 9.10.

Compound 3: mp 104–105 °C; [α]<sub>D</sub><sup>22</sup> = –79.5° (c 1, C<sub>6</sub>H<sub>6</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, Me<sub>4</sub>Si) δ ppm: 0.80 [d, 9H, <sup>3</sup>J(H,H) 6.7]; 0.89 [d, 9H, <sup>3</sup>J(H,H) 6.4]; 0.94 [d, 9H, <sup>3</sup>J(H,H) 6.8]; 0.97–2.10 (m, 30H). MS (*m/z*, relative intensity): 387 [34, (M – C<sub>10</sub>H<sub>19</sub>)<sup>+</sup>], 249 [37, (M – C<sub>20</sub>H<sub>38</sub>)<sup>+</sup>], 137 (76), 55 (100). Anal. Calcd. for C<sub>30</sub>H<sub>57</sub>GeCl: C 68.53; H 10.93. Found: C 68.66; H 10.97.

Compound 4: mp 65–66 °C; [α]<sub>D</sub><sup>22</sup> = –43.7° (c 1, C<sub>6</sub>H<sub>6</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, Me<sub>4</sub>Si) δ ppm: 0.23 (s, 3H); 0.77 [d, 9H, <sup>3</sup>J(H,H) 6.9]; 0.88 [d, 9H, <sup>3</sup>J(H,H) 6.6]; 0.93 [d, 9H, <sup>3</sup>J(H,H) 6.9]; 0.98–1.86 (m, 30H). MS (*m/z*, relative intensity): 367 [1, (M – C<sub>10</sub>H<sub>19</sub>)<sup>+</sup>], 228 [41, (M – C<sub>20</sub>H<sub>38</sub>)<sup>+</sup>], 137 (100). Anal. Calcd. for C<sub>31</sub>H<sub>60</sub>Ge: C 73.67; H 11.96. Found: C 73.48; H 11.92.

Compound 5: IR (NaCl, cm<sup>-1</sup>): ν<sub>Ge-H</sub> 2000; mp 90–91 °C; [α]<sub>D</sub><sup>22</sup> = –105.3° (c 1, C<sub>6</sub>H<sub>6</sub>); <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>, Me<sub>4</sub>Si) δ ppm: 0.89 [d, 9H, <sup>3</sup>J(H,H) 6.9]; 0.92 [d, 9H, <sup>3</sup>J(H,H) 6.2]; 1.00 [d, 9H, <sup>3</sup>J(H,H) 6.9]; 1.21–2.28 (m, 30H); 4.35 (s, 1H, Ge–H). MS (*m/z*, relative intensity): 353 [16, (M – C<sub>10</sub>H<sub>19</sub>)<sup>+</sup>], 215 [50, (M – C<sub>20</sub>H<sub>38</sub>)<sup>+</sup>], 137 (100). Anal. Calcd. for C<sub>30</sub>H<sub>58</sub>Ge: C 73.33; H 11.90. Found: C 73.06; H 11.86.

From the analysis of <sup>1</sup>H and <sup>13</sup>C NMR of 2 and 3 compounds, it was possible to prove that the reaction took place without C1 epimerization. Thus, we demonstrated that direct alkylation of GeCl<sub>4</sub> takes place enantioselectively. This is a very important result that implies a major advantage in the (–)-menthyl germanium compounds synthesis with regard to their organotin analogs [18].

The compounds 4 and 5 were synthesized optically pure from 3. <sup>13</sup>C NMR characteristics of the compounds 2–5 are reported in Table 1.

In Figure 3 it is presented the spatial structure of the chiral modifiers obtained.

### 3.2. Catalysts preparation and characterization

The monometallic catalyst, Pt/SiO<sub>2</sub> (1% w/w measured by atomic absorption spectrometry), was prepared by ionic exchange. This technique allowed obtaining catalysts with high dispersion (H/Pt = 0.65 and CO/Pt = 0.55) [19,20]. The high dispersion is an important characteristic to prepare bimetallic catalysts by controlled surface reaction between the supported transition metal and the organometallic compound. TPR tests showed two distinctive peaks at 250 and 500 °C. The first peak can be assigned to Pt(IV) species formed during calcination. The second one may be attributed to Pt-(O-Si≡)<sub>n</sub><sup>n-y</sup> (n = 2 + or 4+) species, because of the interaction between the support and metallic phase [21]. From TPR results we chose the reduction treatment of monometallic catalyst (H<sub>2</sub> flow at 500 °C during 2 h). Subsequent tests to this treatment demonstrated that the metallic phase was completely reduced. TEM results showed a homogeneous metallic particle size distribution, centered on 2.5 nm.

