ISSN 1070-3632, Russian Journal of General Chemistry, 2014, Vol. 84, No. 12, pp. 2480–2482. © Pleiades Publishing, Ltd., 2014.
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LETTERS TO THE EDITOR

Synthesis and Reactivity of 7-Amino-3-*tert*-butylpyrazolo[5,1-*c*][1,2,4]triazin-4(6*H*)-one

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Received July 21, 2014

Keywords: diazotization, condensation, formolysis, pyrazolo[5,1-*c*][1,2,4]triazine, imidazo[1',2':2,3]pyrazolo-[5,1-*c*][1,2,4]triazine

DOI: 10.1134/S1070363214120287

1,2,4-Triazines are biologically active compounds exhibiting pesticidal and pharmacophore activity. In particular, pyrazolo[5,1-*c*][1,2,4]triazines showed high antiviral, antimicrobial, and antitumor activity [1–3]. Promising synthons for obtaining previously undescribed derivatives are 7-aminopirazolo[5,1-*c*][1,2,4]-triazines containing multiple reaction sites, including the amino group.

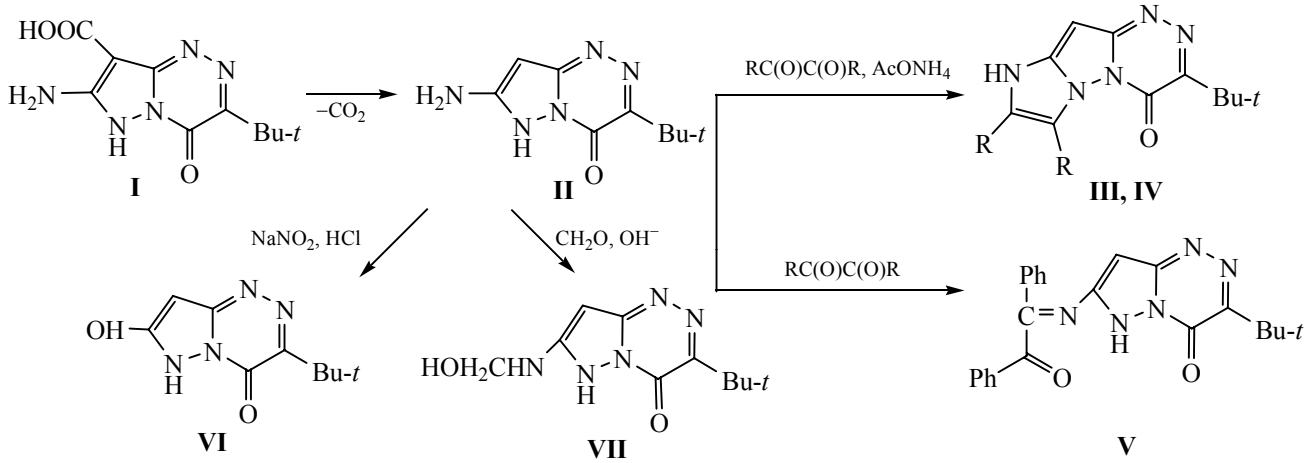
Previously, we have synthesized a series of 7-amino-3-*tert*-butyl-8-R-pyrazolo[5,1-*c*][1,2,4]triazin-4(6*H*)-ones and studied their reactivity [3–5]. In particular, 7-amino-3-*tert*-butylpyrazolo[5,1-*c*][1,2,4]triazin-4(6*H*)-one **II** has been synthesized, and its reactivity has been studied.

7-Amino-3-*tert*-butyl-4-oxo-4,6-dihydropyrazolo-[5,1-*c*][1,2,4]triazine-8-carboxylic acid **I** obtained by alkaline hydrolysis of ethyl 7-amino-3-*tert*-butyl-4-oxo-4,6-dihydropyrazolo[5,1-*c*][1,2,4]triazine-8-carboxylate was used as the starting material. Boiling of compound **I** in DMF for 10–12 h resulted in decarboxylation to give 7-amino-3-*tert*-butylpyrazolo-[5,1-*c*][1,2,4]triazin-4(6*H*)-one **II** (Scheme 1).

