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Preparation of Ethyl 4-Nitrobenzoate Using Ultradispersed Natural Zeolite Catalysts, Ultrasound and Microwave Irradiation

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Abstract

The new possibilities of preparing the ethyl 4-nitrobenzoate by esterification of 4-nitrobenzoic acid (4-NBA) with ethanol under argon at 80°C are shown; particularly, over catalysts: on micrometric (4.8 - 7.0 µm) or ultradispersed crystallites (290 - 480 nm) of hydrogen forms of nanoporous natural zeolites H-CL, H-MOR, H-HEU-M, H-PHI and under irradiation of the reaction mixture with ultrasound (US, 37 kHz, 330 W, 2 h) or microwaves (MW, 2450 MHz, 300 W, 2 h). Ultradispersed crystallites of zeolite catalysts were prepared from hydrogen forms of parent natural zeolites by their treatment with US or MW. In the esterification, the synergism of the actions of catalysts and MW or US was revealed; wherein on the ultradispersed best catalysts H-HEU-M and H-MOR conversion of 4-NBA and yield of ethyl 4-nitrobenzoate reached up to 70% and 67%, respectively. GC/MS, FTIR, NMR methods were used in the study.

Keywords

Ultradispersed Natural Zeolite, Ethyl 4-Nitrobenzoate, Microwaves, Ultrasound

1. Introduction

Ethyl 4-nitrobenzoate is a semi-product in the chemical-pharmaceutical industry for the production of local anesthetics-novocaine (procaine, 2-ethylaminoethyl ester of 4-aminobenzoic acid) and anestezin (benzocaine, ethyl ester of 4-aminobenzoic acid), which are also found in other pain relievers [1]-[6].

Many methods were described for the preparation of ethyl 4-nitrobenzoate with esterification (Fischer esterification) of 4-nitrobenzoic acid with ethanol (Scheme 1); the reaction is reversible and the catalysts for this process are sulfuric acid [7], ammonium hydrogen sulfate [8], however, this catalyst is not commercially available; polyfluoroalkanesulfonic acid [9], silicon tetrachloride [10]. In all these methods, the yield of ethyl 4-benzoate was 75% - 98%. It was shown that in a cascade reactor the esterification of 4-nitrobenzoic acid in the presence of sulfuric acid as a catalyst had some advantages over the same process in a batch reactor [4]. In this case, in a cascade reactor at 110°C - 120°C in a short time (10.5 min), the conversion of 4-nitrobenzoic acid reaches 96%, while in a batch reactor; the same effect is achieved at a higher temperature (180°C) and within 3 hours.

These specified methods for the production of ethyl 4-nitrobenzoate can be considered ecologically unjustified due to the use of large amounts of sulfuric acid, halogenated solvents, the need to regenerate excess alcohol, the presence of a large amount of wastewater and large losses of the target product.

As our study below shows, in the ethanol esterification reaction of 4-nitrobenzoic acid, the use of solid acidic zeolites in synergy with microwaves and ultrasound is promising.

Today more than three thousand chemical reactions are known that occur under the specific activation during microwaves and ultrasound irradiation. They are based on mechanisms of fast dielectric heating of material [11] and acoustic cavitation [12], respectively. Sonication and microwave chemistry are also important in the field of preparation of nanomaterials [13] [14]; nanoparticles have a large surface-to-volume ratio, display increased surface activity and therefore have versus massive materials (adsorbents, catalysts) a great activity [15] [16]. It was shown that pretreatment of H-MOR and H-BEA zeolites with ultrasound causes a change in the morphology of zeolite crystals (unit cell volume, crystal and particle sizes) and their acidic properties [17].

Also by synergistic action of ultrasound and microwaves during the synthesis of type Y zeolite, it was succeeded preparation of micro-mesoporous Y type zeolite in a form of small crystalline nanoparticles, with significantly increased catalytic activity [18].

Due to the synergistic action of microwaves/ultrasound, and catalysts in the esterification and dehydration reactions, an increase in catalytic activity was also observed [19].
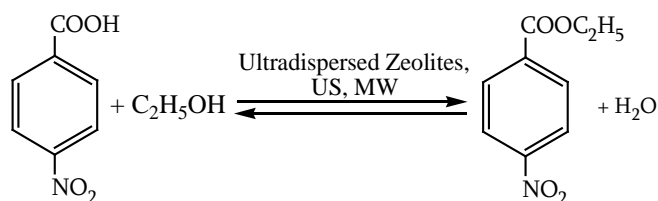
Scheme 1. Reaction for synthesis of ethyl 4-nitrobenzoate.

In the current study, ethyl 4-nitrobenzoate was prepared in two ways by solvent-free esterification of 4-NBA with ethanol in an argon atmosphere at the boiling point of the reaction mixture; with application of nanoporous acid catalysts—hydrogen forms of natural zeolites: H-CL, H-MOR, H-HEU-M, H-PHI with ultradispersed crystallites (290 - 480 nm); as well as by irradiation of the reaction mixture with ultrasound (37 kHz, 330 W, 2 h) or microwaves (2450 MHz, 300 W, 2 h). These methods are simple and environmentally friendly.

2. Materials and Methods

2.1. Chemicals and Materials

In the study was applied 4-Nitrobenzoic acid (≥98%, Sigma-Aldrich, USA), ethyl 4-nitrobenzoate (≥98%, Sigma-Aldrich, USA), ethanol (99.9%, HPLC, CarlRoth, Germany). Argon (99.999%) was used as an inert medium during reactions. As heterogeneous catalysts were used solid acids, hydrogen forms of nanoporous natural zeolites clinoptilolite (CL, 95%, v(Si)/v(Al) = 4.4), mordenite (MOR, 50% - 60%, v(Si)/v(Al) = 6.5), heulandite (as monomineral, HEU-M, v(Si)/v(Al) = 3.4) and phillipsite (PHI, 90%, v(Si)/v(Al) = 2.6), from Georgian deposits of Dzegvi, Bolnisi-Ratevani, Akhaltsikhe and Shukhuti, respectively. Catalysts were prepared from the corresponding natural zeolites according to the method described in section **2.2.**

2.2. Preparation of Catalysts

Catalysts with micrometric crystallites. The catalysts have been prepared from the museum samples of natural zeolites of Georgia. Light pink crystals of monomineral heulandite sample (HEU-M, SiO_2/Al_2O_3 = 6.8, 0.5 cm in size) were selected from natural heulandite manually under a binocular microscope. Starting forms of natural zeolites: clinoptilolite (CL), HEU-M, PHI and MOR were ground down to a powder finer than 6 μm, washed with distilled water and dried. The hydrogen forms of catalysts obtained from them and denoted respectively, H-CL, H-HEU-M, H-PHI, H-MOR were prepared in the way described below.

Catalysts H-CL and **H-MOR**. Natural CL and MOR were leached once with 1M HCI solution (10 mL solution/g zeolite) for 3 h at reflux temperature; the suspension was filtered and the precipitate was washed with hot distilled water until a negative reaction for chlorine ions and dried in air at 40˚C [16].

Catalysts H-HEU-M and **H-PHI**. These were prepared also as a catalyst H-CL and H-MOR from zeolites starting forms HEU-M and PHI; in order to prevent destruction of the HEU-M and PHI crystal structure the 0.25 M solution of hydrochloric acid (10 mL solution/g zeolite) was taken.

Zeolite catalysts with ultradispersed crystallites. For dispersing of micrometric particles of hydrogen forms of the studied zeolites of their suspensions (10%) in water were subjected to ultrasonic or microwave processing. using for this purpose ultrasonic cleaner (Elma P 120 H, Germany, frequency—37 kHz, pow-

er—330 W) and the Ultrasonic-Microwave (hybrid) reactor UMR-300B, Japan; microwave frequency—2450 MHz, power—300 W), respectively. Ultrasonic radiation of samples was carried out for 7.5 h; at the same time before radiation, it is consecutive in 1, 2, 3 and 7.5 h, measured particle size distribution of zeolites. By ultrasound irradiation water temperature in the ultrasonic cleaner rose up to 55°C and it was supported throughout the entire period. Irradiation by microwaves was carried out at 40°C for 2 h.

2.3. Characterization of Catalysts

By X-ray fluorescence analysis using energy dispersive X-ray fluorescence spectrometer EDX3600B (Skyray Instrument Ltd., China) the partial chemical composition of catalysts was determined [16]

Particle size determination. After ultrasonic and microwave treatment the distributions by the sizes of crystallites of catalysts H-CL, H-HEU-M, H-PHI, H-MOR on the laser light scattering particle size analyzer (Laser-Particle Sizer Analysette 12-DynaSizer, Fritsch) by Cumulants and Pade Laplace algorithms were determined. Size distribution was expressed in terms of intensity and volume.

2.4. Catalytic Activity, Analysis of Reaction Products

Before the catalytic experiments, the catalysts were heated for 3 hours in a clean airstream at 310°C for H-CL, H-MOR and at 210°C for H-HEU-M and H-PHI to prevent structural change from heulandite A to heulandite B and thermal decomposition of phillipsite at 250°C.

When using only zeolite catalysts, the reactions were carried out under static conditions in a three-necked flask with a reflux condenser and a thermometer, in an argon atmosphere, on a magnetic stirrer with thermoregulation (MSH-300). The reactions under microwave and ultrasonic irradiation were carried out in a hybrid reactor (UMR-300B) under the same conditions. The regenerated catalyst was added to the flask to a solution of 4-nitrobenzoic acid in hot ethanol and heated to the boiling point of the mixture for several hours; in particular, in the case of zeolite catalysts containing nanosized particles, within 6 hours; while when the reaction mixture was exposed only to radiation (US or MW) or simultaneously to irradiation and a catalyst, for 2 hours.

The solution obtained after the reaction was filtered through a Buchner funnel, the catalyst separated on the funnel was washed with hot ethyl alcohol to remove the reaction mass adsorbed on the catalyst, and wastewater was added to the first filtrate.

The total filtrate obtained (containing the unconverted 4-nitrobenzoic acid, the resulting ethyl 4-nitrobenzoate, ethyl alcohol and water) was added to a 15% soda solution until a weak alkaline reaction (pH = 7.5 - 8). At this time the not reacted 4-nitrobenzoic acid is converted to the salt and completely transferred to the aqueous solution, while the top layer contains alcohol and the 4-nitrobenzoic acid ethyl ester. The mixture was kept in a separation funnel at room temperature to separate the organic-containing top layer, which was then distilled to separate

(detaching) the alcohol. The remaining ethyl 4-nitrobenzoate precipitate was air-dried at 40˚C to a constant weight and weighed.

The catalytic properties were characterized by the conversion of 4-nitrobenzoic acid, the selectivity of the formation of ethyl 4-nitrobenzoate and yield.

GC-MS analysis (Agilent Technologies, 5890B/5977A, USA) of the esterification reaction products was performed in the EI mode, 70 eV, capillary column HP-5ms, Ultra Inert, 30 m × 0.32 mm × 0.25 μm, helium (1.0 mL/min) as a carrier gas, methanol as solvent; analyzes were carried out in program mode: hold at 80˚C for 5 min, ramp to 230˚C at 30˚/min, hold at 230˚C for 10 min. The identification of the compounds was made by comparing the spectra with NIST 2014 library. The amount of 4-NBA and ethyl 4-nitrobenzoate were determined from their calibration curves.

Fourier transform infrared spectroscopy (*FTIR*) *studies* were conducted on a Nicolet™ iS50 FTIR Spectrometer-Thermo Fisher Scientific in the infrared region 4000 - 400 cm^{-1} (scan 32, resolution 4 cm^{-1}); band intensities were denominated in transmittance. Analytical sample: finely dispersed powder (1 - 2 mg).

NMR spectra were recorded on Bruker NMR-400 (400 MHz). Chemical shifts (ppm) are given relative to solvent: references for DMSO were 2.50 ppm (^{1}H-NMR) and 39.50 ppm (^{13}C-NMR).

3. Results and Disscussion

3.1. Composition and Particle Size Distribution of Catalysts

Some characteristics of the catalysts are given in Table 1. It can be seen that after the irradiation of the catalysts with microwaves and ultrasound, the sizes of their particles decrease from the parent micrometric-sized catalysts produces ultradispersed samples with particle sizes 290 - 480 nm.

3.2. Catalytic Activity

3.2.1. Esterification over Micrometric and Ultra Dispersed Zeolite Catalysts

The main product of the 4-NBA esterification reaction with ethanol by catalytic or MW- and US-assisted reactions was ethyl 4-nitrobenzoate (Figure 1); formation of a minor amount of the diethyl ether-product of the ethanol dehydration reaction was observed.

