**AZIDE-TETRAZOLE EQUILIBRIUM IN PYRIDO[3,2-*d*]PYRIMIDINES**

**AZĪDA-TETRAZOLA LĪDZSVARS PIRIDO[3,2-*d*]PIRIMIDĪNOS**

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Heterocycles with an azido-azomethine structural entity are interesting due to their intrinsic dynamic azide-tetrazole tautomeric equilibrium in the solution phase [1] alongside rich azide functional group chemistry [2].

Herein, a method for the synthesis of 5-substituted tetrazolo[1,5-*a*]pyrido[2,3‑*e*] pyrimidines from 2,4-diazidopyrido[3,2-*d*]pyrimidine in SNAr reactions with *N*-, *O*-, and *S*‑ nucleophiles is presented [3]. The tetrazolo[1,5-*a*]pyrimidine derivatives can be regarded as 2‑azidopyrimidines due to present azide-tetrazole valance tautomerism and functionalized in copper(I)-catalyzed azide-alkyne dipolar cycloaddition (CuAAC) and Staudinger reactions.

Equilibrium constants and thermodynamic values were determined using variable temperature 1H NMR and were found to be ΔG298 = −3.33 to −7.52 (kJ/mol), ΔH = −19.92 to −48.02 (kJ/mol) and ΔS= −43.74 to −143.27 (J/mol·K). The negative Gibbs free energy values assert tetrazole as the major tautomeric form in solutions. Furthermore, the key starting material 2,4-diazidopyrido[3,2-*d*]pyrimidine shows a high degree of tautomerization in different solvents presenting up to 7 tautomeric forms.



**Scheme 1.**  Azide-tetrazole equilibrium guided SNAr reaction of azidopyrimidines.

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***References:***

[1] a) