Preparation of Fragrant Allyl Esters

Preparing methyl-cyclohexyloxyacetate, allyl-cyclohexyloxyacetate, methyl-cyclohexylpropionate and allyl-cyclohexylpropionate

Ivana Luštická, Eliška Leitmannová and Libor Červený, Institute of Chemical Technology, Prague, Czech Republic

This article explains the process of preparing methyl-cyclohexyloxyacetate, allyl-cyclohexyloxyacetate, methyl-cyclohexylpropionate and allyl-cyclohexylpropionate—the fragrant odoriferous substances used in the food and perfumery industry.

The objective of these experiments was to find suitable reaction conditions (catalyst, temperature, pressure, and catalyst amount) for the hydrogenation of methyl-phenoxyacetate to methyl-cyclohexyloxyacetate and consequently, apply the discovered conditions to the hydrogenation of methyl-cinnamate to methyl-cyclohexylpropionate (**see F-1**). Further aim was to find a suitable basic or acidic catalyst for the transesterification of the methyl esters acquired by hydrogenation to the relevant allyl esters.

Methyl-cyclohexyloxyacetate is described with a fresh, fruity, herbal to lactone odor.[1] Methyl-cyclohexylpropionate is characterized with a fresh, fruity-green odor, whereas the fragrance of allyl-cyclohexyloxyacetate is perceived to be fruity and pineapplelike.[1,2] Allyl-cyclohexylpropionate is a substance whose aroma can be expressed as sweet, pineapple.[2,3]

Alkyl-cyclohexyloxyacetates can be prepared by hydrolysis of (cyclohexyloxy) acetonitrils using ethanol and chlorine water.[4] Another procedure, described in particular for the production of ethyl-cyclohexyloxyacetate, is the reaction of cyclohexanol with acetic acid diazoethylester.[5] However, as the procedures described above resulted in low yields, the catalytic hydrogenation of alkyl-phenoxyacetates is currently the most common preparation procedure of alkyl-cyclohexyloxyacetates.[1] According to the contemporary scientific knowledge, the most suitable catalysts for hydrogenation of aromatic alkyl-phenoxyacetates are especially metals of VIII.A group and others, such as Rh, Ir, Pd or Pt.[1]

The most common procedure for preparation of methyl-cyclohexylpropionates is the catalytic hydrogenation of methyl-cinnamate, in which suitable catalysts are metals of VIII.A group as in the previous case.[2,3]

Allyl-cyclohexyloxyacetate and allyl-cyclohexylpropionate can be prepared by different procedures.[3] But the most common is transesterification of relevant methyl esters by allyl alcohol (**see F-2**). Transesterification reactions are very important transformations used in both laboratories and industrial processes.[6,7] Transesterifications can proceed in acidic as well as basic environments, as both acids and bases are catalysts suitable to accelerate these reactions.[6,8,9,*]

Experiments

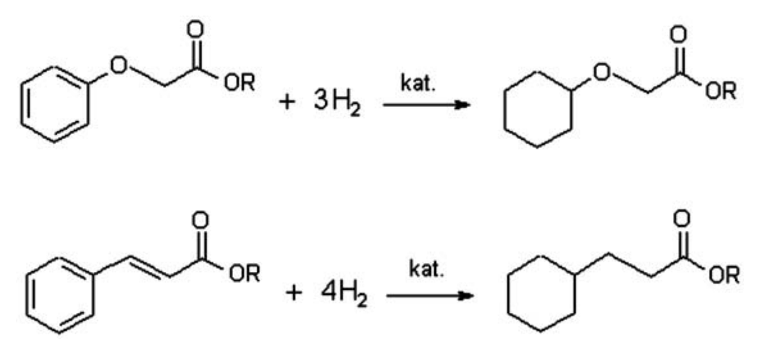
➤ *Hydrogenation of methyl-phenoxyacetate and methyl-cinnamate*

Experiments were carried out in a stainless steel autoclave with a volume capacity of 400 mL. The starting substances for hydrogenation were methyl-phenoxyacetate and methyl-cinnamate, and the catalysts used were: Ni/Al$_2$O$_3$-KL6528-T5 (KataLeuna) (A), Ni/Al$_2$O$_3$-KL6504N-P (KataLeuna) (B), Pt / C (IOT), and Pd / C (Doduco). Methanol (Penta) and decalin (IOT) were used as the solvents. Magnesium oxide (Penta) was used as a modifier. Individual experiments were executed under the temperature range of 160–200°C, pressures 8–14.5 MPa and the catalyst quantity of 1–10 wt.% to the substrate amount.

