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SYNTHESIS OF IONIC COMPOUNDS BASED ON TRIMECAINE IN CLASSICAL CONDITION AND USING ALTERNATIVE METHODS

Abstract. This article presents the results of the synthesis of new and known ionic compounds based on 2-diethylamino-N-(2,4,6-trimethylphenyl)acetamide (trimecaine) in the classical conditions and using microwave and ultrasound activation. Syntheses of ionic compounds were performed via N-alkylation of trimecaine with iodoalkanes. The highest yields were observed when microwave irradiation was used to promote the reaction, ultrasound activation was less effective and mild yields were observed in classical conditions.

Key words: trimecaine, ionic compound, microwave activation, ultrasound activation.

Introduction. Nowadays, the study and application of alternative conditions and ways of synthesis, which consumes less energy, is an important part of green chemistry development. Alternative organic methodologies have become an important part of organic syntheses. Many new organic reaction and methods, in some cases without using catalysts or solvents, and using alternative ways like ultrasonic and microwaves irradiation discussed [1, 2]. It was proposed not to use solution-containing methods completely, since solid-phase reactions proceed efficiently and have advantages such as pollution reduction, low costs, and simplicity of the process [3, 4], even so the problems with mass transfer and reaction (especially exothermic) control arises [3]. In addition, much attention was paid to the use of effective and safe factors for chemical reactions in modern medicinal chemistry, such as ultrasound (US) [5], microwave irradiation (MW) [6]. New methods were described “on the water” using MW without any catalyst [7, 8]. Different natural and bioactive compounds, including food ingredients, cosmetic and pharmaceutical, are reacted under mild conditions with good results [9, 10]. Microwave-assisted extraction and ultrasound-assisted extraction are recognized as efficient extraction techniques that decrease time and rise yield [11]. The Lego chemistry concept [12, 13] promoted to the synthesis of modern molecules like medicines that can accelerate the process of drug production using several safety and practical reactions. The “Lego” chemistry term describes process which are based on readily available starting matters and reactants, need no solvent or nontoxic solvent like water, are high yielding, extensive for using

area, always are specific, easy to carry out and simple to separate product. Ultrasounds and microwaves are various in their working system, however, both of them can essentially optimize the chemical reaction. The using of ultrasound and microwaves has become a real chance for economical, effective and green synthetic process [14-18].

EXPERIMENTAL PART

1. Equipment and General Procedures. The melting points of all ionic compounds were determined in open capillary tube on a OptiMelt (Stanford Research System). The ^1H - and ^{13}C -NMR spectra were recorded using a Varian Mercury-300 spectrometer at 25 or 30°C by using CDCl_3 or DMSO-d_6 as a solvent. IR spectra were recorded on a spectrometer «Nicolet 5700 FT-IR» using KBr pellets. The progress of reactions and purity of products were checked using the TLC method on silica gel plates (Sigma Aldrich®, Germany) with iodine vapors development. The diethylether:ethanol mixtures (4:1 V/V and 5:1 V/V) were used as eluents. The TLC spots on the developed plates were observed in UV light ($\lambda = 254 \text{ nm}$). All reactants and solvents from Sigma Aldrich®. An ultrasonic probe from Cole Parmer (50–60 Hz, 0–240 W) and a domestic microwave generator (0–800 W) were used for the reaction. The separation and purification of substances was carried out by crystallization from appropriate solvents.

