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Hydrogenation of alkyl-substituted phenols over nickel and palladium catalysts

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Abstract

The hydrogenation of alkyl-substituted phenols in the liquid phase was studied using supported nickel and palladium catalysts (<0.02 mm) in stirred reactor. The distribution of hydrogenation products in the final mixture depends not only on the catalyst used, but also on the reactant structure. The palladium catalyst shows higher selectivity with respect to alkylcyclohexanone formation. Also, the number of alkyl-substituents on the aromatic ring and the steric hindrance of hydroxyl group increases the selectivity of alkylcyclohexanone formation. Products of the hydrogenolytic cleavage were observed during hydrogenations on a nickel catalyst.

With the help of molecular modelling (PM3 method) the global energy minima of alkylcyclohexanol isomers were determined. The findings were confirmed by GC–MS, high-energy collision induced decomposition (CID method) and by NMR spectroscopy.

Keywords: Hydrogenation of alkyl-substituted phenols; Palladium; Nickel; Structure effects; Molecular modelling

1. Introduction

Alkyl-substituted phenols represent a valuable source for production of alkyl-substituted cyclohexanones and cyclohexanols. Mixtures of the isomers of alkylcyclohexanols characterised by their odours, and their esters are valuable in the chemistry of fine chemicals and perfume industry. The *trans*-isomers produced alongside *cis*-isomers are not usually of an industrial interest. The hydrogenation of alkyl-substituted phenols is closely connected with a stereoselectivity.

The problem of stereoselectivity has been encountered for many years. The hydrogenation rate and selectivity of alkyl-substituted phenols depend on many factors [1] (nature of the catalyst, substrate structure, solvent, reaction conditions and additives [2]). Two types of the selectivity can be defined in the system of parallel-consecutive reactions: the selectivity of alkylcyclohexanone formation and the selectivity with respect to the ratio of *cis*/*trans*-alkylcyclohexanol isomers. Generally the hydrogenation is carried out on catalysts based on platinum metals and nickel. The highest selectivity of alkylcyclohexanones is shown by palladium catalysts [3–5]. Usually a nickel catalyst is used, but products of hydrogenolytic cleavage can be observed in the reaction mixture [6].

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The main objective of the work was to elucidate influence of the catalyst's active component on the selectivity of alkyl-substituted cyclohexanone formation and on the selectivity of *cis*-alkyl-substituted cyclohexanols formation. Attention is also paid to the influence of bulkiness, location and number of alkyl-substituents on the aromatic ring. For better elucidation of results acquired from hydrogenation of di- and tri-substituted phenols, molecular modelling was successfully used. This approach allowed description of alkylcyclohexanols on molecular level.

2. Experimental

2.1. Chemicals

The reactants were supplied by Schenectady Pratteln^{AG}, USA: their purity was >99%. As a solvent cyclohexane p.a. was used (Penta Chrudim, Czech Republic). Hydrogen Linde-Technoplyn, Prague, was used.

2.2. Catalysts

The commercial catalyst Ni/Al_2O_3 (Contact no. 6524) from Kata-Leuna AG, Germany, was used, the total content of Ni was 50%.

The second catalyst was Johnson-Matthey 5% Pd/Al_2O_3. The grain size of the catalysts was <0.02 mm.

2.3. Measurements and apparatus

All measurements were performed in 400 ml stainless steel autoclave. The hydrogen pressure was maintained between 0.7–0.8 MPa. The reaction was conducted at 453 K for the experiments using nickel catalyst and 393 K using palladium catalyst. All the experiments were carried out in the kinetic region. In a typical run, 0.01 mol of a substrate was used and amount of Ni/Al_2O_3 or Pd/Al_2O_3 was 10% of the substrate weight. The volume of the solvent was 130 ml. A fresh portion of a catalyst was taken for each experiment. During the course of a reaction, samples were taken for GC and GC–MS analyses.

