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SYNTHESIS OF (BENZO)THIAZOLO[3,2-*a*]PYRIDINE DERIVATIVES

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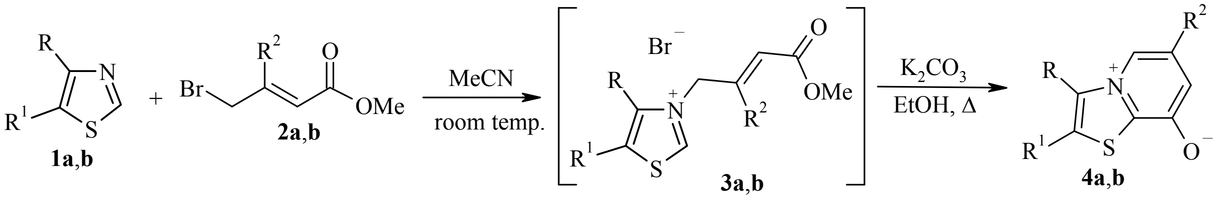
We have previously reported a synthetic method for imidazo[1,2-*a*]pyridines based on the fusion of a pyridine ring to *N*-alkylimidazoles [1]. This method involves quaternization of *N*-alkylimidazoles using γ-halo-α,β-unsaturated ketones and subsequent heterocyclization of the imidazolium salts obtained. This reaction can be successfully extended to the corresponding γ-halocrotonate esters.



1, **3**, **4** **a** R = Me, R^1 = H; **b** R+R^1 = –CH=CH–CH=CH–; **2**, **3**, **4** **a** R^2 = H, **b** R^2 = Me

The γ-halocrotonates **2a**,**b** readily react with the 4-methylthiazole **1a** and benzothiazole **1b**, forming the corresponding thiazolium salts **3a**,**b**. Compounds **3a**,**b** are highly viscous, oily liquids that could not be crystallized, none the less they reached about 95% purity (according to ^{1}H NMR spectroscopy), which was achieved by washing with diethyl ether. The obtained salts **3a**,**b** were dissolved in ethanol in the presence of potassium carbonate and refluxed for 2 h, resulting in cyclization to the thiazolopyridinium olates **4a**,**b**. Thus, the conversion of the thiazoles **1a**,**b** to compounds **4a**,**b** could be performed as a two-stage process involving the intermediates **3a**,**b** without additional purification. Compounds **4a**,**b** were characterized by a mesoionic structure with the charges distributed on the nitrogen and oxygen atoms, and formed crystall hydrates with one molecule of water. The C–O$^-$ bond frequencies in olates studied previously [2] were characteristic to these compounds and appeared at much lower than the normal carbonyl bond stretching frequencies. In our compounds, this vibration appeared at 1573 and 1578 cm^{-1}. The presence of water in the molecules was proven by a low intensity absorption band around 1615 cm^{-1} associated with deformation vibrations and a broad band with a nominal center near 3400 cm^{-1} assigned to stretching vibrations of the O–H bond belonging to the olate associated with a water molecule. It should be noted that the inclusion of water molecules in the structure is typical for mesoionic type substances, e.g., in the *N*-alkylpyridinium-3-olates, reported as hydrates [3].

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In this work we therefore have identified a previously unreported heterocyclization based on γ-bromocrotonates and leading to thiazolopyridinium olates.

IR spectra were recorded on a PerkinElmer Spectrum BX instrument for KBr pellets and UV spectra on a Lambda 20 UV/VIS spectrometer using MeOH. The ^{1}H NMR spectra were recorded on a Bruker Avance DRX-500 instrument (500 MHz) using DMSO-d_6 with TMS as internal standard. Elemental analysis was performed on a vario MICRO cube CHNS-analyzer, and halogens were determined by the Schöniger method. Melting points were measured in Pyrex glass capillaries on a Thiele apparatus and were not corrected.

3-Methyl[1,3]thiazolo[3,2-*a*]pyridin-4-ium-8-olate (4a). A mixture of the 4-methylthiazole **1a** (0.30 g, 3.0 mmol) and methyl 4-bromobut-2-enoate **2a** (0.54 g, 3.0 mmol) was left in MeCN (20 ml) overnight at room temperature. The solution was evaporated, the residue was dissolved in EtOH (20 ml), K_2CO_3 (0.50 g, 3.6 mmol) was added, and the mixture was refluxed for 2 h. The solution was cooled, filtered, and evaporated. The residue obtained was washed with acetone. Yield 0.41 g (82%). Light-brown crystals; mp 259-261°C (acetone). IR spectrum, ν, cm^{-1}: 3483, 3410, 2961, 1615, 1573, 1436, 1276, 1201, 1039, 765. UV spectrum, λ_{max}, nm (log ε): 346 (3.96), 374 (3.38). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.64 (3H, s, CH_3); 6.95 (1H, d, *J* = 8.0, H-7); 7.57 (1H, dd, *J* = 6.0, *J* = 8.0, H-6); 8.04 (1H, s, H-2); 8.17 (1H, d, *J* = 6.0, H-5). Found, %: C 52.16; H 4.90; N 7.58; S 17.13. $C_8H_7NOS \cdot H_2O$. Calculated, %: C 52.44; H 4.95; N 7.64, S 17.50.

2-Methylpyrido[2,1-*b*][1,3]benzothiazol-10-ium-4-olate (4b). A mixture of the benzothiazole **1b** (1.15 g, 8.5 mmol) and methyl 4-bromo-3-methylbut-2-enoate **2b** (1.80 g, 9.4 mmol) in MeCN (60 ml) was left overnight at room temperature. Solvent was removed *in vacuo*, and the residue was dissolved in EtOH (60 ml). K_2CO_3 (1.52 g, 11.0 mmol) was added, and the mixture was refluxed for 2 h. The solution was cooled, filtered, and evaporated, and the residue was washed with acetone. Yield 0.82 g (45%). Brown crystals; mp 224-225°C (acetone). IR spectrum, ν, cm^{-1}: 3431, 3054, 1578, 1542, 1475, 1454, 1364, 1323, 752. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.35 (3H, s, CH_3); 6.64 (1H, s, H-3); 7.70-7.81 (2H, m, H-7,8); 8.30 (1H, d, *J* = 8.0, H-6); 8.61 (1H, d, *J* = 8.0, H-9); 8.64 (1H, s, H-1). Found, %: C 61.59; H 4.69; N 6.11; S 13.71. $C_{12}H_9NOS \cdot H_2O$. Calculated, %: C 61.78; H 4.75; N 6.00; S 13.74.

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