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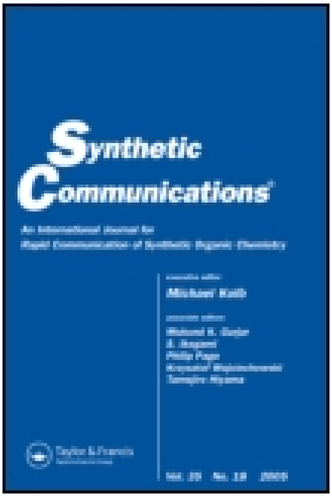

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Synergism of Microwaves and Immobilized Enzyme Catalysis in Synthesis of Adipic Acid Esters in Nonaqueous Media

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Abstract: Low-energy microwave irradiation leads to enhancement by a factor of up to 2.63 in comparison with conventional heating in immobilized lipase-catalyzed esterification of adipic acid with various alcohols and this effect is due to the greater frequency of collision, without any change in activation energy of the two modes of heating.

Keywords: Adipic acid, esterification, diester, immobilized lipase catalysis, monoester, microwave irradiation, synergism

INTRODUCTION

One of the most important classes of synthetic lubricants comprises esters of dicarboxylic acids. Monoesterification and diesterification of aliphatic dicarboxylic acids are both very important.[1] Monoesters of adipic acid are particularly used in Kolbe's synthesis[2,3] and in regioselective transformations, and also as synthons for chiral building block,[4] whereas diesters are extensively used as precursors in the synthesis of biodegradable polymers and as lubricants.[5]

Normally esters are prepared by reaction of an alcohol and a dibasic carboxylic acid in the presence of an acid catalyst. The reaction temperature for adipic acid esters is usually in the range of 100 to 180°C. Several

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homogeneous catalysts, such as sulfuric acid, hydrochloric acid, *p*-toluene sulfonic acid, and methanesulfonic acid, are still used but these are being replaced by heterogeneous catalysts such as cation-exchange resins, activated clay, zeolites, and modified heteropoly acids.[6–9] There are some reports on enzymatic synthesis of esters of adipic acid.[10,11] Mostly all above-mentioned reactions have been carried out using reactors accompanied with traditional heat-transfer equipment. Immobilized lipases have been widely used for esterification in nonaqueous media and our group has studied several industrially relevant reactions.[12–20] Microwave irradiation is being extensively applied to augment rates of chemical reactions. Hence, it was thought worthwhile to combine these two different ways of green chemistry, namely biocatalysis and microwave irradiation, in the current work.

RESULTS AND DISCUSSION

A number of alcohols were reacted with adipic acid with Novozym 435 using both microwave irradiation and conventional heating at a controlled temperature of 60°C. The microwave energy input was below 40 W. The initial rates of reaction of the alcohols with the acid were compared for both modes of operation as shown in Table 1 and Scheme 1. It was found that there was an enhancement in the initial rates of reaction in the presence of microwaves. The overall conversion was higher under microwave irradiation vis-à-vis conventional heating. This shows that the effect may not be purely thermal. Control experiments in the absence of Novozym 435 did not initiate the reaction. Furthermore, microwave irradiation without the enzyme also did not initiate the reaction. Thus, there is a synergistic effect. In the case of nonaqueous enzymology using immobilized enzymes, it is known that the enzyme particle is always surrounded by a thin aqueous layer and all pores of the support are filled with water, and hence the enzyme is not denatured. Because there are no intraparticle diffusion limitations for the reactants, which was studied independently with the most reactive substrate, microwaves affect the rate of reaction on the enzyme surface because of more collisions of the reactant molecules, without affecting the activation energy values. This has been witnessed in chemical catalysis in conjunction with microwaves.[21] Microwaves transfer energy in 10^{-9} s with each cycle of electromagnetic energy. The kinetic molecular relaxation time from this energy is approximately 10^{-5} s. This means that the energy transfers faster than the molecules can relax, which results in nonequilibrium conditions and high instantaneous temperatures that affect the kinetics of the system. Furthermore, microwaves do not influence the orientation of those collisions nor the activation energy.[22] An increase in temperature causes greater movement of molecules, which leads to a greater number of energetic collisions. This leads to enhancement in reaction rates and product yields. The quality of products is better than those obtained with conventional heating.

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Table 1. Esterification of adipic acid with different alcohols

	Microwave irradiation				Conventional heating				ϕ
Alcohol	r_o	% C	% SM	% SD	r_o	% C	% SM	% SD	Enhancement factor
n-Propanol	0.96	77.12	70	30	0.71	73.34	74	26	1.35
n-Butanol	0.98	75.64	69.39	30.61	0.62	72.35	71.56	25.04	1.58
n-Petanol	0.83	70.98	70	30	0.64	64.92	70.92	29.08	1.29
n-Hexanol	0.64	51.41	91	09	0.43	48.12	93	07	1.49
n-Octanol	0.29	27.98	100	—	0.13	21.03	100	—	2.23
n-Decanol	0.29	16.98	100	—	0.11	12.69	100	—	2.63
Iso-propanol	0.89	70.83	79.41	20.59	0.76	64.94	79.36	20.63	1.17
Iso-butanol	0.85	68.73	83.77	16.23	0.61	66.15	81.35	18.65	1.39
2-Ethylhexan-1-ol	0.58	42.85	100	—	0.54	38.59	100	—	1.07
Amyl alcohol	0.75	70.64	80.40	19.59	0.59	64.48	83.24	16.76	1.27
Benzyl alcohol	0.59	70.33	67.64	32.36	0.43	68.00	65.15	34.85	1.37
p-Chlorobenzyl alcohol	0.61	57.90	100	—	0.48	48.70	100	—	1.27
Cyclohexanol		7.5	100	—		4.5	100	—	1.66