The catalysts modified with germanium were obtained by a controlled surface reaction between the monometallic system, previously reduced, and the organogermanium compound

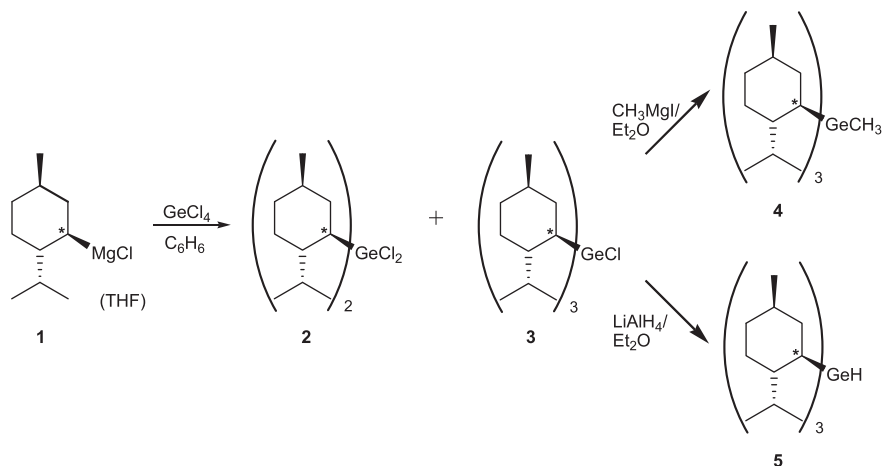


Figure 2. Synthesis of (-)-Men<sub>3</sub>GeMe (4) and (-)-Men<sub>3</sub>GeH (5).

Table 1

<sup>13</sup>C NMR of the compounds 2–5.<sup>a</sup>

Comp. N <sup>o</sup>	R	n
2	Cl	2
3	Cl	3
4	Me	3
5	H	3

C <sub>n</sub>	Comp.2 <sup>b</sup>	Comp.3 <sup>b</sup>	Comp. 4 <sup>c</sup>	Comp. 5 <sup>d</sup>
C <sub>1</sub>	36.31	39.01	34.80	34.91
C <sub>2</sub>	45.22	45.24	45.49	46.42
C <sub>3</sub>	26.43	26.48	26.71	26.61
C <sub>4</sub>	35.37	35.32	35.71	35.97
C <sub>5</sub>	34.53	34.57	32.66	30.56
C <sub>6</sub>	38.80	38.83	39.90	41.00
C <sub>7</sub>	22.84	22.78	23.02	23.10
C <sub>8</sub>	31.07	30.75	30.61	30.46
C <sub>9</sub>	22.05	21.93	22.16	22.23
C <sub>10</sub>	16.48	16.82	16.74	16.23

<sup>a</sup> Chemical shifts.  $\delta$ , in ppm relative to TMS.

<sup>b</sup> In CDCl<sub>3</sub>.

<sup>c</sup> In CDCl<sub>3</sub>, another sign: -1.67 (Me).

<sup>d</sup> In C<sub>6</sub>D<sub>6</sub>.

dissolved in n-decane. At temperature between 90 and 150 °C, the reaction can be represented by the following equation:

The products obtained correspond to bimetallic systems with organic groups anchored to the surface. R represents the remaining organic fragments (hydride, methyl, (-)-menthyl) bonded to Ge, and S the support (SiO<sub>2</sub>). The amount of fixed Ge was determined by gas chromatography and corresponds to the “y” value, expressed by the atomic ratio between Ge and Pt ( $y = \text{Ge}/\text{Pt} = 0.8$ ). So far, it has not been possible to determine in detail the quantity and characteristics of organic groups anchored to the surface. However, the results reported in the present work and others previously published for organotin compounds, have demonstrated that these systems induce enantioselectivity in the hydrogenation of some prochiral carbonyl compounds [17,22]. Therefore, we conclude that at least some (-)-menthyl groups are anchored to the surface. In a previous work, we demonstrated that the Ge–C bond is more stable than the Sn–C bond. Thus, the loss of (-)-menthyl groups in organogermanium systems, during the surface reaction, is more difficult than in organotin catalysts [14].