Initial compound 2-diethylamino-N-(2,4,6-trimethylphenyl)acetamide (trimecaine free base) was synthesized from commercially available hydrochloride by neutralization with the potassium carbonate. 0.01 Mole (2.845 g) of trimecaine hydrochloride was dissolved in 20 mL of water. The initial solution of trimecaine hydrochloride had $\text{pH} < 7$, so potassium carbonate was added till $\text{pH} = 9$. The extraction was carried out three times with benzene. The extract obtained was dried with anhydrous calcium chloride for 12 h. The solvent was removed by simple distillation. The product was dried for two h in vacuum at 80°C. The yield of trimecaine free base is 2.168 g (87.43%). ^{13}C NMR (CDCl_3) δ , ppm: 170.93 (s, $\text{C}=\text{O}$); 136.81 (s, $\text{C}-\text{CH}_{3\text{aromatic}}$); 134.93 (s, $\text{C}-\text{CH}_3$); 131.33 (s, $\text{C}_{\text{aromatic}}-\text{NH}$); 129.03 (s, $\text{C}_{\text{aromatic}}$); 57.54 (s, $\text{CO}-\text{CH}_2-\text{N}^+$); 49.07 (s, N^+-CH_3); 21.02 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 18.56 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 12.77 (s, $\text{N}^+-\text{CH}_2-\text{CH}_3$). ^1H NMR (CDCl_3) δ , ppm: 8.84 (s, $\text{N}-\text{H}$); 6.89 (s, $\text{H}_{\text{aromatic}}$); 3.21 (s, $\text{CO}-\text{CH}_2-\text{N}^+$); 2.65, 2.66, 2.68 ($\text{N}^+-\text{CH}_2-\text{CH}_3$); 3.15 (s, N^+-CH_3); 2.19 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 2.08 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 1.30, 1.28, 1.26 (t, $\text{N}^+-\text{CH}_2-\text{CH}_3$). Calculated for $\text{C}_{15}\text{H}_{24}\text{N}_2\text{O}$, %: C, 72.58; H, 9.68; N, 11.29; O, 6.45. Found %: C, 72.04; H, 9.86.

2. Synthesis of trimecaine based ionic compounds.

2.1. Classical method. Into the 100 mL flask 15 mL of acetonitrile was added and 0.01 mol of trimecaine was dissolved. Thereafter the solution of 0.011 mol of iodoalkane was added and the resulted solution was kept under the reflux.

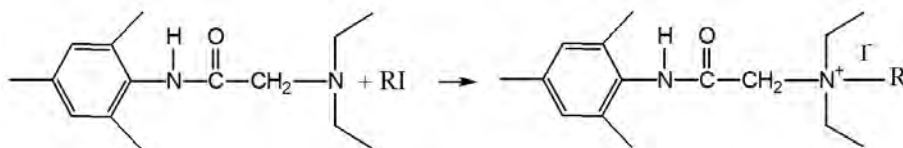


Figure 1 – Synthesis of trimecaine iodoalkanes

Table 1 – The reaction time for N-alkylation of trimecaine in classical method

Iodoalkane*	Time, min
Iodomethane	90
Iodoethane	120
1-Iodopropane	150
1-Iodobutane	180
1-Iodo-2-methylpropane	180
1-Iodohexane	240
*Trimecaine:iodoalkane mole ratio is 0.01:0.011.	

After the process was completed, the volume of solution was reduced twice by evaporation and was cooled down. The obtained isolated product was separated and purified by crystallization and the purity of product was checked by the TLC using a mixture of diethyl ether and ethanol (4:1 or 5:1) as an eluent.

2.2. Ultrasound method. Into the 100 mL flask 15 mL of acetonitrile was added and 0.01 mol of trimecaine was dissolved. Thereafter the solution of 0.011 mol of iodoalkane was added and the reaction mixture was placed in a US reactor and the contents reacted under US conditions characterized by the following parameters: US = 240 W at 30–40 °C.

Table 2 – The reaction time for N-alkylation of trimecaine in US method

Iodoalkane*	Time, min
Iodomethane	30
Iodoethane	40
1-Iodopropane	50
1-Iodobutane	60
1-Iodo-2-methylpropane	60
1-Iodohexane	120
*Trimecaine:iodoalkane mole ratio is 0.01:0.011.	

After the process was complete, the volume of solution was reduced twice by evaporation and was cooled down. The obtained isolated product was separated and purified by crystallization and the purity was checked by the TLC using a mixture of diethyl ether and ethanol (4:1 or 5:1) as an eluent.

2.3. Microwave Method. Into the 100 mL flask 15 mL of acetonitrile was added and 0.01 mol of trimecainewas dissolved. Thereafter the solution of 0.011 mol of iodoalkanewas addedand the reaction mixturewas placed in a MW reactor and the contents reacted under MW conditions at 80 W.

