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SYNTHESIS OF 3-SUBSTITUTED ETHYL ESTERS OF 6-ARYL-5-CYANO-2,4-DIOXO-3-AZABICYCLO-[3.1.0]HEXANE-1-CARBOXYLIC ACID, BASED ON A MODIFIED REFORMATSKY REACTION

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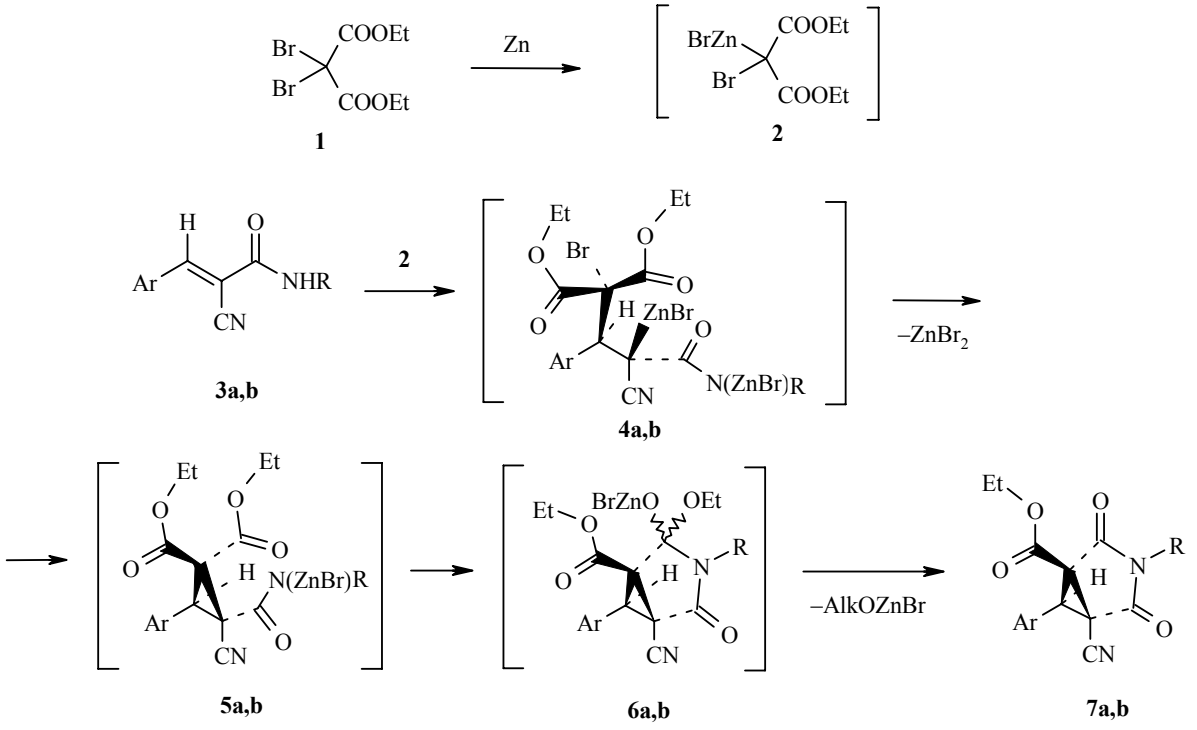
Organozinc reagents formed from alkyl esters of dibromomalonic acid have been previously used for cyclopropanation of alkyl esters of arylidene malonic acids [1].

In this work, we have studied the reaction of the organozinc reagent **2** (formed from the diethyl ester of dibromomalonic acid **1** and zinc) with N-benzyl- and N-cyclohexylamides of 3-aryl-2-cyanopropenoic acid (**3a,b**). As we successfully established, the reaction occurs according to the following scheme:



3-7 a Ar = 4-BrC_6H_4, R = CH_2Ph, **b** Ar = 4-BrC_6H_4, R = C_6H_{11}

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In ether–tetrahydrofuran–HMFT medium, the zinc enolate **2** regiospecifically reacts with electrophilic substrates **3a,b**, attacking the C(3) atom and forming the intermediate compounds **4a,b**. Under the reaction conditions, the latter undergo spontaneous ring closure, which leads to formation of the corresponding cyclopropanation products **5a,b**. The presence in the intermediate compounds **5a,b** of an amide group activated due to replacement of the hydrogen atom by ZnBr, and also an ester group located on one side of the plane of the cyclopropane moiety, makes additional heterocyclization possible. In fact, as shown by the experiments, the amide group attacks the ester group to form intermediates **6a,b**, which leads to the end products of the reaction: 3-substituted ethyl esters of 6-aryl-5-cyano-2,4-dioxo-3-azabicyclo[3.1.0]hexane-1-carboxylic acid **7a,b**.

The composition and structure of compounds **7a,b** have been proven by elemental analysis, IR, and ^{1}H NMR spectroscopy.

In the IR spectra, there are characteristic absorption bands for carbonyls of the ester (1720 cm^{-1}), lactam (1705, 1780 cm^{-1}) and nitrile (2240 cm^{-1}) groups.

In the ^{1}H NMR spectra, we observe characteristic signals in the 3.14 ppm, 3.15 ppm regions that belong to the methine proton (CH) and signals from protons of the ethyl substituent of one ester group in the 1.07, 1.08 ppm (CH_3CH_2O) and 4.08, 4.10 ppm (CH_3CH_2O) regions.

The IR spectra were recorded on a Specord IR-75 in nujol; the ^{1}H NMR spectra were taken on a Tesla BS-567A (100 MHz) in $CDCl_3$, internal standard HMDS (δ, 0.05 ppm).

Ethyl Ester of 3-Benzyl-6-(4-bromophenyl)-5-cyano-2,4-dioxo-3-azabicyclo[3.1.0]hexane-1-carboxylic Acid (7a). Yield 69%; mp 143-144°C. IR spectrum, ν, cm^{-1}: 1705, 1720, 1780, 2240. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.07 (3H, t, *J* = 7.5, CH_3); 3.14 (1H, s, CH); 4.08 (2H, q, *J* = 7.5, CH_2); 4.53 (2H, s, CH_2Ph); 7.0.1-7.42 (9H, m, C_6H_5, 4-BrC_6H_4). Found, %: C 58.21; H 3.72; N 6.11. $C_{22}H_{17}BrN_2O_4$. Calculated, %: C 58.29; H 3.78; N 6.18.

Ethyl Ester of 6-(4-Bromophenyl)-5-cyano-3-cyclohexyl-2,4-dioxo-3-azabicyclo[3.1.0]hexane-1-carboxylic Acid (7b). Yield 78%; mp 221-222°C. IR spectrum, ν, cm^{-1}: 1705, 1720, 1780, 2240. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.08 (3H, t, *J* = 7.5, CH_3); 1.10-2.19 (10H, m, C_6H_{11}); 3.15 (1H, s, CH); 3.79 (1H, m, C_6H_{11}); 4.10 (2H, q, *J* = 7.5, CH_2); 7.11 (2H, d, *J* = 8.0, 4-BrC_6H_4); 7.35 (2H, d, *J* = 8.0, 4-BrC_6H_4). Found, %: C 56.56; H 4.69; N 6.22. $C_{21}H_{21}BrN_2O_4$. Calculated, %: C 56.64; H 4.75; N 6.29.

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REFERENCES

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