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Heterogeneous hydrogenation of substituted phenols over Al_2O_3 supported ruthenium

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Abstract

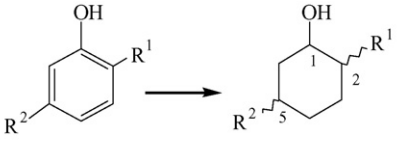
It is shown that catalytic heterogeneous hydrogenation over Ru/Al_2O_3 of mono- and di-substituted phenols (**1**–**4**) works and provides mixtures of the two or four possible isomers. Although *cis* and all-*cis* isomers (corresponding to all-*syn* H_2 additions) are less stable, they are always *major*. It is also observed that large alkyl substituents and carbomethoxy groups have a tendency to increase the diastereoselectivity and that formation of larger amounts of the *trans* isomers is related to the presence of an OH group thus supporting intermediate formation of the corresponding ketone as already suggested.

Keywords: Ruthenium hydrogenation; Hydrogenation of monosubstituted phenols; Hydrogenation of disubstituted phenols

1. Introduction

Stereoselective preparation of poly-substituted cyclic compounds by hydrogenation of the corresponding substituted aromatic compounds using heterogeneous catalysts is a short and challenging route which received growing attention in recent years [1,2] but was devoted to substituted indanes [3,4], toluic ester [5], chiral derivatives of toluic acid [6,7] and aniline [8,9].

We present here a preliminary study of Ruthenium heterogeneous hydrogenation of substituted phenols **1**–**4** to obtain cyclohexanols **5**–**8**. For the sake of comparison *meta*-cresol **9** and *ortho*-toluic methyl ester **10** have also been studied.



1: R^1=Me, R^2=H
2: R^1=CO_2Me, R^2=H
3: R^1= R^2=Me
4: R^1=i-Pr, R^2=Me
5: R^1=Me, R^2=H
6: R^1=CO_2Me, R^2=H
7: R^1= R^2=Me
8: R^1=i-Pr, R^2=Me

for **5** and **6** 1,2-cis
1,2-trans

for **7** and **8** $\mathbf{I}_{ccc}$: 1,2-cis-1,5-cis-2,5-cis
$\mathbf{II}_{ctt}$: 1,2-cis-1,5-trans-2,5-trans
$\mathbf{III}_{tct}$: 1,2-trans-1,5-cis-2,5-trans
$\mathbf{IV}_{ttc}$: 1,2-trans-1,5-trans-2,5-cis

2. Experimental

2.1. General procedure for hydrogenation

A solution of the desired phenol (0.8 mmol, 1 equiv.) in 5 mL of solvent with 0.03 equiv. of the catalyst (Ru/Al_2O_3-9001 from Engelhard) was stirred for the desired time in an autoclave under 20 bar of H_2 (at 40 °C). The autoclave was equipped with a glass-socket and remaining air has been rapidly eliminated through two successive manipulations: vacuum-H_2 admission. The mixture was then filtrated to eliminate the catalyst which was rinsed with solvent and recovered. The joined organic phases were then evaporated under vacuum and the crude products were analyzed by NMR prior to purification. All the compounds

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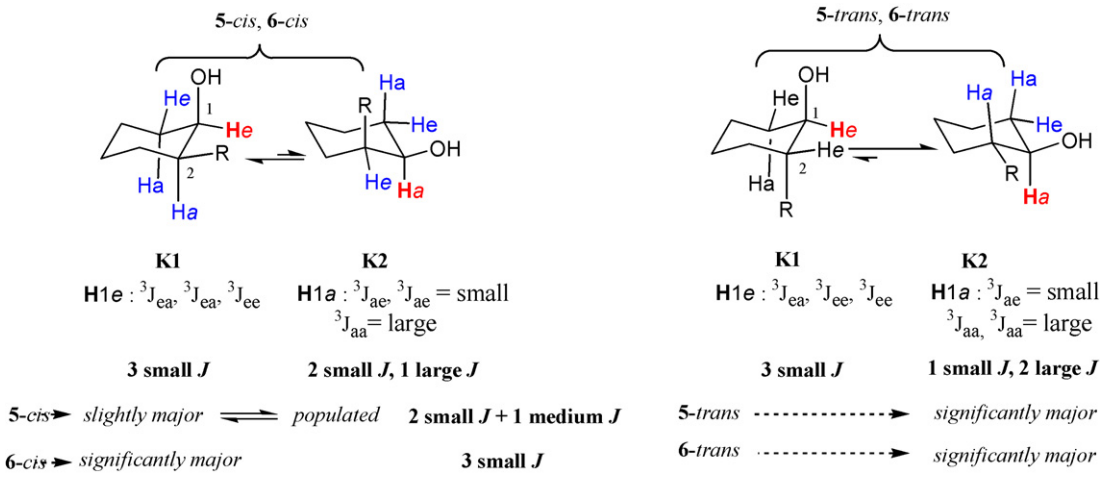