➤ *Transesterification of methyl-cyclohexyloxyacetate and methyl-cyclohexylpropionate*

Methyl-cyclohexyloxyacetate and methyl-cyclohexylpropionate, prepared by the above-described hydrogenation, and allyl alcohol (Sigma-Aldrich) were used as the starting substances. The catalysts used

F-1 Hydrogenation scheme of methyl-phenoxyacetate to methyl-cyclohexyloxyacetate, and methyl-cinnamate to methyl-cyclohexylpropionate



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*http://www.jergym.hiedu.cz/%7Ecanovm/kyseliny/zapisy/alkacet.htm were: potassium carbonate (Penta), TS-1 (UFCHJH), p-sulfobenzoic acid (SAFC), sodium hydroxide (Penta), phosphoric acid (Lachema), sulfuric acid (Penta), p-toluenesulfonic acid (Chemapol), sodium methanolate (BASF), diethylamine (SAFC), dioctylamine (IOT), propylamine (SAFC), and triethylamine (IOT). Other chemicals as toluene (Penta), cyclohexane (Penta), acetone (Lachema) and diethyl ether (Penta) were used as solvents, and magnesium sulphate (Lachema) was used as a desiccant.

➤ *Analytical Conditions*

Chromatographic analysis of products acquired from hydrogenation and transesterification was carried out on the gas chromatograph GC–Varian CP–3800, with FID 11 flame-ionization detection and 1177 injector. Further, non-polar capillary column of the type VA-MS3 was used.

Results and Evaluation

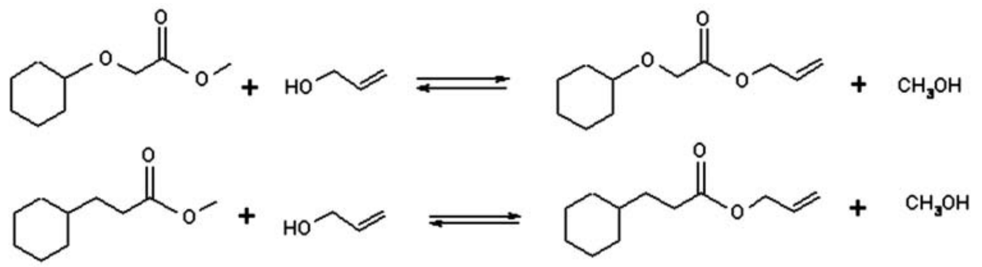
➤ *Hydrogenation of methyl-phenoxyacetate and methyl-cinnamate*

Results suggested that the reaction mixture contained more than just the desired product. It was found that the hydrogenation of methyl-phenoxyacetate hydrogenolyzed not only the starting substances, but also methyl-cyclohexyloxyacetate. This lead to the production of undesirable side-products, thus lowering the yield of the desired products. Cyclohexane, benzene, cyclohexanol, phenol, methyl acetate and methyl glycolate (**see F-3**) were found to be the most abundant representatives of these side-products.

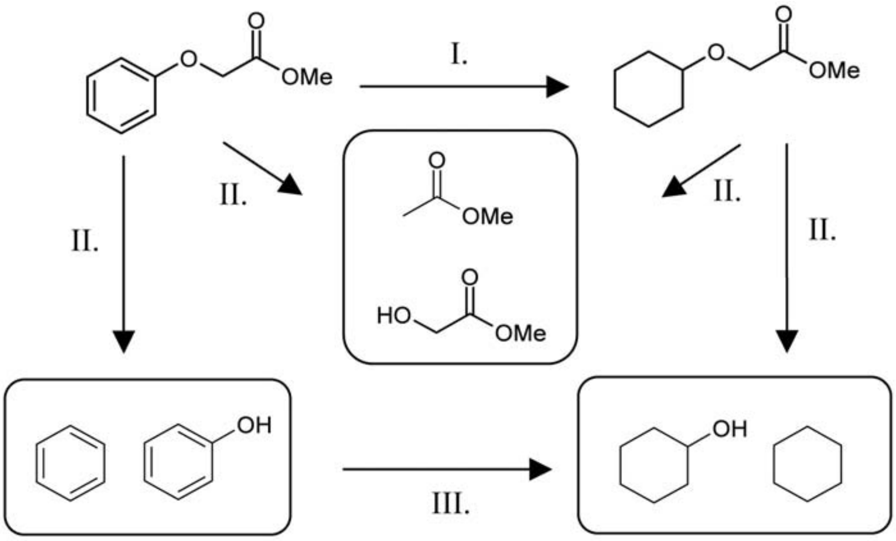
The evaluation process began with the monitoring of the catalyst effect with four different hydrogenation catalysts: 5% Pt/C, 5% Pd/C, 50% Ni/Al_2O_3 (A) and 50% Ni/Al_2O_3 (B); **F-4** depicts the course of each hydrogenation process. It was found that Pd/C and Ni/Al_2O_3 (A) were the appropriate catalysts for methyl-phenoxyacetate hydrogenation, as with their use, total conversion of methyl-phenoxyacetate was achieved at high values of selectivity. For this reason, Ni/Al_2O_3 (A) was selected as the catalyst for consecutive experiments. On the other hand, catalysts Pt/C and Ni/Al_2O_3 (B), when used together with solvents in an effort to increase the selectivity, were found to be unsuitable for this hydrogenation.