2.4. Analysis

Samples, withdrawn at chosen time intervals, were analysed using a gas chromatograph Hewlett–Packard 5890 SERIES II PLUS with a flame-ionisation detector (FID) and chromatographic integration workstation Datamonitor II (Apex). For the analyses capillary column BETADEX 325 (length 30 m, internal diameter 0.25 mm, thickness of the stationary phase 0.25 μm) was used, a temperature program ranging between 373 and 469 K. The overpressure of the carrier gas (N_2) was 150 kPa and the split ratio 1:50.

Compounds in the reaction mixture were determined using the gas chromatograph Varian GC 3800 with mass detector (MS-Ion Trap) Varian Saturn 2000.

The analyses of samples were performed using the column CP-Sil 8 CB lowbleed/(CP index 8), length 30 m, internal diameter 0.25 mm and with the thickness of the stationary phase 0.25 μm. As a carrier gas helium was used. An amount of 0.2 μl of sample was primed to the chromatography column.

2.5. Molecular modelling

Geometry optimisations [7] were carried out using CERIUS^2 (MSI Ltd., USA) Version 3.5 (MSI, USA) on SGI workstation using conjugated gradients minimisation. Calculation were carried out by Dreiding force field. To find the geometry of alkyl-substituted cyclohexanols with minimum of total energy we changed torsional angles between substituents and cyclohexane ring (step size 10°). Conformational search were carried out using grid search method. The van der Waals terms were treated as exponential −6. Switching functions were applied to the model to turn-off van der Waals and Coulombic interactions (spline-on distance 10 Å; spline-off distance 15 Å, force constant 4.18 MJ/mol/Å).

2.6. NMR analysis

NMR measurements were performed using 400 MHz Varian Unity Inova. The measurement was carried out in $CDCl_3$ as a solvent at 303 K. For determination of alkyl cyclohexanol isomers conformation were used experiments as 1H NMR, 13C NMR, APT, DEPT, COSY, TOCSY, J resolved, HMQC,

HMBC, 1D NOE, 1D TOCSY, 1D TOCSY-TOCSY, 1D TOCSY-NOESY.

3. Results and discussion

Alkyl-substituted phenols can be selectively hydrogenated to corresponding cyclohexanols ($S_{cis} = (cis/cis + trans)100$) using many metal catalysts. The reaction can also be conducted to cyclohexanones, which are sometimes preferable products. The highest selectivity of alkylcyclohexanone formation ($S_{\text{ketone}} = (\text{ketone}/\text{ketone} + \text{alcohol})100$) was afforded by palladium catalysts [8,9]. The enol form of this intermediate (alkylcyclohex-1-en-1-ol), is hydrogenated to the *cis*-isomer [10]. It participates apparently in an increase of this isomer in the final mixture. The final product of the alkyl-substituted phenol hydrogenation is a mixture of *cis*- and *trans*-alkylcyclohexanols. The general scheme of hydrogenation is displayed on Fig. 1.

The experiments confirm the consecutive path of alkyl-substituted phenols' hydrogenation. The problem of factors affecting the ratio of *cis*- and *trans*-isomers has been solved for many years [10] as has the effect [11,12] of structure and reaction conditions on the course of hydrogenation and composition of the final mixture.

The measured time dependencies of concentrations of hydrogenated reactants were used to determine values of reaction rates. These were evaluated from the linear region of the dependence $c = f(t)$. Total conversion of the starting mixture of alkyl-substituted phenols was achieved in all the studied systems under the reaction conditions. The reactions were of zero order with respect to the reactant concentration up to high conversions (>95%). Products of the hydrogenolytic cleavage, alkyl-substituted benzenes and cyclohexanes were observed during hydrogenations carried out on the nickel catalyst, and were identified in the reaction mixture in various quantities. Those products of hydrogenolytic cleavage. In samples from the hydrogenation of di-substituted alkylphenols, mono-substituted phenols were detected in the reaction mixture.