Scheme 1.

were known compounds which had analysis within accepted errors.

Al_2O_3 supported ruthenium-5% (Ru/Al_2O_3-9001 from Engelhard) was provided to us by Engelhard Italiana SpA. Solvents and aromatic compounds 99% pure have been purchassed from Aldrich and used without further purification but after having checked their purity by ^1H NMR (300 MHz). All reactions were performed on 0.8 mmol of starting aromatic compound in 5 mL of solvent.

2.2. Calculations

Ring inversions have been modelized and the geometry of the molecules were completely optimized with the Hartree–Fock approximation. The basis set used was 6-31G* for all calculations [10]. All the calculations were done by using the Gaussian 98 program package [11]. The stationary points were characterized by frequency calculations in order to determine that all minimum have zero imaginary frequency. The scale factor 0.91 was used for calculation of the zero-point vibrational energies [12].

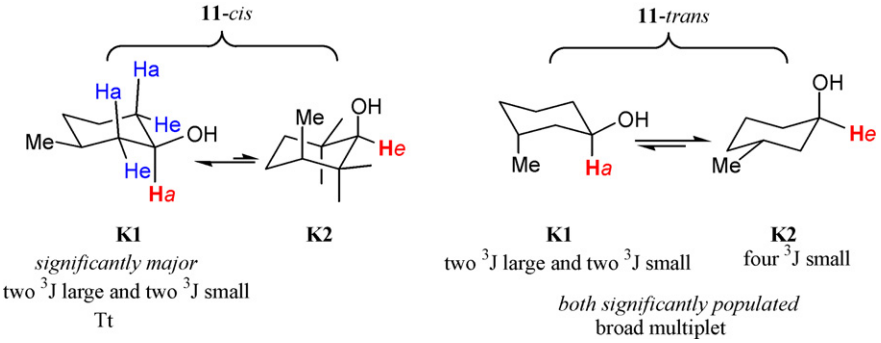
2.3. NMR and structure determination

^1H (300 MHz) NMR spectra were recorded on a Bruker AC 300 spectrometer with $CDCl_3$ as solvent. Chemical shifts (δ) are given in ppm downfield from TMS as an internal standard.

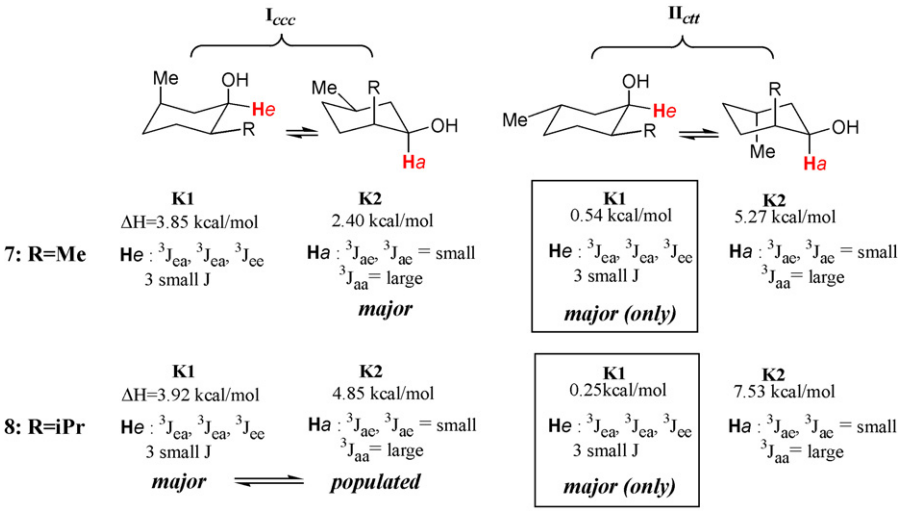
Assignment of all the possible diastereomers for each products has been done using the pattern (multiplicity) of the most isolated H-signal (usualy H1), a very basic and unexpensive NMR method. This method allows simultaneous determination of the three-dimentional structure and of the ratio between the isomers. Ring inversion equilibrium (see Schemes 1–4) have been taken into account as the values observed for the ^3J coupling constants are the weighted average of the values of each conformers. However, exact calculation of the coupling constants values is not necessary, number of different values and relative intensities are enough. It must be noted that in the case of exchanging systems and according to the rates of exchange the lines could be broadened and the mutiplicity badly resolved (indicated as broad or b in the tables).

