Chemistry of Heterocyclic Compounds, Vol. 38, No. 6, 2002

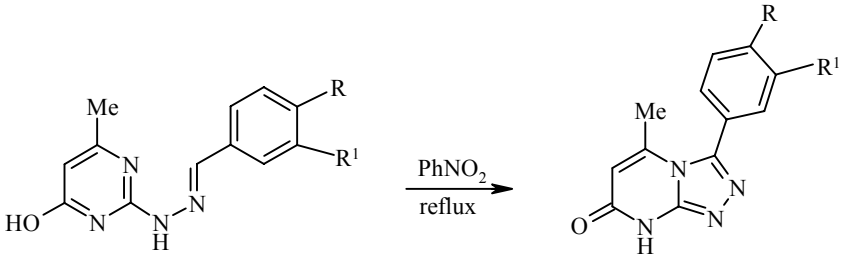
SYNTHESIS OF DERIVATIVES OF 7,8-DIHYDRO[1,2,4]TRIAZOLO[4,3-*a*]-PYRIMIDIN-7-ONE BY THE OXIDATIVE CYCLIZATION OF 2-ARYLIDENEHYDRAZINO-4-HYDROXY-6-METHYLPYRIMIDINES

V. A. Yanchenko and A. M. Demchenko

Keywords: 7,8-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-7-one, nitrobenzene, oxidative cyclization.

One of the methods for the synthesis of condensed *s*-triazoles features the oxidative cyclization of heterocyclic benzylidenehydrazones by means of lead tetraacetate [1, 2]. In addition, the use of acetic acid may lead to isomerization of the reaction products [2].

We have shown that nitrobenzene may act as the oxidizing agent in this reaction. New 3-aryl-5-methyl-7,8 dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-2-ones **1a-e** were obtained by heating 2-arylidenehydrazino-4-hydroxy-6-methylpyrimidines **2a-e** in nitrobenzene. The presence of strong electron-withdrawing substituents in the arylidene fragment leads to inhibition of the reaction and 3-*meta*- and 3-*para*-nitrophenyl analogs of **1** were thus not obtained.



2a–e **1a–e**

1, **2 a** R = Br; **b** R = Cl; **c** R = F; **d** R = OCH_3; **e** RR^1 = –OCH_2O–; **a-d** R^1 = H

The use of nitrobenzene for the oxidative cyclization of arylidenehydrazines **2a-e** leads to a considerable simplification of the reaction, while the high temperature of the reaction mixture leads to the unequivocal formation of the [1,2,4]triazolo[4,3-*a*]pyrimidine system [3].

The structure of the products were supported by ^{1}H NMR spectroscopy.

T. G. Shevchenko Chernigov State Pedagogical University, 14013 Chernigov, Ukraine; e-mail: demch@cn.relc.com. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 850-852, June, 2002. Original article submitted December 6, 2001.

0009-3122/02/3806-0753$27.00©2002 Plenum Publishing Corporation

3-(4-Bromophenyl)-5-methyl-7,8-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-7-one (1a). A solution of **2a** (0.01 mol) in nitrobenzene (50 ml) was heated at reflux for 15 h and then cooled. The precipitate formed was filtered off and dried to give 1.92 g (63%) **1a**; mp 316-317°C (nitrobenzene). IR spectrum, ν, cm^{-1} in KBr pellet: 1605 (C=N), 1680 (C=O). ^{1}H NMR spectrum, δ, ppm (300 MHz, DMSO-d_6, TMS as internal standard): 2.35 (3H, s, CH_3); 5.81 (1H, s, CH); 7.71 (2H, m, *m*-HAr); 8.01 (2H, m, *o*-HAr); 13.4 (1H, br. s, NH). Found, %: Br 25.9; N 18.1. $C_{12}H_9N_4O$. Calculated, %: Br 26.2; N 18.3.

3-(4-Chlorophenyl)-5-methyl-7,8-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-7-one (1b) was obtained analogously in 52% yield; mp 303-304°C (DMF). IR spectrum, ν, cm^{-1} in KBr pellet: 1600 (C=N), 1675 (C=O). ^{1}H NMR spectrum, δ, ppm (300 MHz, DMSO-d_6, TMS as internal standard): 2.34 (3H, s, CH_3); 5.85 (1H, s, CH); 7.56 (2H, m, *m*-HAr); 8.11 (2H, m, *o*-HAr); 13.2 (1H, br. s, NH). Found, %: Cl 13.3; N 21.3. $C_{12}H_9ClN_4O$. Calculated, %: Cl 13.6; N 21.5.

3-(4-Fluorophenyl)-5-methyl-7,8-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-7-one (1c) was obtained analogously in 43% yield; mp 287-288°C (DMF). IR spectrum, ν, cm^{-1} in KBr pellet: 1600 (C=N), 1675 (C=O). ^{1}H NMR spectrum, δ, ppm (300 MHz, DMSO-d_6, TMS as internal standard): 2.35 (3H, s, CH_3) 5.86 (1H, s, CH); 7.37 (2H, m, *m*-HAr); 8.15 (2H, m, *o*-HAr); 13.4 (1H, br. s, NH). Found, %: N 22.7. $C_{12}H_9FN_4O$. Calculated, %: N 23.0.

3-(4-Methoxyphenyl)-5-methyl-7,8-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-7-one (1d) was obtained analogously in 58% yield; mp 295-296°C (DMF). IR spectrum, ν, cm^{-1} in KBr pellet: 1610 (C=N), 1685 (C=O). ^{1}H NMR spectrum, δ, ppm (300 MHz, DMSO-d_6, TMS as internal standard): 2.33 (3H, s, CH_3); 3.84 (3H, s, OCH_3); 5.80 (1H, s, CH); 7.08 (2H, m, *m*-HAr); 8.03 (2H, m, *o*-HAr); 13.0 (1H, br. s, NH). Found, %: N 21.7. $C_{13}H_{12}N_4O_2$. Calculated, %: N 21.9.

5-Methyl-3-(3,4-methylenedioxyphenyl)-7,8-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-7-one (1e) was obtained analogously in 55% yield; mp 301-302°C (DMF). IR spectrum, ν, cm^{-1} in KBr pellet: 1610 (C=N), 1680 (C=O). ^{1}H NMR spectrum, δ, ppm (300 MHz, DMSO-d_6, TMS as internal standard): 2.32 (3H, s, CH_3); 5.85 (1H, s, CH); 6.12 (s, OCH_2O); 7.04-7.64 (3H, m, C_6H_3); 13.2 (1H, br. s, NH). Found, %: N 20.4. $C_{13}H_{10}N_4O_3$. Calculated, %: N 20.7.

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