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Triazolo[4′,3′:4,5] [1,3,4]thiadiazolo[2,3—b]quinazolin-6-one

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3-Methyl-6*H*-[1,2,4]triazolo[4′,3′:4,5] [1,3,4]thiadiazolo[2,3—b]quinazolin-6-one (**6**) has been synthesized by the condensation of isatoic anhydride (**1**) with 4-amino-5-mercapto-3-methyl-[1,2,4]triazole (**2**) and final cyclisation of the intermediate **3** with $POCl_3$ and PCl_3. Alternatively **6** could also be synthesized by the condensation of 3-amino-2-mercapto-3*H*-quinazolin-4-one (**7**) with *N*-carbethoxy hydrazine in presence of hydrochloric acid and final cyclisation of the intermediate **8** with acetic acid. The structures have been confirmed on the basis of IR, PMR and analytical results.

(Keywords: Heterocycles; Infrared; ^{1}H-*NMR)*

Triazolo[4′,3′:4,5] [1,3,4]thiadiazolo[2,3—b]chinazolin-6-on

3-Methyl-6*H*-[1,2,4]triazolo[4′,3′:4,5] [1,3,4]thiadiazolo[2,3—b]chinazolin-6-on (**6**) wurde mittels Kondensation von Isatoesäureanhydrid (**1**) mit 4-Amino-5-mercapto-3-methyl[1,2,4]triazol (**2**) und anschließender Cyclisierung von Zwischenverbindung **3** mit $POCl_3$ und PCl_3 dargestellt. Als Alternative konnte **6** auch über die Kondensation von 3-Amino-2-mercapto-3*H*-chinazolin-4-on (**7**) mit *N*-Carbethoxyhydrazin in Gegenwart von HCl und anschließender Cyclisierung der Zwischenverbindung **8** mit Essigsäure synthetisiert werden. Die Strukturen der Verbindungen wurden mittels IR, ^{1}H-NMR und Mikroanalyse nachgewiesen.

Introduction

Fascinated by the physiological importance of quinazolines, thiadiazoles and triazoles it was considered worthwhile to prepare new compounds incorporating all three rings. In this paper we describe the synthesis of 3-methyl-6*H*-[1,2,4]triazolo[4′,3′:4,5] [1,3,4]thiadiazolo-[2,3—b]quinazolin-6-one (**6**).

Results and Discussion

The synthesis of **6** could be achieved by the condensation of isatoic anhydride (**1**) with 4-amino-5-mercapto-3-methyl[1,2,4]triazole (**2**). The first step led to the formation of *N*-[(3-mercapto-5-methyl-4*H*-[1,2,4]triazol-4-yl) carbamoyl] anthranilic acid (**3**). The structure of **3** has been confirmed on the basis of IR and PMR studies.

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It gave IR absorption bands at 2720, 2660 (OH of COOH), 3210, 3130 (NH), 1715 (C=O of COOH) and 1643 cm^{-1} due to —N—CO—N—. Its PMR (δ/ppm; $CDCl_3 + TFA$) showed a singlet at 2.60 (3H) due to the methyl protons. In addition, it also showed another singlet of one proton intensity at 10.00 assignable to the carboxylic acid proton. The four aromatic protons appeared as a multiplet at 7.27-8.27.

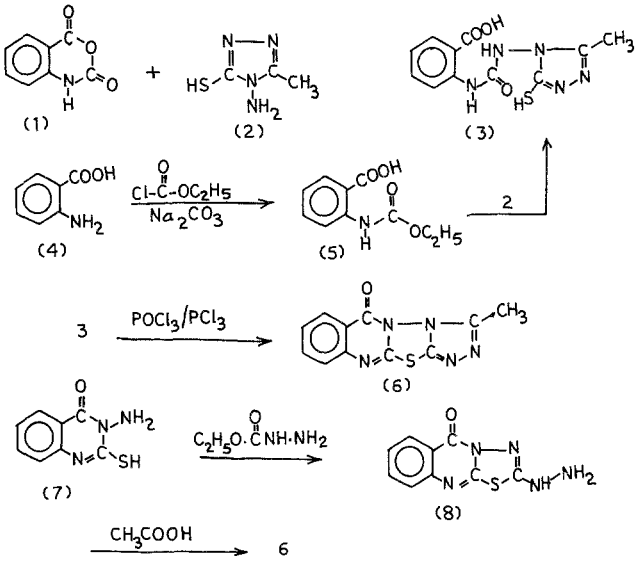
Alternatively the intermediate **3** could also be prepared by treating anthranilic acid (**4**) with ethyl chloroformate in the presence of aqueous sodium carbonate and condensing the intermediate **5** thus formed with **2** in ethanol.

3 underwent cyclisation with $POCl_3$ and PCl_3 to give the final product **6**.

Its IR showed a sharp band at 1660 due to —CO—N<; the bands originally present in **3** had completely disappeared. The PMR spectrum of **6** in *DMSO-d_6* showed a singlet (3H) at 3.13 assignable to methyl while the four aromatic protons appeared as a multiplet (4H) at 7.03-7.94.

In the second approach **6** has been prepared as follows: 3-Amino-2-mercapto-3*H*-quinazolin-4-one (**7**) was condensed with *N*-carbethoxy hydrazine in presence of hydrochloric acid to give 2-hydrazino-5*H*-thiadiazolo[2,3—b]quinazolin-5-one (**8**) which in its IR showed absorption bands at 3240, 3205 and 3160 due to NH and NH_2. It also showed another band at 1653 due to cyclic amide (—CO—N<).