Primarily, the temperature effect (**see F-5**) was studied in the experiments that were conducted at 160°, 180° and 200°C. The temperature of 180°C was selected as optimal, since the selectivity was 84% (i.e. the highest in all the tested temperatures) in 40% of the conversion, which was reached in 30 minutes. At lower temperatures, the reaction time was excessively extended and

Transesterification scheme of methyl-cyclohexyloxyacetate to allyl-cyclohexyloxyacetate, and methyl-cyclohexylpropionate to allyl-cyclohexylpropionate **F-2**



The origin of products and by-products during the hydrogenation of methyl-phenoxyacetate **F-3**

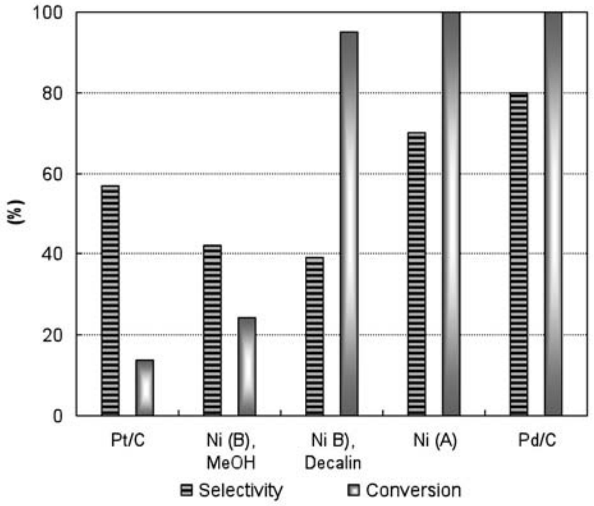


I. Hydrogenation of product and reactant

II. Hydrogenolysis of product and reactant

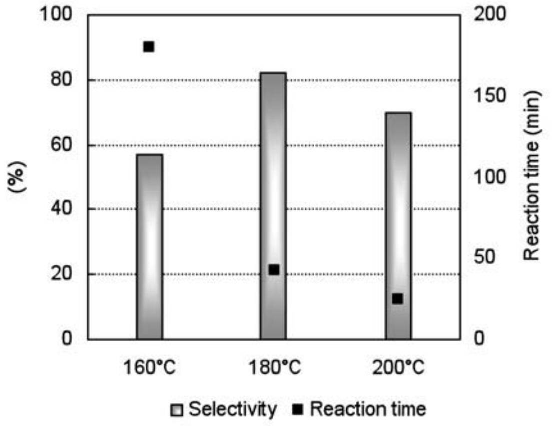
III. Hydrogenation of by-products

F-4 Dependence of selectivity and conversion on catalyst



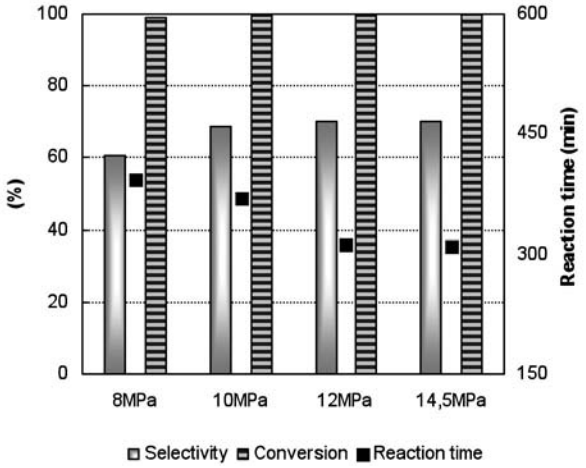
Reaction conditions:
Pt/C
Temperature: 80 °C, Pressure: 7 MPa
Ni/Al_2O_3 KL6504N-P (B)
Solvent: Decalin
Modifier: Magnesium oxide
Temperature: 180 °C, Pressure: 10 MPa
Ni/Al_2O_3 KL6504N-P (B)
Solvent: Methanol
Temperature: 100 °C, Pressure: 10 MPa
Ni/Al_2O_3 KL6528-T5 (A)
Temperature: 180 °C, Pressure: 12 MPa
Pd/C
Temperature: 180 °C, Pressure: 11 MPa

