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LETTERS TO THE EDITOR

An Example of Ultrasonic Activation in the Synthesis of Ethyl 3-(R-Imino)adamantyl-1-carboxylates

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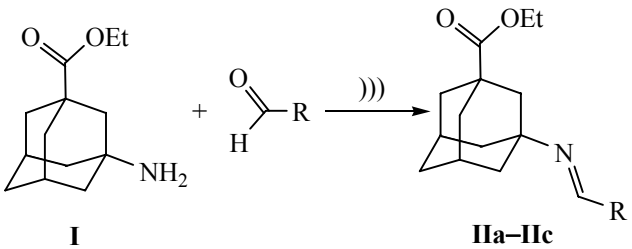
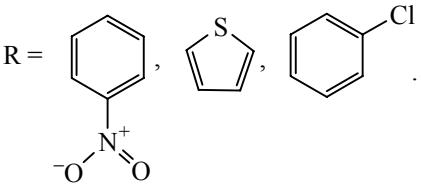
Numerous examples of sonochemical activation of heterophase processes have been reported [1]. The interest in this work consisted in the possibility of effective application of ultrasound as an initiator of the condensation of amine containing adamantane skeleton with an aromatic aldehyde in comparison with the classical method of thermal activation of this reaction.

The synthesis of ethyl 3-(4-nitrobenzylidenimino) adamantyl-1-carboxylate, ethyl 3-[(2-thienyl)methylenimino)adamantyl-1-carboxylate, and ethyl 3-(2-chlorobenzylidenimino)adamantyl-1-carboxylate as potential biologically active substances [2–3] was performed by the condensation of ethyl 3-aminoadamantyl-1-carboxylate with the corresponding aldehydes. The reaction was carried out in two ways: by boiling the reaction mixture for 5–6 h or by the action of ultrasound on the same mixture at room temperature. To remove the liberated water magnesium sulfate was used. This allowed us to achieve greater conversion of the starting amine compared with the azeotropic distillation of water.



I **IIa–IIc**



The sonochemical activation of the reaction of the amines of adamantane series with aromatic aldehydes reduced the reaction temperature. This allowed us to avoid tarring of the aldehyde (which is important at the application of heterocyclic aldehydes) as well as to reduce 2.5–3 times the time of achieving conversion of starting amine as compared with thermal activation. The yields at the sonochemical activation were 28–59% (after recrystallization).

Irradiation was performed in an ultrasonic bath of the Sapphire 2.8 model operating at 35 kHz. The IR spectra of the synthesized compounds were recorded on a Shimadzu FTIR-8400S instrument from KBr pellets. The ^{1}H NMR spectra were recorded on a Varian-400 instrument (400 MHz) with internal reference TMS, solvent DMSO-d_6. The elemental analysis was performed on an elemental analyzer Euro Vektor EA 3000. Purity of the substances and reaction progress were monitored by GLC on a Kristal 2000 device using capillary column BPX-5MS (length 28 m, diameter 0.32 mm, phase thickness 0.25 μm).

Ethyl 3-amino-1-adamantylcarboxylate (I) was obtained as described in [4].

Ethyl 3-(R-imino)adamantyl-1-carboxylates. *a. Thermal activation*. In a 500 ml three-neck flask equipped with a stirrer and a reflux condenser was placed a solution of 0.01 mol of ethyl 3-aminoadamantyl-1-carboxylate in 200 ml of 2-propanol. To this solution was added 0.01 mol of aldehyde and 40 g (0.33 mol) of anhydrous magnesium sulfate. The reaction mixture was heated for 5 h with stirring. The precipitate was filtered off and washed with boiling 2-propanol. The filtrates were combined and concentrated. The residue was recrystallized from anhydrous butanol to give transparent crystals.

b. Sonochemical activation. A mixture of ethyl 3-aminoadamantyl-1-carboxylate (0.01 mol), aldehyde (0.01 mol), $MgSO_4$ (40 g, 0.33 mol) in 200 ml of 2-propanol in a one-neck flask (500 ml), equipped with a reflux condenser, was immersed in an ultrasonic bath and exposed to ultrasound for 2 h. The extraction and purification of the condensation product are similar to the described above.

Ethyl 3-(4-nitrobenzylidenimino)adamantyl-1-carboxylate (IIa). Yield 1.3 g (36%), colorless crystals, mp 72–74°C. IR spectrum, ν, cm^{-1}: 2931, 2900, 2858 (C−H_{Ad}), 1716 (C=O), 1643 (C=N), 1523, 1346 (NO_2), 748, 690 (C–C_{Ar}). ^{1}H NMR spectrum, δ, ppm: 1.14 t (3H, CH_3, *J* 7.0 Hz), 1.5–1.9 m (12H, Ad), 2.20 s (2H, CH_{Ad}), 4.02 q (2H, CH_2), 7.98 d (2H, CH_{Ar}, *J* 8.8 Hz), 8.25 d (2H, CH_{Ar}, *J* 8.8 Hz), 8.45 s (1H, N=CH). Found, %: C 67.38; H 6.80; N 7.84. $C_{20}H_{24}N_2O_4$. Calculated, %: C 67.40; H 6.79; N 7.86.

Ethyl 3-[(thien-2-yl)-methylenimino)adamantyl-1-carboxylate (IIb). Yield 1.9 g (59%), colorless crystals, mp 58–60°C. IR spectrum, ν, cm^{-1}: 2908, 2854 (C−H_{Ad}), 1731 (C=O), 1623 (C=N), 1242 (C–O), 717 (C–S). ^{1}H NMR spectrum, δ, ppm: 1.59–1.78 m (12H, Ad), 2.16 s (2H, CH_{Ad}), 3.56 (3H, CH_3), 7.08 d.d (1H, CH_{Th}, *J* 5.0, *J* 3.6 Hz), 7.43 d. d (1H, CH_{Th}, *J* 3.5, *J* 1 Hz), 7.58 d (1H, CH_{Th}, *J* 5.0 Hz), 8.42 s (1H, N=CH). Found, %: C 68.12; H 7.15; N 4.40. $C_{18}H_{23}NO_2S$. Calculated, %: C 68.10; H 7.30; N 4.41.

Ethyl 3-(2-chlorobenzylidenimino)adamantyl-1-ethylcarboxylate (IIc). Yield 1.0 g (28%), colorless crystals, mp 160–166°C. IR spectrum, ν, cm^{-1}: 2920, 2858 (C−H_{Ad}), 1728 (C=O), 1627 (C=N), 1242 (C–O), 1110 (C–C_{Ar}), 613 (C–Cl). ^{1}H NMR spectrum, δ, ppm: 1.11–1.14 m (3H, CH_3), 1.51–1.8 m (12H, Ad), 2.10 s (2H, CH_{Ad}), 3.99–4.04 q (2H, CH_2), 7.95 d (1H, CH_{Ar}, *J* 7.5 Hz), 7.34–7.50 m (3H, CH_{Ar}), 8.60 s (1H, N=CH). Found, %: C 69.05; H 7.53; N 4.03. $C_{20}H_{26}ClNO_2$. Calculated, %: C 68.90; H 7.50; N 4.01.

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