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FORMATION OF SPIRO[BENZOTHIENO-3,4'-PYRIDINES] BY THE REACTION OF BENZOTHIENO[2,3-*c*]PYRIDINES WITH ACETYLENE DICARBOXYLIC ESTER

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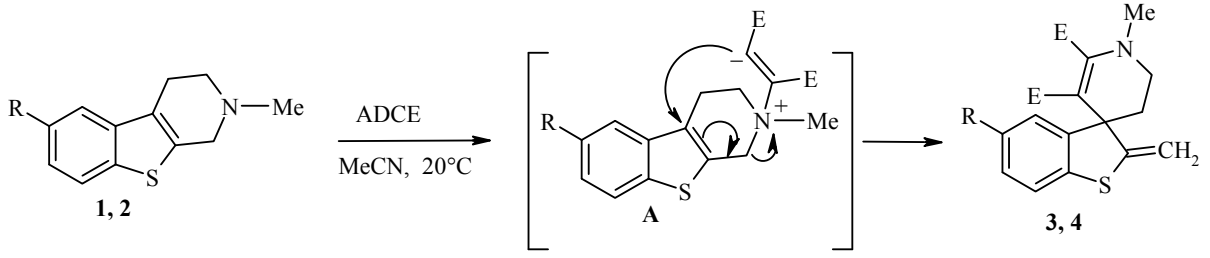
It has previously been shown that 5-*o*-chlorobenzyltetrahydrothieno[3,2-*c*]pyridines react with alkynes only in alcohols to form the products of cleavage of the tetrahydropyridine ring and involving molecules of the solvent and the products of debenzylation (N-vinyltetrahydrothienopyridines) [1]. 2-Trifluoroacetamidotetrahydrothieno[2,3-*c*]pyridines react readily with alkynes both in methanol and in acetonitrile to give a high yield of tetrahydrothieno[3,2-*d*]azocines [2]. 2-Acetamido-substituted thienopyridines react with alkynes in acetonitrile at 20ºC to give modest yields (30-59%) of the thienoazocines. There occur in methanol simul-taneous processes of expansion and cleavage of the tetrahydropyridine fragment to form a mixture of the acetamido-substituted tetrahydrothieno[3,2-*d*]azocines and 2-acetamido-3-ethoxycarbonyl-4-(N-vinyl-N-R)aminoethyl-5-methoxymethylthiophenes [2].

Continuing our study of the dependence of the transformation of tetrahydrothienopyridines with activated alkynes we have shown, for the first time, that the tetrahydrobenzothieno[2,3-*c*]pyridines **1, 2** react with acetylene dicarboxylic ester (ADCE) in acetonitrile to form the spiro[benzothiophene-3,4'-pyridines] **3, 4** in 20-35% yields.



1, 2 **A** **3, 4**

1, 3 R = H; **2, 4** R = Me; E = CO_2Me

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The mechanism for the formation of the spirobenzothienopyridines **3, 4** is given in the Scheme. It involves the formation of an intermediate zwitterion **A** as a result of a Michael addition of the sp^3-hybridized nitrogen atom of the piperidine ring to the ADCE. In methanol, compounds **1, 2** do not react with ADCE, methyl propiolate, or acetyl acetylene. With methyl propiolate in acetonitrile they form a multicomponent mixture difficult to separate chromatographically.

The ^{1}H NMR spectra of the spiro compounds **3, 4** show the presence of two doublets with ^2J = 1.2 Hz in the region 5.07-5.21 ppm due to the protons of a methylene group [3].

IR spectra (KBr) were recorded on an Infralum FT-801 Fourier spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WP-400 (400 and 100 MHz respectively) using $CDCl_3$ and with TMS as internal standard. Mass spectra were taken on a Finnigan MAT-95 XL chromato-mass spectrometer with direct introduction of the sample into the ion source and an ionization energy of 70 eV.

Reaction of the Benzothienopyridines 1,2 with Acetylene Dicarboxylic Ester (General Method). ADCE (3.0 mmol) was added to a solution of the benzothienopyridine **1** or **2** (1.5 mmol) in acetonitrile (25 ml). The reaction was carried out for 10-11 days at room temperature and monitored by TLC. Solvent was distilled off and the residue was placed on an aluminium oxide column (neutral, Brockmann 1). Compounds **3** and **4** were separated by chromatography on aluminium oxide using ethyl acetate–hexane as eluent (1:15).