Table 3 – The reaction time for N-alkylation of trimecaine in MW method

Iodoalkane*	Time, min
Iodomethane	1
Iodoethane	1.5
1-Iodopropane	3
1-Iodobutane	6
1-Iodo-2-methylpropane	6
1-Iodohexane	10
*Trimecaine:iodoalkane mole ratio is 0.01:0.011.	

After the process was complete, the volume of solution was reduced twice by evaporation and was cooled down. The obtained isolated product was separated and purified by crystallization and the purity was checked by the TLC using a mixture of diethyl ether and ethanol (4:1 or 5:1) as an eluent.

3. Spectral and other data for the synthesized compounds.

Trimecaine iodomethane (N,N-Diethyl-2-(mesitylamino)-N-methyl-oxoethanamonium iodide) was separated aswhite crystals after crystallization process.M.p. 205-207.°C. IR (KBr), cm^{-1} : 3173 (N-H) 1692 (C=O amide), 1527 ($\text{C}_{\text{aromatic}}=\text{C}_{\text{aromatic}}$). ^{13}C NMR (DMSO- d_6 , 30°C) δ , ppm: 162.52 (s, C=O); 136.78 (s, CH_3); 135.20 (s, CH_3); 131.27 (s, $\text{C}_{\text{aromatic}}-\text{NH}$); 129.02 (s, $\text{C}_{\text{aromatic}}$); 59.05 (s, $\text{CO}-\text{CH}_2-\text{N}^+$); 57.94 (s, $\text{N}^+-\text{CH}_2-\text{CH}_3$); 48.46 (s, N^+-CH_3); 21.02 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 18.55 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 8.37(s, $\text{N}^+-\text{CH}_2-\text{CH}_3$). ^1H NMR (DMSO- d_6 , 30°C) δ ,ppm:9.81(s, N-H); 6.87 (s, $\text{H}_{\text{aromatic}}$); 4.27 (s, $\text{CO}-\text{CH}_2-\text{N}^+$); 3.52, 3.54, 3.56 ($\text{N}^+-\text{CH}_2-\text{CH}_3$); 3.15 (s, N^+-CH_3); 2.19 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 2.08 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 1.30, 1.28, 1.26 (t, $\text{N}^+-\text{CH}_2-\text{CH}_3$). Mass-spectrum: cation $\text{C}_{16}\text{H}_{27}\text{N}_2\text{O}^+$, 263.2. Calculated for $\text{C}_{16}\text{H}_{27}\text{N}_2\text{OI}$, %: C, 49.23; H, 6.92; N, 7.18; O, 4.1; I, 32.56. Found %: C, 48.96; H, 7.01.

Trimecaine iodoethane (N,N-Diethyl-2-(mesitylamino)-N-ethyl-oxoethanamonium iodide) was separated as white crystals after crystallization process. M.p. 195-197.°C. IR (KBr), cm^{-1} : 3172 (N-H) 1693 (C=O amide), 1526 ($\text{C}_{\text{aromatic}}=\text{C}_{\text{aromatic}}$). ^{13}C NMR (CDCl_3 , 25°C) δ , ppm: 162.49 (s, C=O); 136.71 (s, CH_3); 135.22 (s, CH_3); 131.25 (s, $\text{C}_{\text{aromatic}}-\text{NH}$); 129.01 (s, $\text{C}_{\text{aromatic}}$); 59.04 (s, $\text{CO}-\text{CH}_2-\text{N}^+$); 57.92 (s, $\text{N}^+-\text{CH}_2-\text{CH}_3$); 48.41 (s, N^+-CH_3); 21.03 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 18.54 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 8.36(s, $\text{N}^+-\text{CH}_2-\text{CH}_3$). ^1H NMR (CDCl_3 , 25°C) δ ,ppm:9.82(s, N-H); 6.87 (s, $\text{H}_{\text{aromatic}}$); 4.26 (s, $\text{CO}-\text{CH}_2-\text{N}^+$); 3.51, 3.53, 3.55 ($\text{N}^+-\text{CH}_2-\text{CH}_3$); 3.14 (s, N^+-CH_3); 2.18 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 2.07 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 1.31, 1.29, 1.27

(t, N⁺-CH₂-CH₃). Mass-spectrum: cation C₁₇H₂₉N₂O⁺, 277.2. Calculated for C₁₇H₂₉N₂OI, %: C, 50.49; H, 7.18; N, 6.93; O, 3.96; I, 31.43. Found %: C, 49.95; H, 7.19.