In the cases of disubstituted cyclohexanols (**5**, **6**, **11** and **12**), using the known ΔG° values ('conformational energies or *A* values) [13] for OH (approximately −0.6 kcal/mol), Me (−1.74 kcal/mol) and CO_2Me (−1.25 kcal/mol), one can roughly predict which conformer over the two possible will be significantly *major* or if the populations will be similar (Schemes 1 and 2).

In the cases of trisubstituted cyclohexanols **7** and **8** ab initio simulations/optimizations of ring inversion at the HF/6-31G* level have been performed on the four possible diastereomers. In each case a conformational study (optimization/minimization) around the C–OH bond and around the C–*i*Pr bond has been done to determine the most stable conformation around these



Scheme 2.



Scheme 3.

bonds. The ΔH values obtained are given in Schemes 3 and 4 and in Table 2.

It must be noted that some isomers of the cyclohexanol **8** (menthol and iso-menthol), being commercial compounds and well known in our group, they provided a way to check the mehod.

In the *cis* isomer of compound **5** (Scheme 1) conformer **K1** is expected to be only slightly *major* and **K2** to be reasonably populated (providing an equilibrium between **K1** and **K2**) while in the *trans* isomer conformer **K2** is significantly *major* and **K1** negligible.

In the case of compound **6** (Scheme 1) conformer **K1** in **6**-*cis* and conformer **K2** in **6**-*trans* are stabilized by a mixing entropy due to the presence of two populated conformers of the ester group [14] making these conformers significantly *major*.

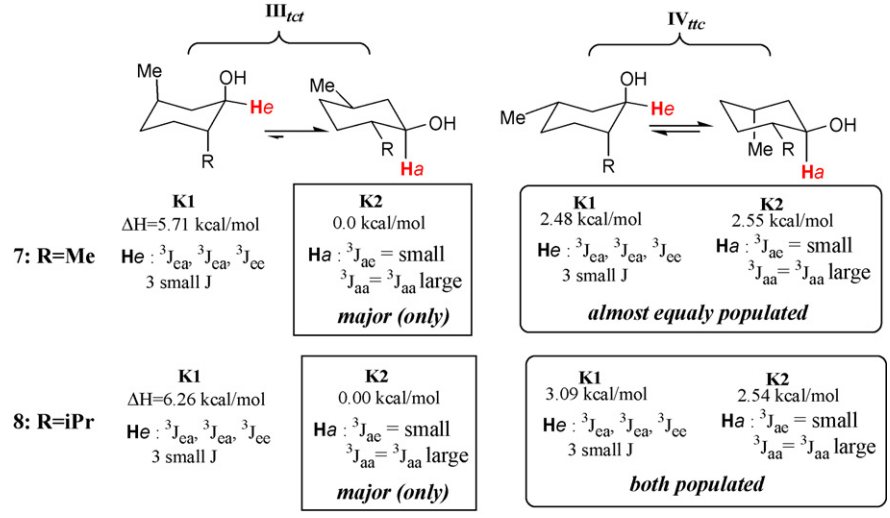
Therefore one can expect that (Table 1):

- **5**-*cis*: Proton H1 (at C1) will appear as a double-triplet with two small coupling constants ($^3J_{HH gauche} \sim 4$ Hz) and one

Table 1
Observed ^{1}H NMR data in $CDCl_3$ (δ, coupling constants, patterns) and predicted patterns of H1 at C1 for the two possible diastereomers of compounds **5**, **6**, **11** and **12**