Table 1 shows values of hydrogenation rates on nickel and palladium catalysts. It implies that the alkylphenol hydrogenation rate decreased with the increasing bulkiness of the alkyl-substituent and with the increasing steric hindrance of hydroxyl group and the number of alkyl-substituents located on the aromatic ring. The palladium catalyst is more active

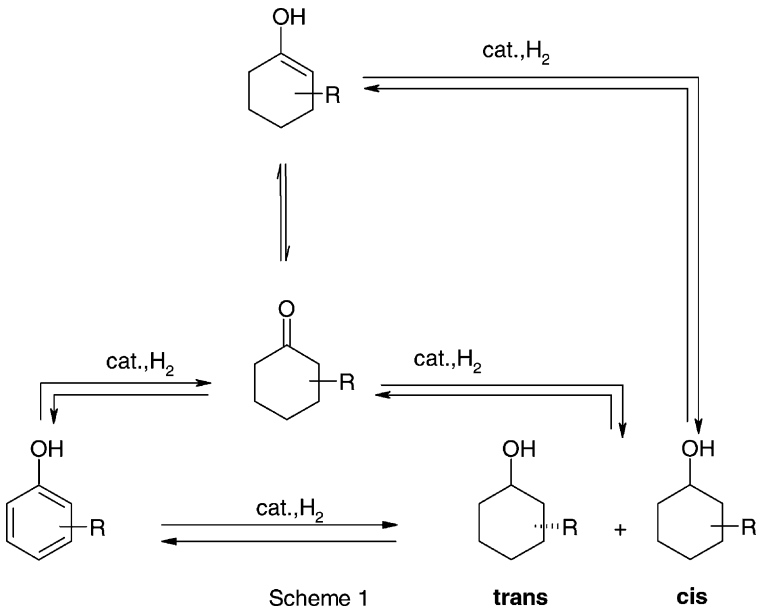


Fig. 1. Reaction scheme of alkylphenol hydrogenation (R stands for alkyl-subtituent).

Table 1
Hydrogenation rates

Substrate	Hydrogenation rates, r (mmol/h per $g_{catalyst}$)	
	Ni/Al_2O_3 (453 K)	Pd/Al_2O_3 (393 K)
2-Methylphenol	45.2	41.2
2-*tert*-Butylphenol	29.3	73.5
2-*tert*-Amylphenol	30.4	67.9
4-Methylphenol	38.8	36.2
4-*tert*-Butylphenol	24.1	75.8
4-*tert*-Amylphenol	29.1	50.6
2,4-Di-*tert*-butylphenol	20.7	38.2
2,4-Di-*tert*-amylphenol	7.4	11.3
2,6-Di-*tert*-butylphenol	6.2	26.8
2,4,6-Tri-*tert*-butylphenol	1.4	36.9
2-*tert*-Butyl-4-methylphenol	15.9	40.7
4-*tert*-Butyl-2-methylphenol	16.6	12.7
4,6-Di-*tert*-butyl-2-methylphenol	13.1	16.7

for hydrogenations of alkylphenols as it is shown in Table 1.

Hindrance of the hydroxyl group also enlarges the selectivity of the alkyl-substituted cyclohexanone formation (as shown in Table 2). During the hydrogenation of 2,4,6-tri-*tert*-butylphenol, the hindrance of the carbonyl group was so strong that the final mixture contained 2,4,6-tri-*tert*-butylcyclohexanone, which was not further hydrogenated. Similar results were found for other substrates with strongly hindered carbonyl groups. On the other hand, if were hydrogenated substrates with only a small alkyl group on nickel catalyst (e.g. 2-methylphenol, 4-methylphenol and others), low concentrations of alkylcyclohexanones were found in the reaction mixture.

Data acquired from the experiments on the palladium catalyst show a significant increase in alkylcyclohexanones' selectivity. The alkylphenols were converted on palladium catalyst to ketones and then hydrogenated to the final mixture of alkylcyclohexanols, if possible. The mono-substituted substrates with smaller alkyl-substituents located on the aromatic ring were hydrogenated to the final mixtures of *cis*- and *trans*-alkylcyclohexanols isomers on both the catalysts.

