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Syntheses of Naphtho[1′,2′:4,5]thiazolo[2,3-*c*]-1,2,4-triazoles and-[3,2-*d*]tetrazole

Darstellung von Naphtho[1′,2′:4,5]thiazolo[2,3-*c*]-1,2,4-triazolen und -[3,2-*d*]tetrazol

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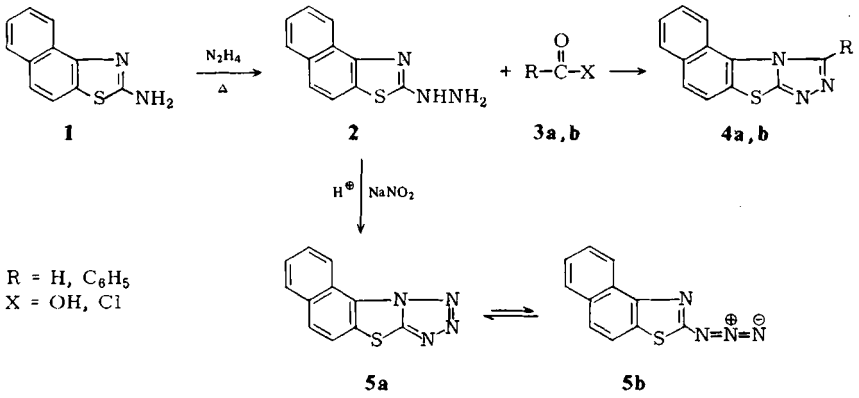
In the course of studying the structure-activity relationships of compounds in the naphthimidazo-thiazole series[1,2], a process of structure modification was developed by increasing the hetero atoms from two to three nitrogens in the imidazole component. Thus, a number of substituted naphtho[1′,2′:4,5]thiazolo[3,2-*b*]-1,2,4-triazoles has been synthesized[3] and subjected to biological evaluation. As a progressive continuation of our study, we wish now to report the method of further modification of the naphthothiazolo-triazole system by changing the fusion site from [3,2-*b*]to [2,3-*c*] and the fusion component from triazole to tetrazole.

The readily available starting material, 2-aminonaphtho[1,2-*d*]thiazole **(1)**[1,4], was converted to 2-hydrazinonaphtho[1,2-*d*]thiazole **(2)** in 96 % yield by exchange amination with hydrazine hydrate and hydrazine monohydrochloride in ethylene glycol on heating under nitrogen atmosphere[5].

Refluxing **2** with excess amount of formic acid **(3a)** or benzoyl chloride **(3b)** provided naphtho[1′,2′:4,5]thiazolo[2,3-*c*]-1,2,4-triazole **(4a)** and its 3-phenyl derivative **4b** in 75 and 53 % yield, resp. Treating **2** with sodium nitrite in acetic acid under cooling afforded the corresponding [3,2-*d*]tetrazole **(5a)** in 77 % yield.



1 **2** **3a,b** **4a,b**

5a **5b**

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The elemental analysis and spectral investigation of the products gave consistent data for the assigned structures **4a, b** and **5a**. However, it has been claimed that many condensed tetrazole ring systems have a tendency to tautomerize to the azide form[6-9]. The azido-tetrazole tautomerism of compound **5** was recognized from the characteristic absorption bands in the IR spectrum. An obscure absorption peak near 2130 cm^{-1} in contrast to the distinct ring stretching bands at 1060, 970 and 720 cm^{-1} demonstrated that the fused tetrazole form **5a** was much favored over the ring-opened azide form **5b** in the solid state at ambient temperature. This finding is also in accordance with those phenomena observed by *Postovskii* and coworkers[7] from the same compound in other medium and at higher temperature.

An attempt made to generate other 3-substituted homologues of **4a** by heating **2** with acetic acid, trifluoroacetic anhydride or triethyl ortho propionate led only to the open-chain acylohydrazides. Ring-closure reactions failed even on prolonged heating at elevated temperature or by treating with polyphosphoric acid.

The pharmacological evaluation of the products for the possible antihypertensive or diuretic activity is still in progress and the results will be reported elsewhere.