	5-*cis*	**5**-*trans*	**6**-*cis*	**6**-*trans*
Predicted pattern[a]	dt-broad	Td	q	Td
Observed δ (ppm)[b]	4.07	3.57	4.06	3.63
Pattern[a]	dt, b[c]	Td	q	Td
^3J (Hz)	7, 4, 4	11.5; 11.5; 4	3; 3; 3	10; 10; 5
	11-*cis*	**11**-*trans*	**12**-*cis*	**12**-*trans*
Predicted pattern[a]	Tt	tt-broad	Dt	Td
Observed δ (ppm)[b]	3.50	4.08	2.5	Not observed
Pattern[a]	Tt	broad multiplet	Dt	–
^3J (Hz)	11.5; 11.5; 4; 4	–	9.5; 4; 4	–

[a] Capital letters correspond to a large coupling constants of about 10 Hz and small letters correspond to smaller coupling constants (1–8 Hz).
[b] ^{1}H NMR in $CDCl_3$ referred to TMS.
[c] b: Broad and badly resolved.



Scheme 4.

medium (averaged between $^3J_{aa}$ and $^3J_{ee}$; >4 and <11 Hz). Moreover, the presence of an exchange may provide a broad and badly resolved signal.

- **5**-*trans*: Proton H1 being mostly axial will appear as a double-triplet with two large coupling constants of ∼11 Hz (two $^3J_{HHtrans}$) and a small of ∼4 Hz (one $^3J_{HHgauche}$).
- **6**-*cis*: Proton H1 being mostly equatorial will appear as a quadruplet with three small coupling constants ($^3J_{HHgauche}$ ∼ 4 Hz).
- **6**-*trans*: Proton H1 being mostly axial will appear as a double-triplet with two large coupling constants of ∼11 Hz (two $^3J_{HHtrans}$) and a small of ∼4 Hz (one $^3J_{HHgauche}$).

This is indeed observed (Table 1):

- The NMR spectrum of product **5** exhibits for H1 a double-triplet with ^3J = 11.5, 11.5 and 4 Hz at 3.57 ppm unambiguously assigned to **5**-*trans* and a broad multiplet (with ^3J ∼ 4, 4 and 7 Hz) at 4.07 ppm (assigned to **5**-*cis*).
- Likewise, the NMR spectrum of product **6** exhibits for H1 a double-triplet with ^3J = 10, 10 and 5 Hz at 3.63 ppm unambiguously assigned to **6**-*trans* and a narrow quadruplet with ^3J ∼ 3, 3 and 3 Hz at 4.06 ppm (assigned to **6**-*cis*).

In the case of compounds **5**-*cis* and **5**-*trans*, the ratios have also been determined/checked using the methyl signals (doublet) which are clearly separated (**5**-*cis*: Me = 0.95 ppm (*major*); **5**-*trans*: Me = 1.01 ppm).

In the case of compounds **6**-*cis* and **6**-*trans* the proton H2 at C2 can also be used for assignment of the *cis* and *trans* relationship and for determining the ratio: in **6**-*cis* H2 is a double-triplet with ^3J = ∼3, ∼3 and 9 Hz at 2.4 ppm and in **6**-*trans* H2 is a double-double-doublet with ^3J = 12, 10 and 4 Hz at 2.15 ppm.

Similarly proton H1 in compound **12** (Table 1), which is now on the carbon having a carboxyl group, is less deshielded but is still in an empty zone of the spectrum and the same method applies (use Scheme 1 with OH=Me and R=CO_2Me): one expect that **12**-*cis* (**K1** only populated) will be a double-triplet (one large ^3J and two small ^3J) and **12**-*trans* (**K2** only populated) will be a triple-doublet (two large ^3J and one small ^3J). A double-triplet with ^3J = 9.5, 4 and 4 Hz is indeed observed at 2.5 ppm fitting with the expected pattern for **12**-*cis* while the *trans* isomer (**12**-*trans*) is not observed.

For the *meta*-substituted cyclohexanol **11** (Scheme 2 and Table 1) four vicinal coupling constants will determine the multiplicities. Isomer **11**-*cis* (conformer **K1** only populated) will exhibit for proton H1 a triple-triplet with two large coupling constant (two $^3J_{trans}$) and two small coupling constant (two $^3J_{gauche}$) while isomer **11**-*trans* (equilibrium between **K1** and **K2**) will exhibit a broad not well resolved multiplet with two averaged and two small coupling constants.