Trimecaine 1-iodopropane (N,N-Diethyl-2-(mesitylamino)-N-propyl-oxoethanamonium iodide) was separated as pale yellow crystals after crystallization process. M.p. 161-163°C. IR (KBr), cm⁻¹: 3171 (N-H) 1691 (C=O amide), 1528 (C_{aromatic}=C_{aromatic}). ¹³C NMR (CDCl₃, 25°C) δ, ppm: 162.51 (s, C=O); 136.75 (s, CH₃); 135.20 (s, CH₃); 131.27 (s, C_{aromatic}-NH); 129.02 (s, C_{aromatic}); 59.05 (s, CO-CH₂-N⁺); 57.94 (s, N⁺-CH₂-CH₃); 48.42 (s, N⁺-CH₃); 21.03 (s, C_{aromatic}-CH₃); 18.55 (s, C_{aromatic}-CH₃); 8.37 (s, N⁺-CH₂-CH₃). ¹H NMR (CDCl₃, 25°C) δ, ppm: 9.81 (s, N-H); 6.87 (s, H_{aromatic}); 4.27 (s, CO-CH₂-N⁺); 3.53, 3.54, 3.55 (N⁺-CH₂-CH₃); 3.16 (s, N⁺-CH₃); 2.19 (s, C_{aromatic}-CH₃); 2.08 (s, C_{aromatic}-CH₃); 1.30, 1.26, 1.24 (t, N⁺-CH₂-CH₃). Mass-spectrum: cation C₁₈H₃₁N₂O⁺, 291.1. Calculated for C₁₈H₃₁N₂OI, %: C, 51.67; H, 7.42; N, 6.70; O, 3.83; I, 30.38. Found %: C, 50.91; H, 7.47.

Trimecaine 1-iodobutane (N,N-Diethyl-2-(mesitylamino)-N-butyl-oxoethanamonium iodide) was separated as yellow crystals after crystallization process. M.p. 145-147 °C. IR (KBr), cm⁻¹: 3174 (N-H) 1692 (C=O amide), 1529 (C_{aromatic}=C_{aromatic}). ¹³C NMR (CDCl₃, 25°C) δ, ppm: 162.51 (s, C=O); 136.75 (s, CH₃); 135.20 (s, CH₃); 131.27 (s, C_{aromatic}-NH); 129.02 (s, C_{aromatic}); 59.05 (s, CO-CH₂-N⁺); 57.94 (s, N⁺-CH₂-CH₃); 48.42 (s, N⁺-CH₃); 21.03 (s, C_{aromatic}-CH₃); 18.55 (s, C_{aromatic}-CH₃); 8.37 (s, N⁺-CH₂-CH₃). ¹H NMR (CDCl₃, 25°C) δ, ppm: 9.81 (s, N-H); 6.87 (s, H_{aromatic}); 4.27 (s, CO-CH₂-N⁺); 3.53, 3.54, 3.55 (N⁺-CH₂-CH₃); 3.16 (s, N⁺-CH₃); 2.19 (s, C_{aromatic}-CH₃); 2.08 (s, C_{aromatic}-CH₃); 1.30, 1.26, 1.24 (t, N⁺-CH₂-CH₃). Mass-spectrum: cation C₁₉H₃₃N₂O⁺, 305.4. Calculated for C₁₉H₃₃N₂OI, %: C, 52.77; H, 7.64; N, 6.48; O, 3.70; I, 29.40. Found %: C, 51.83; H, 7.91.