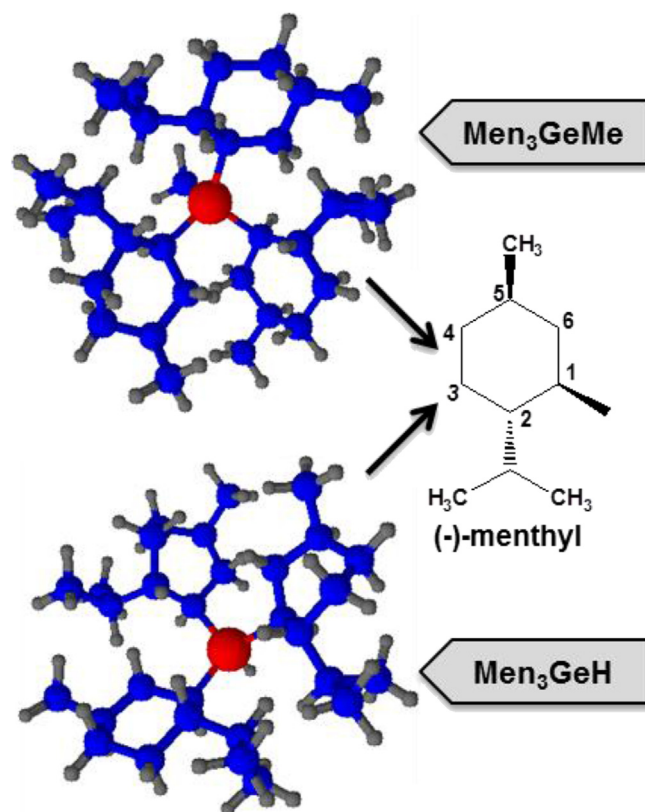
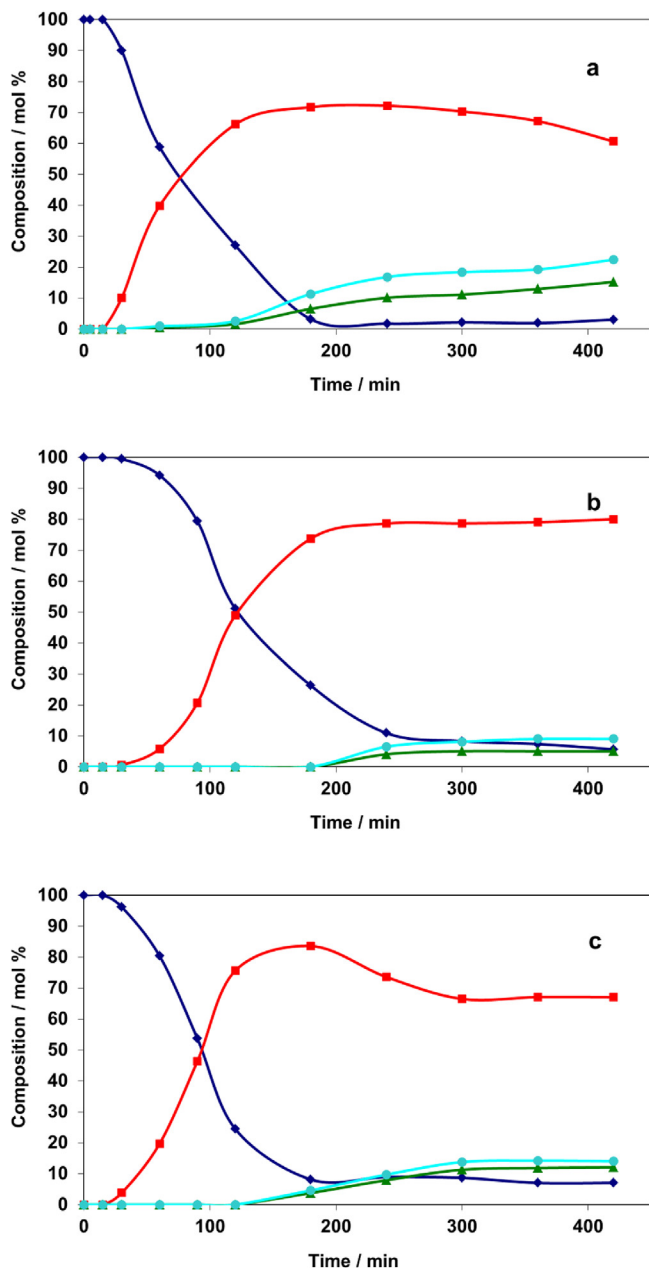


Figure 3. Structure of (-)-menthylgermanium derivatives. (●) H; (●) C; (●) Ge. Pt/S + y GeR<sub>4</sub> + xy/2H<sub>2</sub> → Pt(GeR<sub>4-x</sub>)<sub>y</sub>/S + xy RH.