And this is indeed observed. The NMR spectrum of compound **11** exhibits for H1 a triple-triplet at 3.57 ppm (with two large coupling constants, twice ^3J = 11.5 Hz, and two small coupling constants, twice ^3J = 4 Hz) which is easily assigned to **11**-*cis*; and a broad and badly resolved multiplet at 4.07 ppm assigned to **11**-*trans*.

Table 2
Observed ^{1}H NMR data in $CDCl_3$ (δ, coupling constants, patterns) and predicted patterns of H1 at C1 for the four possible diastereomers of compounds **7** and **8**

	$\mathbf{I}_{ccc}$	$\mathbf{II}_{ctt}$	$\mathbf{III}_{tct}$	$\mathbf{IV}_{ttc}$
7 (R=Me)				
Δ*H* (kcal/mol)[a]	2.40 (**K2**)	0.54 (**K1**)	0.0 (**K2**)	2.48 (**K1**)
Predicted pattern[b]	Dt	q	DDd	td-broad
δ (ppm)[c]	3.7	3.75	3.1	3.46
Pattern[b]	Dt	q	DDd	td, b[d]
^3J (Hz)	12; 4.5; 4.5	3;3;3	11; 10.5; 4.5	7.5; 7.5; 4
8 (R=iPr)				
Δ*H* (kcal/mol)	3.92 (**K1**)	0.25 (**K1**)	0.0 (**K2**)	2.54 (**K2**)
Predicted pattern[b]	dt-broad	q	Td	td-broad
δ (ppm)[c]	4.0	4.1	3.4	3.8
Pattern[b]	dt, b[d]	q	Td	td, b[d]
^3J (Hz)	6.5; 3.5; 3.5	2.5; 2.5; 2.5	10; 10; 4	8; 8; 4

[a] Only the most stable conformer is given (**K1** or **K2**).
[b] Capital letters correspond to a large coupling constants of about 10 Hz and small letters correspond to smaller coupling constants (1–8 Hz).
[c] ^{1}H NMR in $CDCl_3$ referred to TMS.
[d] b: Broad lines/signal.

The Δ*H* values found for the most stable conformers during ring inversions of all the four diastereomers of compounds **7** and **8**, are gathered on Schemes 3 and 4 and in Table 2.

It is observed that the order of stability of the most stable conformer (ring conformation, **K1** or **K2**) is: $\mathbf{III}_{tct}$ (**K2**) < $\mathbf{II}_{ctt}$ (**K1**) < $\mathbf{I}_{ccc}$ (**K2**) ∼ $\mathbf{IV}_{ttc}$ (**K1**) in compound **7** (R=Me) and: $\mathbf{III}_{tct}$ (**K2**) < $\mathbf{II}_{ctt}$ (**K1**) < $\mathbf{IV}_{ttc}$ (**K2**) < $\mathbf{I}_{ccc}$ (**K1**) in compound **8** (R=*iso*Pr)

It is interesting to note that all-*cis* isomers ($\mathbf{I}_{ccc}$) which are always *major* are not the most stable, but third for **7** ($\mathbf{I}_{ccc}$, **K2**) or even last for **8** ($\mathbf{I}_{ccc}$, **K1** on the lists. Isomers *trans–cis–trans* ($\mathbf{III}_{tct}$) are the most stable in both case under the same ring-conformation **K2** (the three substituents being equatorial).

From examination of the Δ*H* values obtained for **K1** and **K2** it appeared for compound 7 that:

- In diastereomer $\mathbf{I}_{ccc}$ (all-*cis*) conformer **K2** is expected to be significantly *major* (ΔΔ*H* = 1.45 kcal/mol) and therefore proton H1 being mainly axial will exhibit a double-triplet (Dt) with one large coupling constant ($^3J_{trans}$) and two small ($^3J_{gauche}$).
- In diastereomer $\mathbf{II}_{ctt}$ (*cis–trans–trans*) conformer **K1** is almost exclusively populated (ΔΔ*H* = 4.73 kcal/mol) and therefore proton H1 being mainly equatorial will exhibit a quadruplet (*q*) with three small coupling constants ($^3J_{gauche}$).
- In diastereomer $\mathbf{III}_{tct}$ (*trans–cis–trans*) conformer **K2** is exclusively populated (ΔΔ*H* = 5.71 kcal/mol) and therefore proton H1 being mainly axial will exhibit a double-triplet (Td) with two large coupling constants ($^3J_{trans}$) and one small ($^3J_{gauche}$).
- In diastereomer $\mathbf{IV}_{ttc}$ (*trans–trans–cis*) conformers **K1** and **K2** are almost equally populated (ΔΔ*H* = 0.07 kcal/mol) and are exchanging making the two large coupling constants smaller than expected while the small remains small, therefore, proton H1 will exhibit a broad (and badly resolved)

double-triplet (td) with two medium coupling constants and one small.

which is observed (cf. Table 2).