The results show that irradiation of hydrogen forms of natural zeolites with US or MW causes a decrease in the size of their crystallites from 4.8 - 7.0 μm to 290 - 480 nm (Table 1); the catalytic activity of the similarly prepared zeolite catalysts (H-CL, H-MOR, H-HEU-M, H-PHI), containing ultradispersed crystallites, is increased in the esterification reaction 4-NBA with ethyl alcohol compared to their parent forms (Figure 2).

The conversion values of 4-NBA on the parent catalysts H-MOR, H-HEU-M, H-CL and H-PHI with micrometric particle sizes (4.80 - 7.00 μm), are inferior (Figure 2), but not significantly, to conversion values on catalysts with ultradispersed particles (290 - 480 nm); except H-PHI, the conversion degree of 4-NBA

over this catalysts is 51% - 58%. In this case, catalysts with a large entrance window size (0.7 - 0.8 nm) turned out to be more active than H-PHI with channel sizes of 0.4 nm; in the presence of H-PHI catalyst, the conversion degree of 4-NBA was less: 27% - 31%.

The effect of decreasing the particle size of the starting catalysts in the esterification of 4-NBA is more pronounced on the values of yield and selectivity for ethyl 4-nitrobenzoate. For example, in the case of ultradispersed H-CL, in comparison with the parent H-CL, the ethyl 4-nitrobenzoate yield increases from 29.7% to 46% - 51%. On the ultradispersed catalysts, obtained by treatment of parent catalysts with either microwaves or ultrasound, the values of both conversions and yields of the target product ethyl 4-nitrobenzoate are close (Figure 2); its

Table 1. Composition of the catalysts and the average particle size of the hydrogen forms of natural zeolites after their ultrasonic (300 W) and microwave (300 W) treatment for 7.5 hours (at 55˚C) and 1 hour (at 40˚C), respectively; sample mass: 1 g.

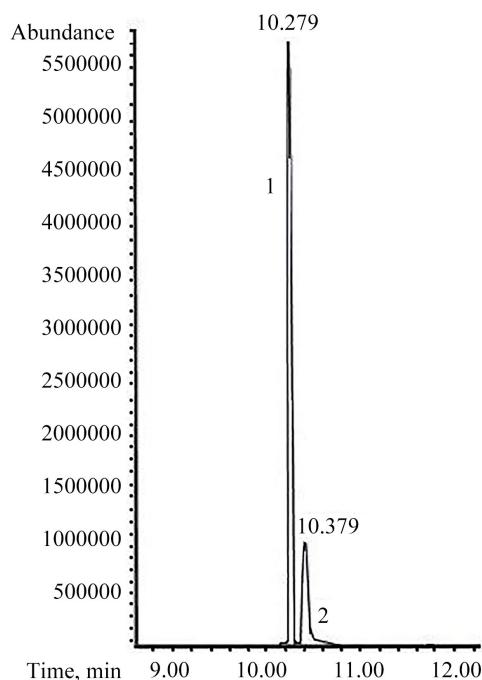| Zeolite catalysts	$\nu(SiO_2)/\nu(Al_2O_3)$	Particles size, nm		
		Before irradiation	After irradiation	
			ultrasound	microwave
H-CL	23.3	5600 - 5800	300 - 325	470 - 480
H-HEU-M	8.2	6000 - 6200	350 - 360	390 - 400
H-PHI	8.0	4800 - 5000	290 - 310	320 - 330
H-MOR	20.1	6500 - 7000	350 - 370	400 - 410