Trimecaine 1-iodo-2-methylpropane (N,N-Diethyl-2-(mesitylamino)-N-isobutyl-oxoethanamonium iodide) was separated as pale yellow crystals after crystallization process. M.p. 153-155 °C. IR (KBr), cm⁻¹: 3173 (N-H) 1693 (C=O amide), 1528 (C_{aromatic}=C_{aromatic}). ¹³C NMR (CDCl₃, 25°C) δ, ppm: 162.51 (s, C=O); 136.75 (s, CH₃); 135.20 (s, CH₃); 131.27 (s, C_{aromatic}-NH); 129.02 (s, C_{aromatic}); 59.05 (s, CO-CH₂-N⁺); 57.94 (s, N⁺-CH₂-CH₃); 48.42 (s, N⁺-CH₃); 21.03 (s, C_{aromatic}-CH₃); 18.55 (s, C_{aromatic}-CH₃); 8.37 (s, N⁺-CH₂-CH₃). ¹H NMR (CDCl₃, 25°C) δ, ppm: 9.81 (s, N-H); 6.87 (s, H_{aromatic}); 4.27 (s, CO-CH₂-N⁺); 3.53, 3.54, 3.55 (N⁺-CH₂-CH₃); 3.16 (s, N⁺-CH₃); 2.19 (s, C_{aromatic}-CH₃); 2.08 (s, C_{aromatic}-CH₃); 1.30, 1.26, 1.24 (t, N⁺-CH₂-CH₃). Mass-spectrum: cation C₁₉H₃₃N₂O⁺, 305.4. Calculated for C₁₉H₃₃N₂OI, %: C, 52.77; H, 7.64; N, 6.48; O, 3.70; I, 29.40. Found %: C, 51.81; H, 7.89.

Trimecaine 1-iodohexane (N,N-Diethyl-2-(mesitylamino)-N-hexyl-oxoethanamonium iodide) was separated as yellow crystals after crystallization process.

M.p. 193-195.°C. IR (KBr), cm^{-1} : 3174 (N-H) 1694 (C=O amide), 1530 ($\text{C}_{\text{aromatic}}=\text{C}_{\text{aromatic}}$). ^{13}C NMR (CDCl_3 , 25°C) δ , ppm: 162.49 (s, C=O); 136.73 (s, CH_3); 135.20 (s, CH_3); 131.27 (s, $\text{C}_{\text{aromatic}}-\text{NH}$); 129.02 (s, $\text{C}_{\text{aromatic}}$); 59.05 (s, $\text{CO}-\text{CH}_2-\text{N}^+$); 57.94 (s, $\text{N}^+-\text{CH}_2-\text{CH}_3$); 48.42 (s, N^+-CH_3); 21.03 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 18.55 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 8.37 (s, $\text{N}^+-\text{CH}_2-\text{CH}_3$). ^1H NMR (CDCl_3 , 25°C) δ , ppm: 9.81 (s, N-H); 6.87 (s, $\text{H}_{\text{aromatic}}$); 4.27 (s, $\text{CO}-\text{CH}_2-\text{N}^+$); 3.53, 3.54, 3.55 ($\text{N}^+-\text{CH}_2-\text{CH}_3$); 3.16 (s, N^+-CH_3); 2.17 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 2.06 (s, $\text{C}_{\text{aromatic}}-\text{CH}_3$); 1.30, 1.26, 1.24 (t, $\text{N}^+-\text{CH}_2-\text{CH}_3$). Mass-spectrum: cation $\text{C}_{21}\text{H}_{37}\text{N}_2\text{O}^+$, 333.1. Calculated for $\text{C}_{21}\text{H}_{37}\text{N}_2\text{OI}$, %: C, 54.78; H, 8.04; N, 6.08; O, 3.48; I, 27.61. Found %: C, 53.97; H, 8.13.

RESULTS AND DISCUSSION

The use of alternative activation factors, ultrasound (US) or microwaves (MW) become very promising and desirable in synthetic methodologies for the efficient and rapid production of organic ionic compounds. In addition to saving energy, these green technologies contribute to faster and more selective conversions. The examples presented in the literature [14-18] clearly show that microwave irradiation and ultrasound, is a practically harmless technological innovation, deserves wide attention in the field of fine chemical and chemical industry. Although the mechanisms of cavitation and microwave effects are not fully understood, processes requiring improved heat transfer and mass transfer will benefit from these green technologies [19]. The results of the alkylation reaction carried out in this work under various reaction conditions confirmed the trends in the literature, and the best results obtained were collected and presented in table 4.