r_o = Initial rate (mol/l-min), C = Conversion, SM = Selectivity toward monoester, SD = selectivity toward diester, ϕ = enhancement of rate.

Reaction Conditions: Adipic acid: 0.01 mol, alcohol: 0.01 mol, speed of agitation: 300 rpm, temperature: 60°C, catalysts loading: 0.0035 g/cc, catalysts: novozym 435, solvent: 1,4-dioxane up to 20 ml, reaction time: 3 h.

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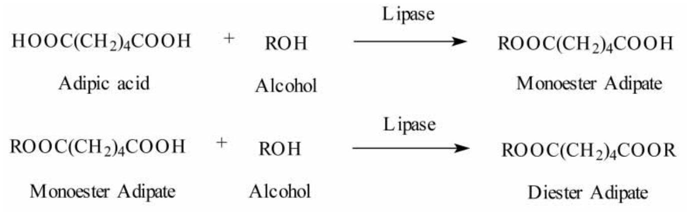

Scheme 1.

In the case of linear alcohols such as *n*-alcohols and *iso*-alcohols, it was found that as the chain length of alcohol increases for *n*-alcohols from *n*-propanol to *n*-decanol and for *iso*-alcohols from *iso*-propanol to 2-ethylhexan-1-ol, the selectivity toward monoester increases and the overall conversion in microwave is more than in conventional heating. The selectivity toward the monoester is more in conventional heating than in microwave irradiation because the consecutive reaction to the disaster formation consumes the monoester. (Table 1 and Scheme 1).

CONCLUSION

The use of low-energy microwaves in the enzyme-catalyzed synthesis of adipic acid mono and diesters in nonaqueous media was studied for the first time. There is significant enhancement in rates of reactions (enhancement factors in the range of 1.07 to 2.63) under microwave irradiation in comparison with conventional heating. The catalyst-reusability studies showed that the catalyst is reusable.

SUPPLEMENTARY DATA

Materials and Methods

Enzymes and Chemicals

The enzymes Novozym 435 (*Candida Antarctica* lipase immobilized on a macroporous polyacrylic resin with an activity 10 PLU/g) was procured as a gift sample from Novo Nordisk, Denmark.

All chemicals were procured from firms of repute and were used without any further purification: adipic acid (Merck India), 1,4- dixoane, *n*-propanol, *n*-butanol, *n*-pentanol, *n*-hexanol, *n*-octanol, *n*-decanol, *iso*-butnaol, amyl alcohol, *iso*-propanol, benzyl alcohol, 2-ethyl hexan-1-ol, *p*-chloro benzyl alcohol, cyclohexanol (all from s.d. Fine Chemicals Pvt. Ltd, Mumbai). All chemicals were AR grade.

Experimental Setup

Conventional Heating

The experimental setup consisted of a 3 cm i.d. fully baffled mechanically agitated glass reactor of 50 cm^3 capacity, which was equipped with four baffles and a six-bladed pitched-turbine impeller. The entire reactor assembly was immersed in a thermostatic water bath maintained at the desired temperature with an accuracy of $\pm 1°\mathrm{C}$.

In a typical experiment, the reaction mixture consisted of 0.01 mol of adipic acid and 0.01 mol alcohol, diluted to 20 ml with 1, 4-dioxane as a solvent. The reaction mixture was agitated at 60°C for 15 min at a speed of 300 rpm and a known quantity of immobilized enzyme was then added to initiate the reaction typically ($0.0035\ \mathrm{g/cm}^3$). Clean samples were withdrawn periodically and analyzed by HPLC.

Microwave Reactor

The experimental setup consisted of the "Discover" system (CEM Corporation, USA). This system consists of a circular single-mode cavity design which directs the microwave energy into a defined area, resulting in a homogenous field pattern surrounding the sample. The Discover System incorporates temperature and pressure feedback systems for complete control on reaction conditions. The same reaction conditions as used for experiments with conventional heating were used.

Analysis

The concentration of the reactants and products were determined on HPLC equipped with a UV detector using the following conditions:

Column = Merck 50938 column with a stationary phase of Lichrosphere 100 RP-8 particle size 5 μm, prepacked on a 125 × 4 mm ID. **Mobile phase** = Acetonitrile: Water (60:40 by vol.) **Flow rate** = $0.8\ \mathrm{ml\,min}^{-1}$. **Detector** = Knauer K-2501 UV detector set at 214 nm.

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