### 3.3. Hydrogenation of de 3,4-hexanedione

Figure 4 shows the composition of the reaction mixture versus time for the three systems studied: Pt (a), Pt-Men<sub>3</sub>GeMe (b), and Pt-Men<sub>3</sub>GeH (c). In the first step, 4-hydroxy-3-hexanone was produced. Subsequently, by hydrogenation of the hydroxy ketone, the corresponding diols were obtained. The figure shows that all three systems were active in the reaction, reaching approximately 95% of conversion after 200 min of reaction. Therefore, as there was no decrease in the activity, we concluded that the presence of Ge on the Pt surface did not cause a significant blocking effect.



**Figure 4.** Concentration profiles (mol%) along the reaction. (♦) 3,4-hexanedione, (■) 4-hydroxy-3-hexanone, (▲) 3,4-hexanediol, (●) meso-3,4-hexanediol. Pt (a); Pt-Me<sub>3</sub>GeMe (b) and Pt-Me<sub>3</sub>GeH (c).

In Figure 4 we can see an induction time that is commonly observed in this kind of reactions. The origin of the induction period it is not known with certainty. A possible explanation is the competitive adsorption between substrate molecules and hydrogen. Because of the catalyst is reduced in H<sub>2</sub> flow before reaction, it is possible that the surface could be covered by ad-atoms of hydrogen. When substrate molecules are introduced into the reaction medium they can gradually occupy active sites over Pt surface observing an increment in the conversion [23].

The selectivity to products at two conversions is reported in Table 2. As shown in the table, all of systems were highly selective. For PtGe catalysts, only the hydroxy ketone was produced about 150 min of reaction time (75% of conversion). Thus, these catalysts are very efficient from the chemoselectivity point of view.

**Table 2**  
Selectivity to products at two conversions.

	Conv.%	Catalyst		
		Pt	Pt-Me <sub>3</sub> GeMe	Pt-Me <sub>3</sub> GeH
S <sub>I</sub> % <sup>a</sup>	X = 75	92	100	100
	X = 95	71	83	71
S <sub>II</sub> % <sup>a</sup>	X = 75	3	–	–
	X = 95	12	7	13
S <sub>III</sub> % <sup>a</sup>	X = 75	5	–	–
	X = 95	17	10	16
ee <sub>I</sub> % <sup>b</sup>	X = 75	–	16	23
	X = 95	–	18	25
ee <sub>II</sub> % <sup>b</sup>	X = 75	–	–	–
	X = 95	–	10	10

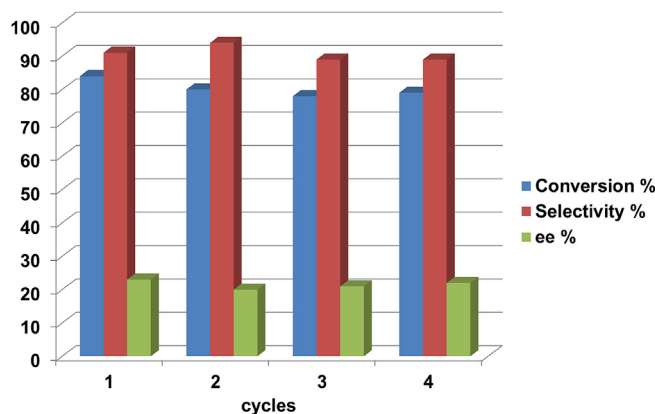
<sup>a</sup> I = (4S)- y (4R)-hydroxy-3-hexanone; II = (3S,4S)- y (3R,4R)-hexanediol; III = meso hexanediol.

<sup>b</sup> ee% = 100(S - R)/(S + R).

Table 2 also lists the enantiomeric excess obtained in the hydrogenation of 3,4-hexanedione with the chiral catalysts. The enantiomeric excess has not significantly varied during the reaction. These results are in agreement with those reported by others authors for enantioselective hydrogenation of diketones with classic systems Pt/cinchonidine [24]. These results are very interesting since they are comparable to those obtained in previous work with similar PtSn systems [13]. It is very important to mark that the PtGe catalysts proposed in this report have interesting advantages over their PtSn analogous systems. On one hand, epimerization of C1 was not observed during the synthesis of organogermanium compounds. Thus, the synthesis by direct alkylation allowed us to obtain more easily the enantiopure compounds. On the other hand, organogermanium compounds derived from (–)-menthyl are more stable and less toxic than the corresponding organotin. An additional advantage of PtGe systems is that the enantiomeric excess reached for diols is twice compared to that obtained with PtSn catalysts [13].