From examination of the ΔH values obtained for **K1** and **K2** it appeared for compound 8 that:

- In diastereomer $\mathbf{I}_{ccc}$ (all-*cis*, racemic neoisomenthol) conformer **K1** is expected to be *major* ($\Delta\Delta H = 0.93$ kcal/mol) but **K2** is populated and **K1** and **K2** exchange, therefore proton H1 will exhibit a broad (and badly resolved) double-triplet (dt) with two small coupling constants ($^3J_{gauche}$) and one medium (average value between $^3J_{gauche}$ and $^3J_{trans}$).
- In diastereomer $\mathbf{II}_{ctt}$ (*cis–trans–trans*, racemic neomenthol) conformer **K1** is exclusively populated ($\Delta\Delta H = 7.28$ kcal/mol) and therefore proton H1 being mainly equatorial will exhibit a quadruplet (q) with three small coupling constants ($^3J_{gauche}$).
- In diastereomer $\mathbf{III}_{tct}$ (*trans–cis–trans*, racemic menthol) conformer **K2** is exclusively populated ($\Delta\Delta H = 6.26$ kcal/mol) and therefore proton H1 being mainly axial will exhibit a double-triplet (Td) with two large coupling constants ($^3J_{trans}$) and one small ($^3J_{gauche}$), a well known signal in natural menthol.
- in diastereomer $\mathbf{IV}_{ttc}$ (*trans–trans–cis*, racemic isomenthol) conformers **K1** and **K2** are almost equally populated ($\Delta\Delta H = 0.55$ kcal/mol) and are exchanging making the two large coupling constants smaller than expected while the small remains small therefore proton H1 will exhibit a broad (and badly resolved) double-triplet (td) with two medium size coupling constant and one small.

which is observed (cf. Table 2).

3. Results and discussion

3.1. Hydrogenation of disubstituted phenyls *1*, *2*, *9* and *10*, Scheme 5

Ru/Al_2O_3 heterogeneous hydrogenation of *o*-cresol **1** in EtOH as solvent shows that 70 bar H_2 pressure is not necessary and that 20 bar with a substrate/catalyst ratio of 30 provides full conversion in 1 h reaction time (Table 3, entries 1–4).

When less catalyst is used ($n_S/n_C = 100$, Table 1, entries 7, 8) a longer reaction time is necessary of course (14 h), however, it is worth noting that, whatever the pressure, the reaction time or the yield, the *cis-trans* ratio does not change much (62/38–60/40) and that the *cis* isomer is always *major*.

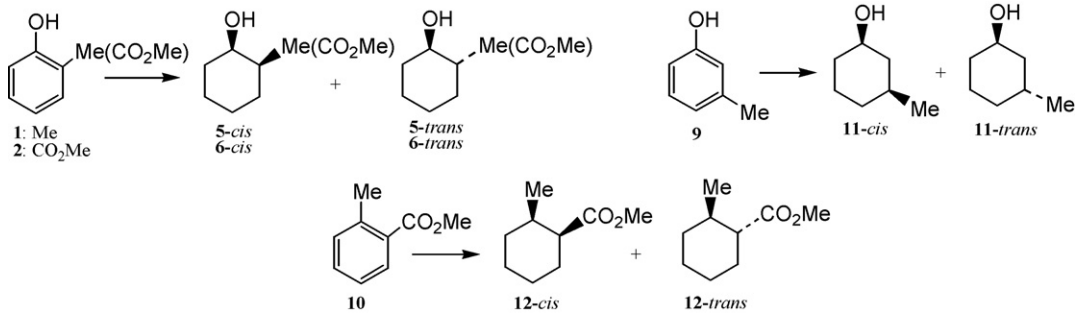
Table 3
Hydrogenation over Ru/Al_2O_3 of *o*-cresol **1** at 40 °C in EtOH as solvent