In the ^{1}H NMR spectrum of **II** there was the signal of the C^{8}H proton of heterocycle at 8.4 ppm. The IR spectrum of compound **II** contained no absorption band of the carboxy group at 1720 cm^{-1} (C=O).

Refluxing (15 h) of compound **II** in glacial acetic acid in the presence of diphenylethanedione and an excess of ammonium acetate led to the formation of 3-*tert*-butyl-7,8-diphenyl-9*H*-imidazo[1',2':2,3]pyrazolo-[5,1-*c*][1,2,4]triazin-4-one **III**. The reaction of **II** with diphenylethanedione in the absence of ammonium

Scheme 1.



acetate (AcOH, reflux, 2 h) resulted in 3-*tert*-butyl-7-[(benzoylphenylmethylidene)amino]pyrazolo[5,1-*c*]-[1,2,4]triazin-4(6*H*)-one **V**. Mass spectra of compounds **III** and **V** contained peaks of molecular ions $[M + H]^+$ with *m*/*z* 383.1741 and 400.1768, respectively.

3-*tert*-Butyl-7,8-dimethyl-9*H*-imidazo[1',2':2,3]pyrazolo[5,1-*c*][1,2,4]triazin-4-one **IV** was obtained similarly to compounds **III** using diacetyl.

Diazotization of **II** in diluted HCl was performed by adding a solution of sodium nitrite at 0°C over 1–1.5 h. The resulting diazo compound was separated and boiled in a solution of 2N hydrochloric acid, resulting in the formation of 3-*tert*-butyl-7-hydroxypyrazolo[5,1-*c*][1,2,4]triazin-4(6*H*)-one **VI**.

3-*tert*-Butyl-7-[(hydroxymethyl)amino]pyrazolo[5,1-*c*]-[1,2,4]triazin-4(6*H*)-one **VII** was obtained by treating compound **II** in an alkaline medium (pH 9–10) with formaldehyde solution at room temperature.

All obtained compounds were high melting crystalline substances insoluble in water and oxygen-containing organic solvents. Composition and structure of the compounds obtained were established by elemental analysis, UV, IR, ^{1}H, ^{13}C NMR spectroscopy, and mass spectrometry data.

Compound **I** was obtained by procedure [5] (mp >300°C).

7-Amino-3-*tert*-butylpyrazolo[5,1-*c*][1,2,4]triazin-4(6*H*)-one (II). A solution of 0.25 g (1 mmol) of 7-amino-3-*tert*-butyl-4-oxo-4,6-dihydropyrazolo[5,1-*c*]-[1,2,4]triazine-8-carboxylic acid **I** in 10 mL of DMF was refluxed for 10–12 h, then cooled, and filtered. Then distilled water was added to the filtrate (1 : 1). The precipitate was filtered off and recrystallized from 2-propanol. Yield 0.14 g (69%), pale pink crystals, mp >300°C. IR spectrum, ν, cm^{-1}: 3437, 3298, 3162, 2951, 2615, 1618 (C=O), 1585, 1531, 1457, 1389, 1360, 1321, 1209, 1104, 947, 814, 781, 738. UV spectrum, λ_{max} (log ε), nm: 211 (2.005), 256 (2.078), 332 (0.681). ^{1}H NMR spectrum, δ, ppm: 1.4 s (9H, Bu-*t*), 5.7 s (2H, NH_2), 8.4 s (1H, CH), 13.71 s (1H, NH). Found, %: C 52.19, 52.18; H 6.31, 6.30; N 33.83, 33.80. $C_9H_{13}N_5O$. Calculated, %: C 52.16; H 6.32; N 33.79.