Experimental Part

2-Hydrazinonaphtho[1,2-d]thiazole **(2)**

A suspension of 10.0 g (0,05 mol) of **1**, 5.9 g (0.1 mol) of 85 % hydrazine hydrate and 3.5 g (0.05 mol) of hydrazine monohydrochloride in 40 ml of ethylene glycol was heated at 140° in nitrogen atmosphere for 4 h. After cooling, the reaction mixture was diluted with 40 ml of water and the precipitate was recrystallized from DMF/ethanol to give 10.5 g (97 %) of light yellow crystalline powder, mp. 226–227°. IR (KBr): 3350 (N-H), 3060 (=C-H), 1640, 1560 (C=N/C=C), 1370 (C-N), 910 (=C-H), 750 (C-S) cm^{-1}. NMR (DMSO-D_6): δ (ppm) = 5.16 (s, NH_2), 7.40–7.65 (m, 4H, ArH), 7.90 (m, H-4), 8.39 (d, H-9, J = 6.5 Hz), 9.20 (s, NH). $C_{11}H_9N_3S$ (215.3) Calcd. C 61.4 H 4.21 N 19.5 S 14.9; Found C 61.7 H 4.07 N 19.4 S 15.1.

Naphtho[1',2':4,5]thiazolo[2,3-c]-1,2,4-triazole **(4a)**

A solution of 2.2 g (0.01 mol) of **2** in 36.6 g (0.8 mol) of **3a** was refluxed for 3 h. The excess formic acid was distilled off i. vac. and the residue was recrystallized from ethanol to give 1.7 g (75 %) of white needles, mp. 228–229°. UV (MeOH): λmax (logε) = 225 (4.45), 246 (4.53), 290 (3.84), 334 (3.20) nm; λmin (logε) = 232 (4.39), 281 (3.70), 329 (3.01) nm. IR (KBr): 3060 (=C-H), 1600, 1480 (C=N/C=C), 1320 (C-N), 760 (C-S) cm^{-1}. NMR (DMSO-D_6): δ (ppm) = 7.71 (m, H-6,7), 7.98–8.16 (m, 3H, ArH), 8.55 (d, H-10, J = 6.5 Hz), 10.08 (s, H-3). $C_{12}H_7N_3S$ (225.3) Calcd. C 64.0 H 3.13 N 18.7 S 14.2; Found C 64.0 H 3.13 N 18.3 S 14.3.

3-Phenylnaphtho[1',2':4,5]thiazolo[2,3-c]-1,2,4-triazole **(4b)**

A solution of 2.2 g (0.01 mol) of **2** in 14.1 g (0.1 mol) of **3b** was refluxed for 5 h. After cooling, the solid product was washed with ethanol and recrystallized from ethanol and from benzene to give 1.6 g (53 %) of white needle crystals, mp. 219–220°. UV (MeOH): λmin (logε) = 217 (4.53), 247 (4.44), 336 (3.38) nm; λmin (logε)= 238 (4.41), 330 (3.26) nm. IR (KBr): 3040 (=C-H), 1640, 1580 (C=N/C=C), 1370 (C-N), 710 (C-S) cm^{-1}. NMR (DMSO-D_6): δ (ppm) = 6.98 (m, H-6, 7), 7.50–7.80 (m, 7H,

ArH), 8.14 (m, H-5, 10). $C_{18}H_{11}N_3S$ (301.4) Calcd. C 71.7 H 3.67 N 13.9 S 10.6; Found C 71.4 H 4.07 N 13.7 S 11.0.

Naphtho[1',2':4,5]thiazolo[3,2-d]tetrazole **(5a)**

A solution of 2.2 g (0.01 mol) of **2** in 150 ml of 50 % acetic acid was kept at 0° in an ice-bath and treated with a solution of 2.1 g (0.03 mol) of sodium nitrite in 10 ml of water under stirring. The reaction mixture was diluted with 300 ml of ice-water and the precipitate was decolorized in dioxane and recrystallized from ethanol to give 1.8 g (77 %) of light yellow needle crystals, mp. 119–120°. UV (MeOH): λmax (logε) = 236 (4.57), 306 (3.93), 333 (3.80) nm; λmin (logε) = 271 (3.72), 329 (3.71) nm. IR (KBr): 3060 (=C-H), 2130 (N_3), 1580, 1560 (C=N/C=C), 1335 (C-N), 1060, 970, 720 (tetrazole), 710 (C-S) cm^{-1}. NMR (DMSO-D_6): δ (ppm) = 6.98 (m, H-6, 7), 7.50–7.80 (m, 3H, ArH), 8.14 (d, H-10, J = 7.0 Hz). $C_{11}H_6N_4S$ (226.3) Calcd. C 58.4 H 2.67 N 24.8 S 14.2; Found C 58.5 H 2.82 N 24.4 S 14.3.

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