8 on refluxing with acetic acid underwent cyclisation to give **6** as established by its m.p., m.m.p., tlc, superimpossable IR and identical PMR spectrum with the compound obtained by the first method.



Experimental

Melting points were determined in open glass capillaries using a liquid paraffin bath and are uncorrected. IR spectra were recorded in nujol on a Perkin-Elmer 377, 621 and PMR on a Varian EM-390 90 MHz spectrometer using *TMS* as the internal reference. The analytical values (C, H, N) agree with the proposed structures of **3**, **5**, **6**, and **8**.

4-Amino-5-mercapto-3-methyl-[1,2,4]-triazole (**2**)

2 was prepared starting from thio-carbohydrazide[1] and excess of acetic acid according to the procedure described by *Saikachi* and *Kanaoka*[2].

N-[(3-mercapto-5-methyl-4H-[1,2,4]-triazol-4-yl) carbamoyl] anthranilic acid (**3**)

Isatoic anhydride (**1**)[3] (**1**,63 g, 0.01 mol) and 4-amino-5-mercapto-3-methyl-[1,2,4]triazole (**2**) (1.43 g; 0.011 mol) were suspended in dry xylene (400 ml). The reaction mixture was refluxed for 8 h. It was filtered while hot to remove unreacted reactants. On cooling a fluffy material separated out. It was filtered under suction and crystallized from ethanol, m.p. 198°; yield 2 g (62%). $C_{11}H_{11}N_5O_3S$.

IR (in nujol): 3 210, 3 130, 2 720, 2 660, 1 715, 1 643, 1 565, 1 437, 1 360, 1 300, 1 240, 1 205, 1 050, 1 030, 910, and 735 cm^{-1}.

PMR ($CDCl_3$ + *TFA*): 2.60 (s, 3 H, CH_3), 7.27-8.27 (m, 4 H, aromatic), 10.00 (s, 1 H, —COOH).

N-Carbethoxy anthranilic acid (**5**)

It was prepared by the modification of the method reported in [4]. To a solution of anthranilic acid (1.37 g; 0.01 mol) in 5% aqueous sodium carbonate (10.6 ml, 0.53 g, 0.01 mol) was added a solution of ethyl chloroformate (0.96 ml, 0.01 mol) in ethanol (20 ml) dropwise with stirring at room-temperature when the product separated out immediately. After keeping overnight, the mixture was diluted with water, filtered under suction, washed with water and crystallized from ethanol, m.p. 126°; yield, 1.70 g (85%). $C_{10}H_{11}NO_4$.

IR (in nujol): 3 265, 2 685, 2 595, 1 715, 1 700, 1 635, 1 560, 1 490, 1 430, 1 385, 1 300, 1 230, 1 200, 1 145, 1 050, 760, and 745 cm^{-1}.

PMR ($CDCl_3$): 1.40 (t, 3 H, CH_2—C**H**$_3$), 4.36 (q, 2 H, C**H**$_2$—CH_3), 7.03-8.67 (m, 4 H, aromatic), 10.33 (s, 1 H, —COOH) and 10.97 (s, 1 H, —NH, exchangeable with D_2O).

Formation of **3** *via* **5**

To a solution of **5** (1.045 g; 0.005 mol) in ethanol (25 ml) was added the solution of 4-amino-5-mercapto-3-methyl-[1,2,4]triazole (**2**) (0.65 g; 0.005 mol) in the same solvent (50 ml). The contents were refluxed on a steam bath for 8 h. Ethanol was distilled off and the residue was crystallized from ethanol. It was found to be compound **3** as established by m.p., m.m.p. 198°, tlc and superimposable IR spectrum with the compound obtained in step 2; yield 1.025 g (70%). $C_{11}H_{11}N_5O_3S$.

3-Methyl-6H-[1,2,4]triazolo[4',3':4,5] [1,3,4]thiadiazolo[2,3--b] quinazolin-6-one (**6**) *via* **3**

A mixture of **3** (200 mg), phosphoryl chloride (3 ml) and phosphorous trichloride (3 ml) was stirred at room temperature for 3 h. Finally it was refluxed for 1 h, cooled to room temperature and poured over crushed ice. A solid separated after keeping it overnight was collected under suction and crystallized from a mixture of ethanol and chloroform, m.p. 240°; yield 100 mg (57%), $C_{11}H_7N_5OS$.

2-Hydrazino-5H-thiadiazolo[2,3—b]quinozolin-5-one (**8**)

To a solution of 3-amino-2-mercapto-3*H*-quinazolin-4-one (**7**)[5] (1 g) in ethanol (250 ml) was added *N*-carbethoxy hydrazine[6,7] (0.54 g) and hydrochloric acid (0.25 ml). The contents were refluxed for 10 h. Ethanol was distilled off completely. On basification with 10% sodium carbonate solution, the solid thus separated was collected under suction, washed with water and crystallized from ethanol, m.p. 199°; yield 745 mg (62%), $C_9H_7N_5OS$.

IR (in nujol): 3 240, 3 205, 3 160, 1 653, 1 615, 1 530, 1 460, 1 377, 1 265, 1 225, 1 180, 1 162, 980, 920, 770, and 660 cm^{-1}.

Formation of **6** *via* **8**

8 (0.466 g; 0.002 mol) was taken in excess of glacial acetic acid (20 ml). The contents were refluxed over a sand bath. The suspended material changed into a clear solution after one h of refluxing but with the advancement of refluxing a new solid started separating out. It was refluxed for 4 h in all to ensure completion of reaction. On cooling, the separated solid was filtered under suction, washed with dilute sodium carbonate solution and finally with water. Crystallization from ethanol gave the required product **6** with m.p. 238 in 53% yield.

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