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Synthesis of [1,2,4]triazolo[1,5-*a*]quinazolines from 7-methyl-5-phenyl-4,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidine

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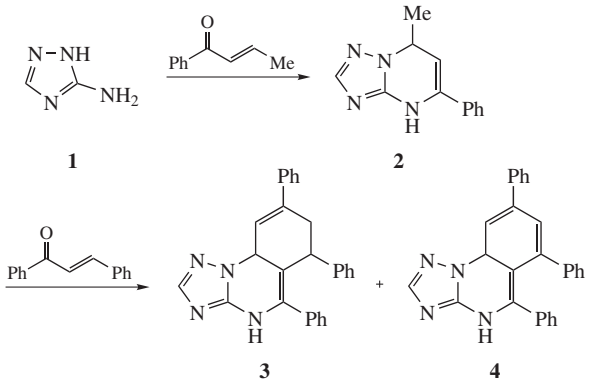
Tetrahydro- and dihydrotriazolo[1,5-*a*]quinazolines were prepared by reaction of 7-methyl-5-phenyl-4,7-dihydro[1,2,4]triazolo-[1,5-*a*]pyrimidine with chalcone.

During our recent studying of dihydroazolopyrimidines[1,2] we have found[3–5] that under basic catalysis C(6)-positioned carbon atom can act as a nucleophilic centre and add to α,β-unsaturated ketones to form Michael adducts. Under the same conditions, [1,2,4]triazolo[1,5-*a*]dihydropyrimidines[3,4] and some other azoloazines[4,5] bearing the methyl group at the 5-position of six-membered heterocycle undergo deprotonation at this methyl group and produce azoloquinazolines as a result of intramolecular cyclization. Interestingly, 5-methyl-4,7-dihydrotetrazolo[5,1-*a*]pyrimidines do not react with aldehydes (other type of electrophiles) at C(5)-Me group.[5]

In the present study we have performed a similar reaction of chalcone with dihydroazolopyrimidine bearing methyl group at the 7-position (Scheme 1). The required 7-methyl-5-phenyl-4,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidine **2** was prepared from 3-aminotriazole **1** and 1-phenylbut-2-en-1-one as described previously.[†,1,2]

Reaction of compound **2** with chalcone in methanol in the presence of sodium methoxide at 40–50 °C[4,5] resulted in a mixture of two cyclocondensation products **3** and **4**, which were separated by crystallization from propan-2-ol.[‡] According to the elemental and spectral analyses, they have structures of tetrahydro (**3**) and dihydro (**4**) triazoloquinazolines. The ^{1}H NMR spectrum of tetrahydrotriazoloquinazoline **3** contained the following characteristic signals: ABX system of protons at 2.8, 3.1, 4.4 ppm (*J* 14.1, 8.0 and 6.0 Hz), and the AB system of protons at 5.3 and 6.6 ppm (*J* 6.0 Hz), assigned to =C(9)H and C(9a)H protons. The spectrum of dihydrotriazoloquinazoline **4** contained AB system of =C(9)H and C(9a)H protons at 5.4 and 6.6 ppm (*J* 6.2 Hz), while the signal of =C(7)H overlapped with aromatic protons in the broad multiplet in the range of 6.9–8.3 ppm.



Scheme 1

In summary, 7-methyl-4,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidines in the reaction with α,β-enones undergo similar cyclization like their 5-methyl analogues.

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† Melting points were determined on a Kofler apparatus. The ^{1}H NMR spectra were recorded at 200 MHz on a Varian Mercury VX-200 spectrometer with TMS as an internal standard in [^{2}H$_6$]DMSO. Mass spectra were taken on a Finnigan MAT 4651P instrument (EI, 70 eV). TLC was used to monitor the reactions and control the purity of products on Silufol UV-254; eluents acetone–hexane (1:1), chloroform–hexane (1:1) and pure chloroform; visualized under UV light or in iodine camera.

*7-Methyl-5-phenyl-4,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidine* **2**. A solution of aminotriazole **1** (0.1 mol) and 1-phenylbut-2-en-1-one (1 mol) in 20 ml of *n*-butanol was refluxed for 30–90 min. After cooling, crystals of triazolopyrimidine **2** were filtered off, washed with methanol and dried. Yield, 72%. White solid, mp 186–188 °C. IR (KBr, ν_{max}/cm^{-1}): 1680 (C=C–NH), 1614 (C=C). ^{1}H NMR, δ: 1.9 (d, 3H, Me, *J* 8.2 Hz), 4.6 (dd, 1H, CH, *J* 8.2 Hz, *J* 6.0 Hz), 6.2 (d, 1H, CH, *J* 6.0 Hz), 6.8–7.8 (m, 5H, Ar), 7.9 (s, 1H, C*H*-triazole), 10.0 (br. s, 1H, NH). MS (EI), *m*/*z* (%): 212 (100, M$^+$), 197(18), 171(46), 135(30), 130(26). Found (%): C, 68.12; H, 5.54; N, 26.12. Calc. for $C_{12}H_{12}N_4$ (%): C, 67.90; H, 5.70; N, 26.40.

‡ *5,6,8-Triphenyl-4,6,7,9a-tetrahydro[1,2,4]triazolo[1,5-*a*]quinazoline* **3** *and 5,6,8-triphenyl-4,9a-dihydro[1,2,4]triazolo[1,5-*a*]quinazoline* **4**. A solution of triazolopyrimidine **2** (0.01 mol) and chalcone (0.01 mol) in 10 ml of methanol containing 0.015 mol of sodium methoxide was refluxed for 5 min, cooled and filtered. The crystals were washed with methanol to give 77% of the crude material. Recrystallization from propan-2-ol or propan-2-ol–DMF (10:1) mixture gave crystals which were washed with acetone to afford tetrahydrotriazoloquinazoline **3**, yield 30%. The mother liquor was concentrated and recrystallised in the same manner to give 18% of dihydrotriazoloquinazoline **4**.

For **3**: white solid, mp 238–240 °C. IR (KBr, ν_{max}/cm^{-1}): 1668 (C=C–NH), 1608 (C=C). ^{1}H NMR, δ: 2.8 (dd, 1H, CH_AH$_B$–CH$_X$, *J* 14.1 Hz, *J* 6.0 Hz), 3.1 (dd, 1H, CH$_A$H$_B$–CH$_X$, *J* 14.1 Hz, *J* 8.0 Hz), 4.4 (dd, 1H, CH$_A$H$_B$–C*H*$_X$, *J* 8.0 Hz, *J* 6.0 Hz), 5.3 (d, 1H, C*H*$_A$–CH$_B$, *J* 6.0 Hz), 6.6 (d, 1H, CH$_A$–C*H*$_B$, *J* 6.0 Hz), 6.8–8.2 (m, 16H, Ar + C*H*-triazole), 10 (s, 1H, NH). MS (EI), *m*/*z* (%): 402 (100, M$^+$), 325 (58), 320 (24). Found (%): C, 80.51; H, 5.54; N, 13.89. Calc. for $C_{27}H_{22}N_4$ (%): C, 80.57; H, 5.51; N, 13.92.

For **4**: white solid, mp 161–163 °C. IR (KBr, ν_{max}/cm^{-1}): 1589 (C=C), 1592, 1598 (C=C). ^{1}H NMR, δ: 5.4 (d, 1H, C*H*$_A$–CH$_B$, *J* 6.2 Hz), 6.6 (d, 1H, CH$_A$–C*H*$_B$, *J* 6.2 Hz), 6.9–8.3 (m, 17H, Ar + C*H*-triazole), 10.6 (s, 1H, NH). MS, *m*/*z* (%): 400 (M$^+$, 100), 323 (67). Found (%): C, 80.95; H, 5.08; N, 14.01. Calc. for $C_{27}H_{20}N_4$ (%): C, 80.98; H, 5.03; N, 13.99.

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