Entry	Pressure (bar)	Time (h)	n_S/n_C	Convers (%)	**5**-*cis*/**5**-*trans*
1	70	4	30	100	62/38
2	70	1	30	100	62/38
3	35	1	30	100	61/39
4	20	1	30	100	61/39
5	20	0.5	30	95	60/40
6	20	0.25	30	55	60/40
7	20	1	100	60	60/40
8	20	14	100	100	62/38
9	10	1	30	80	61/39

Using the pressure, temperature and amount of catalyst determined for *o*-cresol **1** in EtOH (20 bar, 40 °C and $n_S/n_C = 30$), other substrates and other solvents (non-polar, polar-protic and polar-aprotic) have been tested, Table 4. Solubility and therefore concentration in substrate are the main problem together with *trans*-esterification of ester functions in alcoholic solvent. No clear-cut effect is observed but it is worth noting that *o*-toluic ester **10**, although soluble in hexane, reacted but slowly in this solvent (Table 4, line 10) and that, in consistency with Lemaire co-workers results [5], hydrogenation of *o*-toluic ester **10** does not proceed in MeOH (Table 4, line 12).

In all the solvents the *cis* diastereomers are still *major*, in consistency with the well accepted *syn* addition of hydrogen to carbon=carbon double bonds [15,16] which was first proposed by Vavon in 1926 [17]. However, the *trans* isomers are always present in consistency with literature results where many examples of *trans* additions can be found (hydrogenation of 1,2-cyclohexene [18], racemization and deuterium exchange of (+)-3-methylhexane [19]) and for which various explanations have been proposed such as: dissociative adsorption [20], rollover mechanism [16], 1,3-hydrogen shift over the top side of an adsorbed double bond [21] or top side addition of hydrogen [22].

Although no ketone have been detected/isolated in these cases, larger percentages of *trans* isomers (19–45%) are obtained when an OH group is present on the substrate (Table 4, compare entries 1–9 with 10–11) which support the hypothesis that a ketone [23–25] can be formed as intermediate.



Scheme 5.

Table 4
Hydrogenation over Ru/Al_2O_3 of *o*-cresol **1**, *o*-carbomethoxy phenol **2**, *m*-cresol **9** and *o*-toluic ester **10** (at 20 bar, 40 °C, $n_S/n_C = 30$) in various solvents

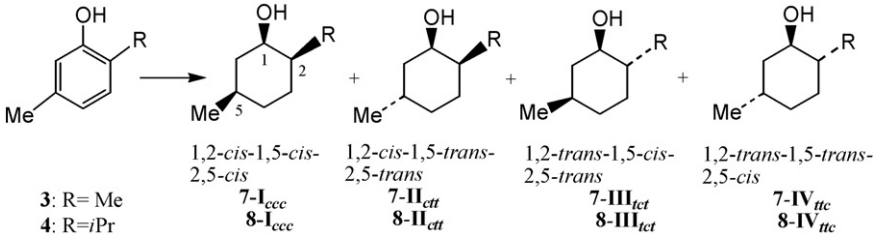
Entry	Start substance	Solvent	Reaction time (h)	Conversion (%)	Product: *cis*/*trans*
1	*o*-Cresol **1**	Hexane	1	100	**5**: 59/41
2	*o*-Cresol **1**	EtOH	1	100	**5**: 62/38
3	*o*-Cresol **1**	MeOH	1	60	**5**: 65/35
4	*o*-Cresol **1**	THF	1	30	**5**: 55/45
5	*m*-Cresol **9**	EtOH	1	100	**11**: 57/43
6	*o*-Carbomethoxy phenol **2**	Hexane		Not soluble	
7	*o*-Carbomethoxy phenol **2**	MeOH[a]	3	100	**6**: 81/19
8	*o*-Carbomethoxy phenol **2**	THF	3	60	**6**: 84/16
9	*o*-Carbomethoxy phenol **2**	THF	o.n.[b]	100	**6**: 80/20
10	*o*-Toluic ester **10**	Hexane	3	10	**12**: 100/0[c]
11	*o*-Toluic ester **10**	THF	3	100	**12**: 100/0
12	*o*-Toluic ester **10**	MeOH	o.n.[b]	0	

[a] EtOH lead to partial formation of ethyl ester and is not a suitable solvent for methyl esters.
[b] o.n.: Over night.
[c] 20% Conversion was obtained when the reaction was maintained over night, and only the *cis* isomer was detected.