F-5 Dependence of reaction time and selectivity on temperature (°C) at identical conversion (40%)



Reaction conditions:
Catalyst quantity: 10 wt. %
Pressure: 12 MPa

F-6 Dependence of selectivity, conversion and reaction time on pressure (MPa)

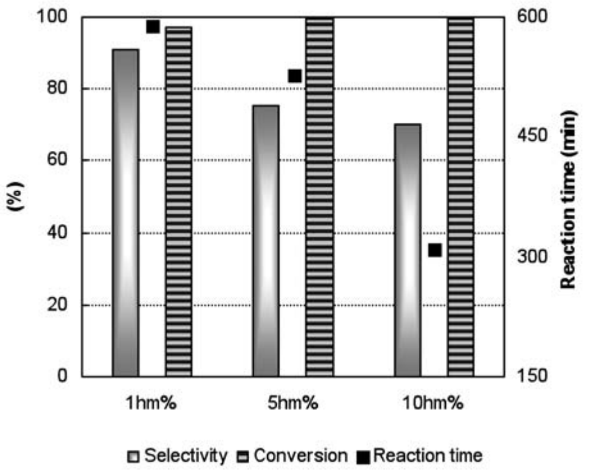


Reaction conditions:
Catalyst quantity: 10 wt. %
Temperature: 180 °C

at higher temperatures, it was not possible to maintain the highly exothermic reaction in the range of the temperature limits. This lead to overheating of the reaction mixture, and the consequent catalyst deactivation. To monitor the impact of pressure, 8, 10, 12 and 14.5 MPa were used (**see F-6**). The pressure of 12 MPa was found to be optimal, because under a higher pressure, no substantial positive effect on the selectivity was observed and the reaction rate increased only in the context of measurement errors. Under lower pressures as 8 MPa and 10 MPa, the selectivity slightly decreased and the total reaction time increased. Next, the effect of the catalyst amount was studied (**see F-7**). 10, 5 and 1 wt.% of the catalyst to the substrate amount were used, respectively, in individual experiments. Even though the reaction time was longer compared to the one using a higher catalyst amount, the optimal amount was 1 wt.%, since the production of the undesired hydrogenolytic products did not occur to the extent of higher catalyst quantities. Thus, high values of selectivity (90%) were achieved.

This was followed by the application of the optimal conditions (found for hydrogenation of methyl-phenoxyacetate) to the hydrogenation of methyl-cinnamate. In this process, hydrogen was added to a C=C double bond of a linear chain to produce methyl-phenylpropionate, followed by a saturated methyl-cyclohexylpropionate. The advantage of this reaction was a high selectivity of the overall process, without creation of hydrogenolytic products.

Dependence of selectivity, conversion and reaction time on catalyst amount to substrate amount wt.% **F-7**



Reaction conditions:
Temperature: 180 °C
Pressure: 12 MPa

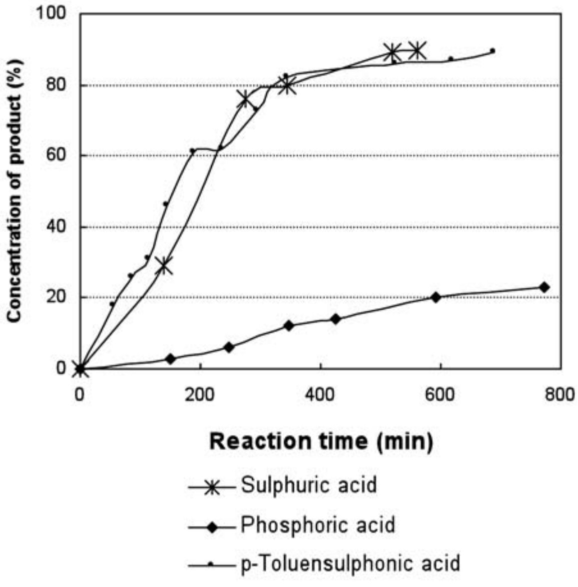
➤ ***Transesterification of methyl-cyclohexyloxyacetate and methyl-cyclohexylpropionate***

Transesterification as well as esterification is an equilibrium reaction and thus the equilibrium can be positively affected by an excess of, for instance, allyl alcohol. In order to remove even trace residues of allyl alcohol, which may cause the product's non-conformation to sensory parameters, toluene (azeotrope of toluene-allyl alcohol), was used in this case as an azeotropic agent. Both basic and acid catalysts were used for the transesterification.