It was found that the content of alkylcyclohexanol in the reaction mixture is much lower with respect to its content acquired on nickel catalyst. During the hydrogenations on nickel catalyst, products

Table 2
Selectivity of alkylcyclohexanones formation

Substrate	Maximal selectivity, S_{ketone} [a]	
	Ni/Al_2O_3	Pd/Al_2O_3
2-Methylphenol	$6.0^{10.0}$	$99.6^{8.0}$
2-*tert*-Butylphenol	$93.0^{50.0}$	$99.3^{57.6}$
2-*tert*-Amylphenol	$80.2^{53.0}$	$99.0^{98.5}$
4-Methylphenol	$25.0^{20.0}$	$90.0^{11.0}$
4-*tert*-Butylphenol	$19.9^{20.0}$	$100.0^{23.3}$
4-*tert*-Amylphenol	$37.0^{5.0}$	$94.1^{25.7}$
2,4-Di-*tert*-butylphenol	$66.2^{22.0}$	$89.4^{15.0}$
2,4-Di-*tert*-amylphenol	$53.7^{18.0}$	$88.0^{7.0}$
2,6-Di-*tert*-butylphenol	$69.1^{99.0}$	$71.7^{100.0}$
2,4,6-Tri-*tert*-butylphenol	$99.0^{100.0}$	$100.0^{100.0}$
4,6-Di-*tert*-butyl-2-methylphenol	$90.0^{32.3}$	$100.0^{7.3}$

[a] Conversion of alkylphenol at the maximal content of alkylcyclohexanone.

of hydrogenolytic cleavage were detected, alkyl-substituted benzenes and cyclohexanes.

In Table 3 are shown the selectivities with respect to the ratio of *cis*/*trans*-isomers for mono-substituted alkylcyclohexanols.

The global energy minima of alkylcyclohexanols isomers were computed with the use of molecular modelling. The semi-empirical method PM3 [13,14] was applied. That way the most stable isomers of alkylcyclohexanols were probably determined. These global minima were determined by scanning of the conformation space. These computed data were compared with results from the GC–MS. The CID method was used for determination of the most stable isomer. The isomer with the highest energy C–O bond cleavage was marked as the most stable isomer of an appro-

Table 3
Selectivity of alkylcyclohexanols formation on the nickel catalyst at total conversion of alkylphenols

Substrate	S_{cis}
2-Methylphenol	66.9
2-*tert*-Butylphenol	81.9
2-*tert*-Amylphenol	70.7
4-Methylphenol	59.3
4-*tert*-Butylphenol	32.4
4-*tert*-Amylphenol	32.5
2,4-Di-*tert*-butylphenol	58.6
2,4-Di-*tert*-amylphenol	53.7
2,6-Di-*tert*-butylphenol	95.8
2,4,6-Tri-*tert*-butylphenol	–

Table 4
Molecular modeling data for 4-*tert*-butyl-2-methylcyclohexanol

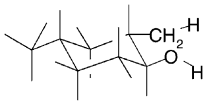
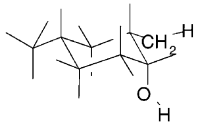
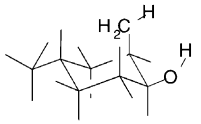
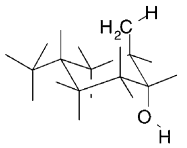
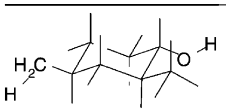
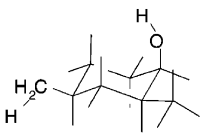
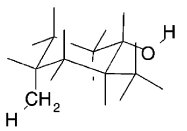
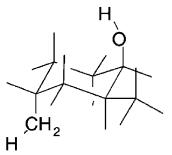
Diastereomer		Orientation of substituent	Torsion	Value of torsion (°)	Length of bond (Å)		Energy (kJ/mol)
					C–O	C–CH_3	
	A1	OH *e* CH_3 *e* *t*Bu *e*	H–O–C1–C2 CH_3–C4–C3 *t*Bu–C2–C1	179.4 −55.6 −57.7	1.426	1.558	62.0
	A2	OH *a* CH_3 *e* *t*Bu *e*	H–O–C1–C2 CH_3–C4–C3 *t*Bu–C2–C1	−60.7 −58.0 −58.3	1.426	1.557	67.4
	A3	OH *e* CH_3 *a* *t*Bu *e*	H–O–C1–C2 CH_3–C4–C3 *t*Bu–C2–C1	63.2 61.6 −58.79	1.423	1.561	78.0
	A4	OH *a* CH_3 *a* *t*Bu *e*	H–O–C1–C2 CH_3–C4–C3 *t*Bu–C2–C1	−179.4 58.3 −58.8	1.429	1.561	72.5