In the beginning, trimecaine base was reacted under classical conditions (heating under the reflux) using acetonitrile as a solvent. These reactions give only moderate yields while the reaction time is long. The classical condition promoted the alkylation reaction, but the use of microwaves and ultrasound waves proved to be more effective in reducing the reaction time and increase the chemical efficiency (yield of the product). In all the reactions, identical molar ratio of reactants was used, corresponding to the reaction equation. In all the cases acetonitrile was used as a solvent and all the reagents were soluble. Electromagnetic radiation with a frequency in the range from 0.3 to 300 GHz, heats the substance using a dielectric mechanism, which may include dipolar polarization and ionic conductivity. It is the ability of a material to absorb MW energy and convert it into heat that causes mass heating; temperature of the entire sample rises simultaneously, in stark contrast to conventional conductive heating [20]. Although non-thermal heating and ultrasonic waves are among the simplest, cheapest, and most valuable tools in applied chemistry. Besides saving energy, these green methods contribute to faster and more selective transformations. The device is often subject to additional hazard restrictions. However, recent events suggest that such combination is certainly possible and safe starting from simple

Table 4 – The parameters of N-alkylation reaction

Reagents		Products	Synthesis/reaction conditions	Time/min	Yield, %
2-diethylamino-N-(2,4,6-trimethylphenyl)acetamide (trimecaine)	CH ₃ I	N,N-Diethyl-2-(mesitylamino)-N-methyl-oxoethanamonium iodide	Classical conditions	90	45
			US activation	30	70
			MW activation	1	87
	C ₂ H ₅ I	N,N-Diethyl-2-(mesitylamino)-N-ethyl-oxoethanamonium iodide	Classical conditions	120	42
			US activation	40	65
			MW activation	1.5	83
	1-C ₃ H ₇ I	N,N-Diethyl-2-(mesitylamino)-N-propyl-oxoethanamonium iodide	Classical conditions	150	39
			US activation	50	66
			MW activation	3	80
	1-C ₄ H ₉ I	N,N-Diethyl-2-(mesitylamino)-N-butyl-oxoethanamonium iodide	Classical conditions	180	33
			US activation	60	57
			MW activation	6	71
	(CH ₃) ₂ CHCH ₂ I	N,N-Diethyl-2-(mesitylamino)-N-isobutyl-oxoethanamonium iodide	Classical conditions	180	39
			US activation	60	61
			MW activation	6	76
	1-C ₆ H ₁₃ I	N,N-Diethyl-2-(mesitylamino)-N-hexyl-oxoethanamonium iodide	Classical conditions	240	27
			US activation	120	46
			MW activation	10	62

modifications to flow systems that are suitable for automation and scaling. The effects are more visible for reactions in which the transition state is more polar than the ground state [21]. It is generally accepted that the increase in speed is largely due to thermal effects. In fact, the average photon energy in the microwave area is even lower than the transmitted energy of Brownian motion. A final note also applies to the US in its practical range from 20 to 100 kHz, the rotational or vibrational molecular states do not even change as ultrasonic frequencies. US is not absorbed by individual molecules, although it is partially converted into heat. Accordingly, the frequency effects that are sometimes observed cannot be easily rationalized. Ultrasonic effects come from a unique nonlinear phenomenon of cavitation, i.e. micrometer-sized creation, growth and destruction of bubbles which are generated when a pressure wave of sufficient intensity propagates through the fluid. Bubble explosion creates the local conditions of thousands of degrees Kelvin and hundreds of atmospheres are