Figure 1. Typical GC/MS chromatogram of the esterification reaction product of 4-NBA with ethanol by the catalytic or US- and MW-assisted conversions at 40˚C - 80˚C under argon atmosphere, US or MW (300 W, 2 h). 1: Ethyl 4-nitrobenzoate, $C_9H_9NO_4$, 2: 4-Nitrobenzoic acid, $C_7H_5NO_4$.
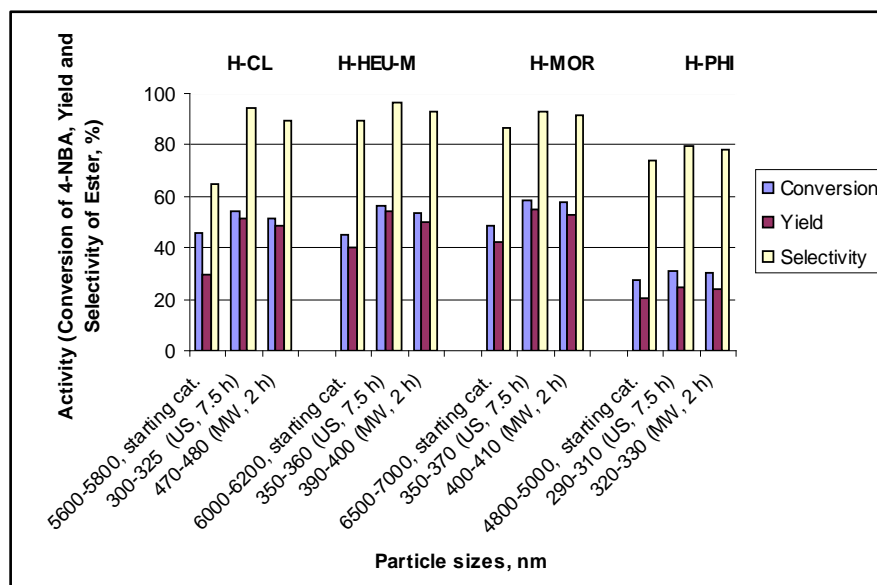
Figure 2. Dependence of the catalytic activity on the particle size for the parent micrometric-sized catalysts (H-CL, H-HEU-M, H-MOR and H-PHI) and their sonicated for 7.5 h (US, 7.5 h) and microwaved for 2 h (MW, 2 h) ultradispersed samples in the esterification of 4-NBA. Mass of catalysts: 0.1 g, mass of 4-NBA: 0.5 g, molar ratio of 4-NBA and ethanol: 1:35; reaction conditions: argon atmosphere, temperature: 80˚C, duration of run: 6 h.

highest yield (about 55%) is found on H-MOR and H-HEUM.

There is the following selectivity series for the formation of ethyl 4-nitrobenzoate for the initial catalysts at approximately the same conversions of 4-NBA (45% - 49%):

H-HEU-M (89.5%) > H-MOR (86.5%) > H-CL (65.0%).

For the same zeolite catalysts but with ultradispersed particles at comparable conversions of 4-NBA (55% - 59%), the selectivity range is as follows:

H-HEU-M (96.5%) > H-MOR (93.3%) > H-CL (94.1%).

On the investigated zeolite catalysts, with the micrometric and ultradispersed particles, in the esterification 4-NBA the obtained series of selectivity in ethyl 4-nitrobenzoate are similar, which indicates the same nature of the active centers in them.

3.2.2. Sinergic Action Ultradispersed Natural Zeolites and Ultrasonic or Microwave Radiations in Esterification

When the 4-NBA was irradiated only with ultrasound or microwaves, the selectivity of the formation of ethyl-4-nitrobenzoate (about 93%) and the conversion of 4-NBA (about 58%) are the same as in the case of ultradispersed zeolites H-HEU-M, H-MOR, H-CL (Table 2); these parameters exceed those for the parent micrometric zeolites (Figure 2).

In the esterification reaction of 4-NBA with the simultaneous action of ultrasound or microwaves and as a catalysts hydrogen forms of natural zeolites with ultradisperse particles, the process is accelerated in comparison with the thermocatalytic reaction; in particular, for the most active ultradispersed catalysts

Table 2. Effect of ultrasound (300 W, 37 kHz) and microwave (300 W, 2450 MHz) irradiation on the esterification reaction of 4-nitrobenzoic acid, and effect of these irradiations together with catalysts—hydrogen forms of natural zeolites with ultradispersed particles; m (4-NBA) = 0.5 g, catalyst weight: 0.1 g, molar ratio v(4-NBA)/v(C_2H_5OH) = 1/35, reaction atmosphere: argon, reaction temperature: 80˚C, reaction run time: 2 h.