Table 5
Molecular modeling data for 2-*tert*-butyl-4-methylcyclohexanol

Diastereomer		Orientation of substituent	Torsion	Value of torsion (°)	Length of bond (Å)		Energy (kJ/mol)
					C–O	C–CH_3	
	B1	OH *e* CH_3 *e* *t*Bu *e*	H–O–C1–C2 CH_3–C4–C3 *t*Bu–C2–C1	−179.1 −59.1 −56.5	1.427	1.553	34.5
	B2	OH *a* CH_3 *e* *t*Bu *e*	H–O–C1–C2 CH_3–C4–C3 *t*Bu–C2–C1	−64.1 −58.9 −48.4	1.425	1.553	44.7
	B3	OH *e* CH_3 *a* *t*Bu *e*	H–O–C1–C2 CH_3–C4–C3 *t*Bu–C2–C1	−179.1 57.9 −56.4	1.427	1.555	45.4
	B4	OH *a* CH_3 *a* *t*Bu *e*	H–O–C1–C2 CH_3–C4–C3 *t*Bu–C2–C1	−64.3 55.6 −48.4	1.425	1.556	56.6

priate alkylcyclohexanol. The real structure (relative configuration) of the isomers was confirmed by NMR spectroscopy. It was found that the most stable isomer of alkylcyclohexanol (isomer with as many equatorial substituents as possible) is contained in the final mixture in the highest content. The content of the isomer with alkyl-substituents orientated to the equatorial positions is for 4-*tert*-butyl-2-methylcyclohexanol 61% and for 2-*tert*-butyl-4-methylcyclohexanol 46%. The hydrogenation led to the most thermodynamically stable products.

Molecular modelling data for 4-*tert*-butyl-2-methylcyclohexanol and 2-*tert*-butylcyclohexanol are assigned in the Tables 4 and 5. From values of global energies noted in Tables 4 and 5 show that the most stable cyclohexanols isomers are configurations, where the maximum number of alkyl-substituents are orientated to the equatorial positions. It is further evident that bulky *tert*-butyl groups are orientated always to the equatorial positions. This is in harmony with conformation energy and with the effective size of a given alkyl-substituent.

4. Conclusions

Alkyl-substituted phenols hydrogenated on nickel based catalyst acquire mainly mixture of *cis*- and *trans*-isomers of an appropriate alkylcyclohexanols, while palladium catalyst is selective for the alkylcyclohexanones formation. The most stable relative configurations of the isomers were successfully defined and distinguished by molecular modelling and with the help of GC–MS and NMR spectroscopy.

Among important factors which have also an influence on the course of hydrogenation is the structure of the compound, viz. the bulkiness of the alkyl-substituent and its position on the aromatic ring of phenol. The increase of the steric hindrance of the hydroxyl group increases the selectivity with respect to alkylcylohexanone formation on the both catalysts. The selectivity of alkylcyclohexanone formation grows with increasing alkyl-substituent located in the position 2 on the aromatic ring and also with a number of alkyl-substituents. In the systems with low hindered substrates, the ketone stage is usually passed over, or low selectivity of alkylcyclohexanone formation is observed.

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