3-*tert*-Butyl-7,8-diphenyl-9*H*-imidazo[1',2':2,3]-pyrazolo[5,1-*c*][1,2,4]triazin-4-one (III). To a suspension of 0.41 g (2 mmol) of compound **II** in 5 mL of glacial acetic acid was added 1.54 g (20 mmol) of ammonium acetate and 0.63 g (3 mmol) of diphenylethanedione. The reaction mixture was refluxed for 15 h, cooled and filtered. The precipitate was dried in air and recrystallized from pyridine. Yield 0.39 g (52%), yellow crystals, mp 241–242°C. IR spectrum, ν, cm^{-1}: 3478, 3252, 3168, 1683 (C=O), 1622, 1482, 1330, 1133, 930, 685. UV spectrum, λ_{max} (log ε), nm: 326 (0.718). ^{1}H NMR spectrum, δ, ppm: 1.4 s (9H, Bu-*t*), 6.35 s (1H, CH), 7.7–7.4 m (10H, Ph), 11.4 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 28.06 [C($\underline{C}H_3)_3$], 37.06 [$\underline{C}(CH_3)_3$], 126.33 (C^{11}), 129.08 (Ph), 130.18 (Ph), 133.18 (C^{10}), 141.5 (C^7), 142.45 (C^8), 146.97–147.22 (C^4), 160.08 (C^3), 166.05 (C^{12}). Mass spectrum, *m*/*z*: 383.1741 $[M + H]^+$, 405.1560 $[M + Na]^+$, 421.1299 $[M + K]^+$. Found, %: C 72.05, 72.04; H 5.46, 5.45; N 18.23, 18.25. $C_{23}H_{21}N_5O$. Calculated, %: C 72.06; H 5.48; N 18.27.

3-*tert*-Butyl-7,8-dimethyl-9*H*-imidazo[1',2':2,3]-pyrazolo[5,1-*c*][1,2,4]triazin-4-one (IV). To a suspension of 0.41 g (2 mmol) of compound **II** in 5 mL of glacial acetic acid was added 1.54 g (20 mmol) of ammonium acetate and 0.44 mL (5 mmol) of diacetyl. The reaction mixture was stirred at 45–50°C for 15 h, then cooled and filtered. The residue was recrystallized from 1-butanol. Yield 0.3 g (57%), beige crystals, mp 269–270°C. IR spectrum, ν, cm^{-1}: 3456, 3334, 3248, 3166, 2958, 1672 (C=O), 1625, 1590, 1532, 1460, 1418, 1352, 1269, 1118, 964, 901, 772, 704. UV spectrum, λ_{max} (log ε), nm: 253 (0.745), 361 (0.721). ^{1}H NMR spectrum, δ, ppm: 1.35 s (9H, Bu-*t*), 2.05 s (3H, Me), 2.2 s (3H, Me), 6.0 br. s (1H, CH), 10.65 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 10.10 (CH_3), 24.16 (CH_3), 27.58–27.79 [C($\underline{C}H_3)_3$], 36.76 [$\underline{C}(CH_3)_3$], 83.49 (C^{11}), 142.44 (C^3), 146.59–147.22 (C^4), 148.45 (C^{12}), 158.9 (C^8), 163.64 (C^7), 179.23 (C^{10}). Found, %: C 60.45, 60,41; H 6.61, 6.59; N 26.91, 26.88. $C_{13}H_{17}N_5O$. Calculated, %: C 60.23; H 6.56; N 27.03.

3-*tert*-Butyl-7-[(benzoylphenylmethylidene)amino]-pyrazolo[5,1-*c*][1,2,4]triazin-4(6*H*)-one (V). To a suspension of 0.41 g (2 mmol) of compound **II** in 5 mL of glacial acetic acid was added 0.63 g (3 mmol) of diphenylethanedione. The reaction mixture was refluxed for 2 h, cooled and filtered. The precipitate was dried in air. Yield 0.67 g (84%), yellow crystals, mp 207–209°C (decomp.). IR spectrum, ν, cm^{-1}: 3442, 3377, 3253, 3176, 2970, 2929, 1700 (C=O), 1683 (C=O), 1630, 1536, 1502, 1444, 1352, 1327, 1151, 1122, 1082, 954, 828, 768, 743, 696. UV spectrum, λ_{max} (log ε), nm: 341.4 (0.264), 256.4 (0.356). ^{1}H NMR spectrum, δ, ppm: 1.4 s (9H, Bu-*t*), 6.65 s (1H, CH), 7.4–7.6 m (10H, Ph), 13.15 s (1H, NH). Mass spectrum, *m*/*z*: 400.1768 $[M + H]^+$, 422.1587 $[M + Na]^+$, 438.1327

$[M + K]^+$. Found, %: C 69.2, 69.18; H 5.3, 5.28; N 17.56, 17.57. $C_{23}H_{21}N_5O_2$. Calculated, %: C 69.17; H 5.26; N 17.54.