Dimethyl 1'-methyl-2-methylene-5',6'-dihydro-1'H-spiro[1-benzothiophene-3,4'-pyridine]-2',3'-dicarboxylate (3). Yield 35%. Colorless crystals, mp 122-123ºC, R_f 46 (Sorbfil, ethyl acetate–hexane, 1:3). IR spectrum, ν, cm^{-1}: 1740 (CO), 1679 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.81-1.91 (1H, m, CH_2); 2.03 (1H, td, *J* = 3.9 and *J* = 13.7, CH_2); 2.97 (3H, s, NCH_3); 3.11 (1H, td, *J* = 4.3 and *J* = 12.9, CH_2); 3.30 (3H, s, CO_2CH_3); 3.48 (1H, ddd, *J* = 3.9, *J* = 11.2, and *J* = 12.9, CH_2); 3.95 (3H, s, CO_2CH_3); 5.12 (1H, d, *J* = 1.1, C=CH_2); 5.21 (1H, d, *J* = 1.1, C=CH_2); 6.95-6.97 (1H, m, H-4); 7.02 (1H, dt, *J* = 1.5 and *J* = 7.3, H-5); 7.09-7.17 (2H, m, H-6,7). ^{13}C NMR spectrum, δ, ppm: 23.8, 35.8, 39.7, 44.8, 50.6, 52.8, 87.1, 105.2, 121.3, 122.7, 124.7, 127.3, 136.8, 146.7, 151.6, 155.7, 166.1, 166.5. Found, %: C 62.67; H 5.50; N 9.25. M^+ 345. $C_{18}H_{19}NO_4S$. Calculated, %: C 62.59; H 5.54; N 9.27. M 345.

Dimethyl 1',5-dimethyl-2-methylene-5',6'-dihydro-1'H-spiro[1-benzothiophene-3,4'-pyridine]-2',3'-dicarboxylate (4). Yield 20%. Colorless crystals, mp 123-124ºC, R_f 0.41 (Sorbfil, ethyl acetate–hexane, 1:3). IR spectrum, ν, cm^{-1}: 1740 (CO), 1679 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.82 (1H, ddd, *J* = 4.2, *J* = 11.3, and *J* = 13.8, CH_2); 1.97 (1H, td, *J* = 3.8 and *J* = 13.8, CH_2); 2.23 (3H, s, $ArCH_3$); 2.94 (3H, s, NCH_3); 3.07 (1H, td, *J* = 4.2 and 12.9, CH_2); 3.28 (3H, s, CO_2CH_3); 3.42-3.46 (1H, m, CH_2); 3.93 (3H, s, CO_2CH_3); 5.07 (1H, d, *J* = 1.3, C=CH_2); 5.17 (1H, d, *J* = 1.3, C=CH_2); 6.75 (1H, s, H-4); 7.02 (1H, d, *J* = 7.8, H-6); 6.92 (1H, d, *J* = 7.8, H-7). ^{13}C NMR swpectrum, δ, ppm: 21.0, 35.8, 39.7, 44.8, 50.7, 52.9, 54.0, 96.6, 105.1, 121.0, 123.4, 128.2, 133.2, 134.5, 146.7, 151.6, 156.1, 166.2, 166.6. Found, %: C 63.59; H 5.81; N 3.88. M^+ 359. $C_{19}H_{21}NO_4S$. Calculated, %: C 63.49; H 5.89; N 3.90. M 359.

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REFERENCES

1. L. G. Voskressensky, T. N. Borisova, A. V. Listratova, E. A. Sorokina, S. V. Tolkunov, and A. V. Varlamov, *Izv. Akad. Nauk, Ser. Khim.*, 1003 (2007).
2. L. G. Voskressensky, A. V. Listratova, T. N. Borisova, S. A. Kovaleva, R. S. Borisov, and A. V. Varlamov, *Tetrahedron*, **64**, 10443 (2008).
3. H. Günther, *Introduction to an NMR Spectroscopy Course* [Russian translation], Mir, Moscow (1984), p. 418.