We consider that enantiodifferentiating capacity of the catalysts prepared in this work is interesting. As mentioned before, the classic systems Pt/cinchona alkaloids are effective for hydrogenation of  $\alpha$ -ketoesters. The enantiomeric excess achieved for diketones is much lower [5,7,24]. Particularly, the enantiomeric excesses obtained for the 3,4-hexanedione hydrogenation with Pt/cinchonidine catalysts were between 17 and 22% depending on the reaction conditions [5,25].

It is well known that the main advantage of heterogeneous catalysts is their easy recovery and reuse. For example, we reused



**Figure 5.** Conversion, selectivity and enantioselectivity to 4-hydroxy-3-hexanone, at 150 min of reaction, in four subsequent cycles on Pt-Me<sub>3</sub>GeH catalyst.

PtMen<sub>3</sub>GeH in four consecutive hydrogenation cycles. In each of them, the catalyst was washed and reused. In Figure 5 are shown the conversion and selectivity to 4-hydroxy-3-hexanone at about 150 min of reaction. As can be seen, during the four cycles the catalyst maintained its activity, chemoselectivity and enantioselectivity (80% of conversion, 90% of selectivity and more than 20% of ee). Similar results have been obtained by our group with analogous PtSn catalysts [17]. Then, these systems are reusable without adding new amounts of chiral modifier and without pretreatment. This is an important advantage respect to classic systems Pt/cinchonidine.

This is a very important result since the possibility of catalyst reusing and its effect on the catalytic activity and selectivity after a large number of reaction cycles are a main issue in heterogeneous hydrogenation reactions. In matters of asymmetric hydrogenations, only a few authors have reported reuse test results of chiral catalysts, but only using the so-called “classic” systems, i.e., a supported metal modified with a chiral compound (typically cinchonidine). It is well known that cinchonidine can be hydrogenated on Pt catalysts under mild reaction conditions, affording products with certain degree of molecule saturation that are more soluble in the reaction medium and so less efficient as a chiral modifier. Vorlop *et al.* found that the Pt-alumina catalyst can be suitably reused for 10 cycles in the hydrogenation of ethyl pyruvate (EP), keeping total substrate conversion and enantioselectivity almost constant, without the addition of chiral modifier in each reaction [26]. This is achieved by stopping each reaction at 70% conversion and then starting the next one. Bartók *et al.* studied the reuse of chiral Pt-alumina catalysts (Engelhard E4759) modified with dihydrocinchonine in EP hydrogenation, at 1 bar hydrogen pressure and reaction temperatures between –20 and 25 °C. They found that the catalyst activity and enantiomeric excess always decreased with the number of reuses [27].

#### 4. Conclusions

The main conclusions of the present work are summarized below:

- Organogermanium compounds derived from (–)-menthyl were obtained. These compounds were synthesized with retention of configuration of the chiral inductor. The reaction was carried out without epimerization of C1, demonstrating that the direct alkylation of GeCl<sub>4</sub> takes place enantioselectively. This result is very interesting and shows a fundamental advantage with respect to the synthesis of analogous organotin compounds.
- The organogermanium compounds presented in this work have advantages over their analogous organotin compounds, mainly due to their higher stability and nontoxicity.
- New heterogeneous organobimetallic catalysts were prepared by controlled surface reaction between the chiral organogermanium compound and the monometallic catalyst. The catalysts preparation method allowed obtaining stable and reproducible systems. These characteristics are very important for potential applications.
- The systems obtained were effective in the liquid-phase hydrogenation of 3,4-hexanedione. All of them presented similar activity. PtGe catalysts were 100% chemoselective to 4-hydroxy-3-hexanedione at 75% of conversion.
- Pt-Men<sub>3</sub>GeMe and Pt-Men<sub>3</sub>GeH catalysts were enantioselective. They allowed to reach approximately 20% and 25% of

enantiomeric excess to 4-hydroxy-3-hexanone, respectively. This enantiomeric excess was comparable to that previously obtained with similar PtSn catalysts and to the one reported in literature for classic Pt/cinchonidine systems. The enantiomeric excess achieved for 3,4-hexanediol was 10%; this value is two times the enantiomeric excess obtained with similar organotin systems.

- The Pt-Men<sub>3</sub>GeH catalyst was stable during four consecutive hydrogenation cycles, keeping its activity, chemoselectivity and enantioselectivity. Thereby, it is a real heterogeneous catalyst since it can be reused without further addition of chiral inducer and without any treatment.
- These systems are potentially versatile; we could obtain enantioselective catalysts for different families of compounds through the adequate design of chiral modifier structure.

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