3-*tert*-Butyl-7-hydroxypyrazolo[5,1-*c*][1,2,4]-triazin-4(6*H*)-one (VI). A solution of 0.41 g (6 mmol) of sodium nitrite in 4 mL of distilled water was added to a mixture of 0.41 g (2 mmol) of compound **II** in 5 mL of 15% HCl at 0°C under stirring within 1 h. The reaction mixture was stirred for 0.5 h at the same temperature, and then filtered. The precipitate was washed with distilled water and refluxed in 10 mL of 2 N HCl for 2 h. After cooling, the precipitate was filtered off, washed with distilled water, re-dissolved in chloroform, filtered, and concentrated. Yield 0.12 g (29%), brown crystals, mp 189–191°C (decomp.). IR spectrum, ν, cm^{-1}: 3170 (OH), 2968, 2930, 1695 (C=O), 1602, 1530, 1458, 1364, 1310, 1271, 1158, 1122, 946, 867, 752. UV spectrum, λ_{max} (log ε), nm: 193.2 (3.284), 200.2 (3.180), 254.8 (2.665), 325.2 (1.310). ^{1}H NMR spectrum, δ, ppm: 1.4 s (9H, Bu-*t*), 3.35 s (1H, OH), 8.3 s (1H, CH), 13.7 br.s (1H, NH). Found, %: C 51.89, 51.90; H 5.78, 5.80; N 26.88, 26.90. $C_9H_{12}N_4O_2$. Calculated, %: C 51.92; H 5.77; N 26.92.

3-*tert*-Butyl-7-[(hydroxymethyl)amino]pyrazolo-[5,1-*c*][1,2,4]triazin-4(6*H*)-one (VII). To a suspension of 0.41 g (2 mmol) of compound **II** and 0.5 mL (6 mmol) of formaldehyde water solution in 5 mL of water under stirring was added dropwise 10% NaOH solution to pH 9–10. The reaction mixture was stirred at room temperature for 18–20 h and then filtered. The filtrate was acidified to pH 7. The formed precipitate was filtered off, washed with hot water, and dried in air. Yield 0.8 g (68%), white crystals, mp 258–260°C (decomp.). IR spectrum, ν, cm^{-1}: 3361 (OH), 2960, 1690 (C=O), 1604, 1536, 1458, 1364, 1290, 1169, 1020, 934, 861, 773, 706. UV spectrum, λ_{max} (log ε), nm: 211.4 (1.496), 265 (1.352), 319.2 (0.761). ^{1}H NMR spectrum, δ, ppm: 1.38 s (9H, Bu-*t*), 4.05 s (1H, OH), 4.3 s (2H, CH_2), 4.85 (1H, NH), 6.9 s (1H, CH), 13.4 s (1H, NH). Found, %: C 50.61, 50.60; H 6.37, 6.36; N 29.56, 29.58. $C_{10}H_{15}N_5O_2$. Calculated, %: C 50.63; H 6.33; N 29.54.

IR spectra were recorded on an Agilent Cary 660 Fourier spectrometer from a thin layer. UV spectra were registered on a Shimadzu UV-1800 spectrophotometer. ^{1}H (300 MHz) and ^{13}C NMR spectra (75.47 MHz) were taken on a Bruker AM-300 spectrometer in DMSO-d_6 solutions, internal reference HMDS. Mass spectra were recorded on a Bruker micrOTOF II mass spectrometer. Purity of the obtained compounds was monitored by TLC using Silufol UV-254 plates, eluting with a chloroform–methanol mixture (9 : 1) and detecting with UV light.

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