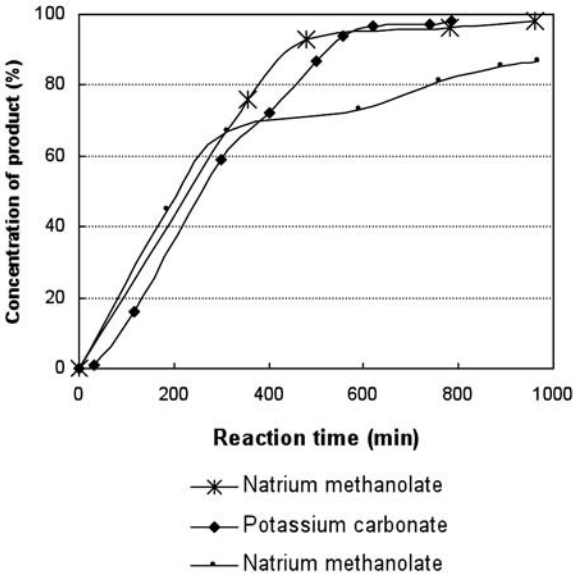
When acidic catalysts like sulfuric acid, particularly p-toluenesulfonic acid and phosphoric acid were used, total methyl-ester conversion was achieved (**see F-8**). However, polymer compounds were produced from allylic compounds. Polymeric compounds are a result of the acidic environment and thus the acidic catalysts were not found to be appropriate for the transesterification. The production of these substances had been monitored on a gas chromatograph using the method of the external standard, which was nonane. Other acidic catalysts were applied; zeolite TS-1 and p-benzosulfonic acid in particular, but these did not catalyze the transesterification.

The basic catalysts used were: potassium carbonate, sodium methanolate and sodium hydroxide (**see F-9**). Potassium carbonate and sodium methanolate were selected as suitable catalysts, which yielded total conversion of methyl ester, minimal production of the polymer compounds and achieved 72–75% selectivity. When the identical catalyst amount and sodium hydroxide solution were used, total conversion of methyl ester was not

Transesterification course in acidic environment **F-8**



Transesterification course in basic environment **F-9**



reached at the same reaction time, and other tested basic catalysts as pyridine, urea, triethylamine, diethylamine, propylamine and dioctylamine were found to be catalytically inactive during the transesterification.

Sensory Analysis

Following refining by vacuum distillation, individual products acquired from the hydrogenation and transesterification underwent sensory analysis at Aroma, a.s. and were compared to the standards. Fragrant characteristics of all prepared substances offered solid prospects for industrial application.

Conclusion

All experiments highlighted these conditions as optimum for the hydrogenation of methyl-phenoxyacetate to methyl-cyclohexyloxyacetate: a temperature of 180°C, pressure of 12 MPa and 1 wt. % of the catalyst Ni/Al_2O_3 related to the substrate amount. Under these conditions, the highest selectivity (90%) to the desired methyl-cyclohexyloxyacetate was achieved. It was observed that applying a higher catalyst amount decreased the reaction time, but it also decreased the selectivity. This had a negative effect on the yield of the desired product. Higher temperatures led to the deactivation of the catalyst, whereas higher pressures did not have any significant impact on the selectivity of the entire process. Acquired conditions were used in the hydrogenation of methyl-cinnamate.

Methyl-cyclohexyloxyacetate and methyl-cyclohexylpropionate, produced by hydrogenation, were utilized as starting substances for transesterification by allyl alcohol to produce allyl-cyclohexyloxyacetate and allyl-cyclohexylpropionate. Basic catalysts have proved to be more suitable, as in their presence, the side products derived from allylic compounds were not produced to such a high quantity as in the case of acid catalysts. Potassium carbonate and sodium methanolate were found to be the most suitable catalysts. Using both of these catalysts, 100% conversion of methyl esters and the selectivity of 95% to desired allyl esters was achieved. The yields of allyl-cyclohexyloxyacetate and allyl-cyclohexylpropionate, acquired in the experiment on a preparation scale, were 72% and 74%, respectively, calculated to the starting methyl-cyclohexyloxyacetate and methyl-cyclohexylpropionate. All products acquired by hydrogenation (methyl-cyclohexyloxyacetate, methyl-cyclohexylpropionate) and transesterification (allyl-cyclohexyloxyacetate, allyl-cyclohexylpropionate) were purified by a vacuum distillation and were sensory evaluated. The results of the complete study offered solid prospects for industrial application of the prepared substances.

Acknowledgments

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