Entry	1	2	3
Irradiation type (frequency and power)/catalysts (particle size, nm)	Conversion of 4-NBA, %	Yield of Ethyl 4-Nitrobenzoate, %	Selectivity of Ethyl 4-Nitrobenzoate, %
US (37 kHz, 330 W)	57.1	52.7	92.2
MW (2450 MHz, 300 W)	58.6	54.8	93.4
US/H-CL (300 - 325)	61.5	58.1	94.5
MW/H-CL (470 - 480)	69.4	64.9	93.5
US/H-HEU-M (350 - 360)	66.4	61.2	92.2
MW/H-HEU-M (390 - 400)	68.1	65.6	96.3
US/H-PHI (290 - 310)	34.7	28.0	80.7
MW/H-PHI (320 - 330)	36.7	32.5	88.6
US/H-MOR (350 - 370)	69.6	66.4	95.4
MW/H-MOR (400 - 410)	70.3	67.4	95.9

H-MOR and H-HEU-M, the degree of 4-NBA conversion increases to 70% and the yield of ethyl 4-nitrobenzoate to 67% (Table 2).

3.2.3. Identification of Synthesized Ethyl 4-Nitrobenzoate

Synthesized ethyl 4-nitrobenzoate was identified by its melting point, GC/MS, FTIR, ^{1}H and ^{13}C NMR spectra. Melting point of ethyl 4-NBA samples prepared on zeolite catalysts H-CL, H-HEU and H-HEU-M, and re-crystallized in ethanol was equal to 55˚C - 57˚C.

The FTIR spectra of initial 4-Nitrobenzoic acid and Ethyl 4-nitrobenzoate, synthesized by synergic action of H-MOR (400 - 410 nm) and MW (300 W, 2450 MHz) irradiation, are shown in Figure 3; the strongest peak for ethyl 4-nitrobenzoate is 1712.26 cm^{-1} which corresponds to the C=O ester peak region; conjugation with an aromatic ring shifts the peak characteristic of the C=O group from 1750 - 1735 cm^{-1} to 1712.26 cm^{-1}. Peaks at 1366.77, 1520.06, 869.81, 711.51 and 505.53 cm^{-1} correspond to the NO_2 group [20]. Two strong spectral bands at 1269.03 and 1100.94 cm^{-1} correspond to the symmetric and antisymmetric C-O stretches of the ester COO group and the band at 1008.72 cm^{-1} is the ether CO stretch of the OC2H5 group [21] [22]. The presence in the FTIR spectrum of said characteristic frequencies and their comparison with the spectrum of the starting 4-nitrobenzoic acid unambiguously indicates the formation of Ethyl 4-nitrobenzoate (Figure 3), which corresponds to the standard ethyl 4-nitrobenzoate FTIR spectrum [23].

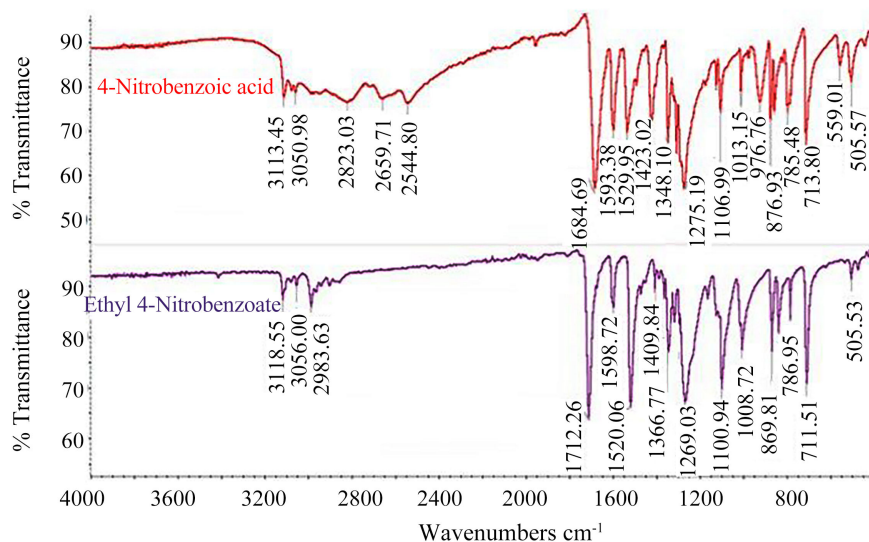The NMR spectra data of the prepared ethyl 4-nitrobenzoate was as follows.

