INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN CHEMISTRY AND PHARMACEUTICAL SCIENCES

(p-ISSN: 2348-5213: e-ISSN: 2348-5221)
www.ijcrcps.com

Research Article

HETEROCYCLIZATION OF ETHYL 2-AMINO-4,9-DIOXO-4,9-DIHYDRONAPHTHO [2,3-B]THIOPHENE-3-CARBOXYLATE WITH ARYLISOCYANATES

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Abstract

The synthesis of new 3-arylnaphtho[2',3':4,5]thieno[2,3-d]pyrimidine-2,4,5,10(1H,3H)-tetraones was carried out by the heterocyclization of ethyl-2-amino-4,9-dioxo-4,9-dihydronaphtho[2,3-b]thiophene-3-carboxylate with a series of arylisocyanates in the presence of pyridine.

Keywords: ethyl 2-amino-4,9-dioxo-4,9-dihydronaphtho[2,3-b]thiophene-3-carboxylate, arylisocyanates, 3-arylnaphtho[2',3':4,5]thieno[2,3-d]pyrimidine-2,4,5,10(1H,3H)-tetraones

Introduction

One of the most important tasks of organic and pharmaceutical chemistry is creation, development and implementation in practical healthcare of high-potent and low-toxic medicinal drugs. Heterocyclic compounds take important place in the list of used medicinal products, where special role is played by azoles, azines, and condensed systems. The most attention is paid to pyrimidinediones because many of them participate in physiological processes, are found in the nucleic acids, ferments and other biologically important systems. A series of derivatives of such pyrimidines, including barbituric acids, is widely used as medicinal products (5-fluorouracil, potassium orotate, barbiturates, etc.). On the other hand, these compounds are widely applied to resolving general problems of heterocycle chemistry [1-13].

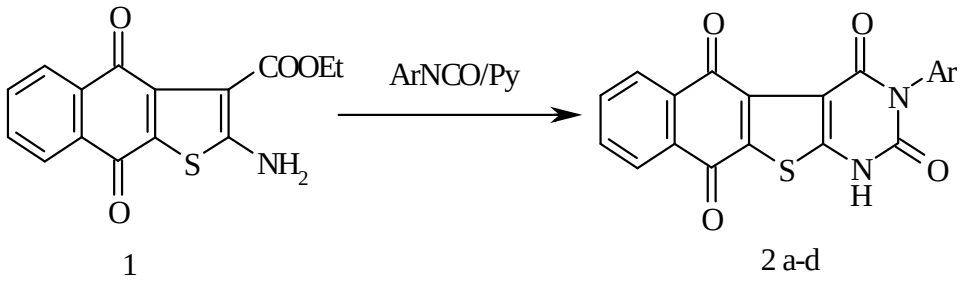
By this time, a great deal of condensed quinoid systems including in their structures nitrogen-bearing or other heterocycles have been synthesized in the world. At the same time, the scientific literature contains far less information about such compounds with sulphur-bearing heterocycles, in particular, thiophene or pyrimidinedione.

Taking into account the above-mentioned, we conducted an interaction of ethyl 2-amino-4,9-dioxo-4,9-dihydronaphtho[2,3-b]thiophene-3-carboxylate **1** with a series of arylisocyanates in the presence of pyridine along with creation of 3-arylnaphtho[2',3':4,5]thieno[2,3-d]pyrimidine-2,4,5,10(1H,3H)-tetraones **2 a-d**:

All the chemicals used for the synthesis of the compounds were purchased from Aldrich, Merck AG and Acros Chemicals. Melting points of the compounds were recorded on an electrothermal-9200 digital melting points apparatus and are uncorrected.

NMR spectra ^{1}H и ^{13}C are recorded on the device Varian Mercury-400 (400 and 100 MHz respectively) under 25^{o}C in the solution DMSO-d_6 (dimethylsulphoxide), internal standard TMS (tetramethylsilane). IR-spectra are obtained on spectrophotometer Specord M80 in KBr

tablets. Reaction path was controlled by TLC (thin layer chromatography) method on UV-254 plates in the system of eluents benzol-acetonitrile, 5:1. Element analysis was carried out on the analyzer Thermo Finnigan Flash EA 1112.



Ar= Ph (a); p-ClPh (b); p-NO2Ph (c); p-MePh (d)

Scheme 1. Synthetic route of the preparation of 3-arylnaphtho[2',3':4,5]thieno[2,3-d]pyrimidine-2,4,5,10(1H,3H)-tetraones **2a-d**

3-arylnaphtho[2',3':4,5]thieno[2,3-d]pyrimidine-2,4,5,10(1H,3H)-tetraones 2 a-d (general procedure).