accompanied by shock waves of extremely short duration [22]. In other words, cavitation can be seen as a quasi-adiabatic process that releases enough kinetic energy to trigger chemical reactions. Although it is still poorly understood, current theory (commonly referred to as the theory of hot spots) explains the majority of experimental observations, such as fragmentation of particles, splitting of radicals and the formation of excited species as a result of pyrolytic cleavage of solvent or substrate molecules [23]. In fact, cavitation is more dependent on physical properties, such as vapor pressure, viscosity and surface tension, compared to chemical characteristics commonly evaluated (acidity/basicity or polarity). Although practicing microwave ovens often refer to the existence of hot spots, it is still unclear whether they represent cavitation media. In chemistry MW, hot spots should be understood as hot areas approaching molecular measurements that arise due to heterogeneities electromagnetic field. They cause a nonlinear dependence of the thermal and electromagnetic properties of the heated material on temperature [24]. Also, bond strength affect the reactivity of iodoalkanes. By increasing weight of radical, bond between carbon and iodine getting stronger:

Bond strength: $\text{CH}_3\text{—I} < \text{C}_2\text{H}_5\text{—I} < \text{C}_3\text{H}_7\text{—I} < \text{C}_4\text{H}_9\text{—I} < \text{C}_6\text{H}_{13}\text{—I}$.

Stronger bonds are more difficult to break, making them less reactive. So iodomethane most reactive and reactivity decreases by increasing carbon number in radical.

In all the cases studied the reaction time for the synthesis of particular trimecaine alkyl derivative decreases with changing classical reaction conditions (reflux) to US activation and further to MW activation. Also, the yield of the reaction product increases in the same order. Due to the following observations it is possible to choose MW activation as the most potent method for the synthesis of ionic derivatives of trimecaine.

Conclusion. Therefore, the results of the experiments performed confirmed the positive effect of non conventional reaction conditions. In this study, we analyzed the reactions of N-alkylation of trimecaine with iodoalkanes that can be used for rapid production of ionic compounds. Ultrasonic and microwave processes can successfully compete with classical synthesis methods. Results of our study confirm the literature data describing tendency of growing effectiveness of reaction assistance in the sequence: classical method, ultrasound activation and microwave activation. The obtained ionic compounds can be successfully used in further transformations with other active molecules, effective plant growth stimulants and production of drugs.

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Резюме

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ТРИМЕКАИН НЕГІЗІНДЕ
ИОНДЫҚ ҚОСЫЛЫСТАРДЫ КЛАССИКАЛЫҚ ЖӘНЕ
БАЛАМА ЖОЛДАР АРҚЫЛЫ СИНТЕЗДЕУ

Мақалада 2-диэтиламино-N-(2,4,6-триметилфенил)ацетамид (тримекаин) негізінде микротолқын мен ультрадыбыстық активтендіруді қолдану арқылы жаңа және белгілі иондық қосылыстардың синтезі туралы баяндалады. Иондық қосылыстардың синтезі тримекаинді йодалкандармен N-алкилдеу арқылы жүзеге асырылды. Ең жоғарғы шығым микротолқынды сәулеленуді қолданылған кезде байқалды. Ультрадыбыстық активтендіруде шығым орташа, ал классикалық жағдайда реакция өнімі төмен шығымды көрсетті.

Түйін сөздер: тримекаин, иондық қосылыс, микротолқынды және ультрадыбысты активтендіру.

Резюме

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СИНТЕЗ ИОННЫХ СОЕДИНЕНИЙ НА ОСНОВЕ ТРИМЕКАИНА
В КЛАССИЧЕСКИХ УСЛОВИЯХ
С ИСПОЛЬЗОВАНИЕМ АЛЬТЕРНАТИВНЫХ МЕТОДОВ

В работе приведены результаты синтеза новых и известных ионных соединений на основе 2-диэтиламино-N-(2,4,6-триметилфенил) ацетамида (тримекаин), которые были получены в классических условиях, а также с использованием микроволновой и ультразвуковой активации, путем N-алкилирования тримекаина йодалканами. Самые высокие выходы продуктов наблюдались при микроволновом облучении реакционных смесей. Тогда как активация ультразвуком была чуть менее эффективной по сравнению с микроволновой. Наименьший выход продуктов получен при проведении реакции в классических условиях при нагревании реакционной смеси при температуре кипения растворителя.

Ключевые слова: тримекаин, ионное соединение, микроволновая и ультразвуковая активация.