Figure 3. FTIR spectra of parent 4-Nitrobenzoic acid and Ethyl 4-nitrobenzoate, synyhe-sized by synergic action of H-MOR (400 - 410 nm) and MW (300 W, 2450 MHz) irradiation in esterification reaction of 4-Nitrobenzoic acid; m(H-MOR) = 0.1 g, molar ratio ν(4-NBA)/ν(C$_2$H$_5$OH) = 1/35, reaction atmosphere: argon, reaction temperature: 80°C, duration of run: 2 h.

^{1}H NMR (400 MHz, DMSO-d6): δ 8.35 - 8.34 (2H, m), 8.21 - 8.18 (2H, m), 4.41 - 4.35 (q, 2H, J = 7.1 Hz), 1.37 - 1.34 (t, 3H, J = 7.1 Hz);

^{13}C NMR (100 MHz, DMSO-d6) δ (ppm) 164.77 (C=O), 150.70 (C-NO$_2$), 135.76, 131.07 (2C), 124.37, 62.15, 14.51.

This NMR spectra (^{1}H NMR and ^{13}C NMR) data of ethyl 4-nitrobenzoate, synthesized on the zeolite catalysts and under influence of US or MW irradia-tion, completely coincide with the literature data [23].

4. Conclusion

1) The synthesis reaction of ethyl 4-nitrobenzoate was investigated by esteri-fication of 4-nitrobenzoic acid with ethanol under argon at the boiling point of the reaction mixture; heterogeneous catalytic synthesis is carried out in the presence of acidic catalysts, hydrogen forms of natural zeolites: H-CL, H-MOR, H-HEU-M, H-PHI with ultradispersed crystallites (290 - 480 nm); and also ethyl 4-nitrobenzoate was synthesized by irradiation of the reaction mixture with ul-trasound (37 kHz, 330 W, 2 h) or microwaves (2450 MHz, 300 W, 2 h). Ethyl 4-nitrobenzoate is identified by GC/MS, FTIR and NMR (^{1}H, ^{13}C) spectroscopy.

2) Zeolite catalysts with ultradispersed crystallites were prepared from hydro-gen forms of parent natural zeolites with micrometric crystallites (4.8 - 7.0 μm) by their indirect treatment with ultrasound (US, 300 W, 37 kHz, 7.5 h) or by di-rect influence of microwaves (MV, 300 W, 2450 MHz, 2 h) on the catalysts; these irradiations cause a reduction in the size of zeolite crystallites as determined by means of the laser light scattering particle size analyzer. The zeolite catalysts par-ticle sizes obtained by both types of irrradiations are close to each other and the

particle size was in a range of 290 - 480 nm.

3) The 4-NBA conversion, ester yield and selectivity are higher on zeolite catalysts with ultradispersed particles than on catalysts with micrometric crystallites. Thus, the size effect is observed here. With the simultaneous exposure of the reaction mixture to irradiation (ultrasound or microwaves) and ultradispersed zeolite catalysts, there is a synergistic effect; catalysts activity increases and on the best of them (H-MOR and H-HEU-M) conversion and yield of ethyl 4-nitrobenzoate reach up to 70% and 67%, respectively.

The activities (conversion, yield) of one ultrasound or microwaves in the esterification of 4-NBA are comparable with the activity of ultradispersed catalysts, but in the latter, the reaction time is three times longer (6 h).

4) In contrast to the known methods for the production of ethyl 4-nitrobenzoate, which use halogen-containing solvents, catalysts that are aggressive for the environment (sulfuric acid, ammonium hydrogen sulfate, sulfuryl chloride, polyfluoroalkanesulfonic acid) and complex apparatus design, esterification of 4-NBA under the influence of ultrasound, microwaves or ultradispersed natural zeolites is a simple and cheap way.

The use of microwaves, ultrasound or catalysts of ultra-dispersed natural zeolites allows the successful synthesis of ethyl 4-nitrobenzoate in an argon atmosphere at about 80°C without the use of solvents, aggressive substances and multistage processes; at the same time, providing conversions of about 60 - 70 and yields of 55% - 67%, as well as a high selectivity (more than 90%) according to the ester.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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