Table 5
Hydrogenation over Ru/Al_2O_3 of **3** and **4** (at 20 bar, 40 °C, $n_S/n_C = 30$) in hexane and EtOH

R	Solvent	React. time	Conv. (%)	$\mathbf{I}_{ccc}/\mathbf{II}_{ctt}/\mathbf{III}_{tct}/\mathbf{IV}_{ttc}$[a]	1,2-*cis*/1,2-*trans*	1,5-*cis*/1,5-*trans*	2,5-*cis*/2,5-*trans*	all-*cis*
3 Me	Hexane	o.n.[b]	100	60/6/6/28	66/34	66/34	88/12	60
3 Me	EtOH	3 h	100	64/6/6/24	70/30	70/30	88/12	64
4 i-Pr	Hexane	o.n.[b]	100	48/5/3/44	53/47	51/49	92/8	48
4 i-Pr	EtOH	3 h	100	79/5/6/10	84/16	85/15	89/11	79

[a] ccc: 1,2-*cis*-1,5-*cis*-2,5-*cis*; ctt: 1,2-*cis*-1,5-*trans*-2,5-*trans*; tct: 1,2-*trans*-1,5-*cis*-2,5-*trans*; ttc: 1,2-*trans*-1,5-*trans*-2,5-*cis*.
[b] o.n.: Over night.



Scheme 6.

One also observes that, roughly, replacement of a methyl group with a carbomethoxy group (compound **1** versus compound **2**) led to higher diastereoselectivity (compare Table 4, entries 1–4 with 6–9) likewise replacement of an OH with a methyl (compound **2** versus compound **10**, Table 4, compare entries 6–9 with 10–11) and that *m*-substitution provides lower diastereoselectivity (Table 4, entries 2 and 5) than *o*-substitution.

3.2. *Hydrogenation of trisubstituted phenyls, **3** and **4**, Scheme 6*

EtOH (Table 5), is the best solvent with quantitative conversion in 3 h in both cases and higher diastereoselectivity (Table 5, compare entries 1 and 3 with 2 and 4).

A rapid overlook of Table 5 shows that the all-*cis* isomer ($\mathbf{I}_{ccc}$) of compounds **7** and **8** is always *major* although less in hexane than in EtOH. All-*cis* isomer corresponds to all-*syn* H_2 addition from the metal surface to the side of the molecule facing the surface as expected from literature results and proposed mechanisms (cf. above). Isomers $\mathbf{II}_{ctt}$ (5–6%), $\mathbf{III}_{tct}$ (3–6%) and $\mathbf{VI}_{ttc}$ (10–44%) are observed but are *minor*, also in consistency with literature proposed mechanisms.

4. Conclusion

It is shown that catalytic heterogeneous hydrogenation over Ru/Al_2O_3 of mono- and di-substituted phenols (**1**, **2**, **3** and **4**) works smoothly and provides mixtures of all the possible isomers apart *o*-toluic ester **10** which provides only the *cis* isomer [23].

Moreover, although they are less stable than the other isomers (cf. Schemes 1–4 and Table 3), the *cis* isomers (compounds **5**, **6**) and all-*cis* isomers (compounds **7**, **8**) are always *major* which supports the proposed litterature mechanism of a *syn* hydrogen addition from the metal surface to the side of the molecule facing the surface [13–15].

It is also observed that large alkyl substituents and carbomethoxy groups have a tendency to increase the diastereoselectivity.

No cyclohexanones have been isolated nor detected during hydrogenations of substituted phenols **1**-**4** over Ru/Al_2O_3 contrary to what was observed during hydrogenation of cresols over rhodium catalyst by Takagi et al. [24,25] and of thymol either over supported Pt by Besson et al. [23] or over $Ni–Cr_2O_3$ by Allakhverdiev et al. [26]. But observation of larger amount of *trans* isomers obtained in the cases of phenols supports transitory formation of the corresponding keto group.

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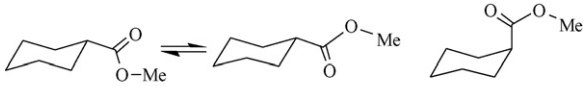

equatorial ester axial ester

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