To the solution (0.654 mmol) of 2-amino-3-carbetoxynaphtho[2,3-b]thiophen-4.9-dione 1 in pyridine with permanent mixing an equimolar amount of arylisocyanate is added. The reaction mixture is warmed under 75-80^{o}C for 5 hours. The reaction mixture is filtered and washed with water. The resultant precipitate of the product is dried in vacuum.

3-Phenylnaphtho[2',3':4,5]thieno[2,3-d]pyrimidine-2,4,5,10(1H,3H)-tetraone 2a. Yield 75%, mp >250 ^{o}C. ^{1}H NMR spectrum, δ, ppm: 8.43 (1H, s, NH); 8,25-7,98 (2H, m, HAr), 7.77-7.66 (2H, m, HAr); 7,19-7,55 (5H, m, HPh). ^{13}C NMR spectrum, δ, ppm: 108.76, 123.39 (C thiophene); 126.59 (C Ar); 127.23 (C Ar); 128.93, 129.22 (C Ph); 129.72 (C thiophene); 129.77 (2C Ph); 130.4, 132.04, 133.15, 134.13 (C Ar); 135.86 (C Ph); 149.18 (C=O); 150.96 (C thiophene); 158.38 (C=O); 176.46 (C=O); 179.25 (C=O). Found, %: C 64.22; H 2.76; N 7.41; S 8.53. $C_{20}H_{10}N_2O_4S$. Calculated, %: C 64.16; H 2.69; N 7.48; S 8.57.

3-(4-Chlorophenyl)naphtho[2',3':4,5]thieno[2,3-d]pyrimidine-2,4,5,10(1H,3H)-tetraone 2 b. Yield 81%, mp >250 ^{o}C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.51 (1H, s, NH); 8,10-7,95 (4H, m, HAr), 7.72, 7.70, 7.65, 7.64 (4H, dd, ^{2}J= 8.21, HAr). ^{13}C NMR spectrum, δ, ppm: 108.75, 123.40 (C thiophene); 126.57 (C Ar); 127.23 (C Ar); 129.58 (2C Ar); 129.72 (C thiophene); 130.41, 132.04 (C Ar); 132.38 (2C Ar), 133.15, 134.13 (2C Ar); 134.68, 134.93 (2C Ar); 148.85 (C=O); 150.96 (C thiophene); 158.05 (C=O); 176.45 (C=O); 179.25 (C=O). Found, %: C 58.71; H 2.25; Cl 8.61; N 6.91; S 7.89. $C_{20}H_9ClN_2O_4S$. Calculated, %: C 58.76; H 2.22; Cl 8.67; N 6.85; S 7.84.

3-(4-Nitrophenyl)naphtho[2',3':4,5]thieno[2,3-d]pyrimidine-2,4,5,10(1H,3H)-tetraone 2c. Yield 79%, mp >250 ^{o}C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.57 (1H, s, NH); 8.54, 8.52, 8.45, 8.43 (4H, dd, ^{2}J= 9.21, HAr); 8.13-7.87 (4H, m, HAr). ^{13}C NMR spectra, δ, ppm: 108.76, 123.39 (C thiophene); 124.8 (2C Ar); 126.29 (C Ar); 127.23 (C Ar); 129.72 (C thiophene); 130.4 (C Ar), 131.42 (2C Ar); 132.04 (C Ar); 133.15 (C Ar); 134.13 (C Ar); 140.75 (C Ar); 149.35 (C=O); 149.45 (C Ar); 150.96 (C thiophene); 158.55 (C=O); 176.46 (C=O); 179.25 (C=O). Found, %: C 57.23; H 2.23; N 10.09; S 7.71 $C_{20}H_9N_3O_6S$. Calculated, %: C 57.28; H 2.16; N 10.02; S 7.65.

3-(*p*-Tolyl)naphtho[2',3':4,5]thieno[2,3-d]pyrimidine-2,4,5,10(1H,3H)-tetraone 2d. Yield 72%, mp >250 ^{o}C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.45 (1H, s, NH); 8,12-7,93 (4H, m, HAr), 7.64, 7.62, 7.44, 7.42 (4H, dd, ^{2}J= 8.2, HAr). ^{13}C NMR spectrum, δ, ppm: 20.89 (C CH_3); 108.76, 123.39 (C Thiophene); 126.59 (C Ar); 127.23 (C Ar); 128.93, 129.22 (C Ph); 129.72 (C Thiophene); 129.77 (2C Ph); 130.4, 132.04, 133.15, 134.13 (C Ar); 135.86 (C Ph); 149.18 (C=O); 150.96 (C thiophene); 158.38 (C=O); 176.46 (C=O); 179.25 (C=O). Found, %: C 64.91; H 3.15; N 7.28; S 8.19. $C_{21}H_{12}N_2O_4S$. Calculated, %: C 64.94; H 3.11; N 7.21; S 8.26.

Conflicts of Interest

The authors declare no conflict of interest

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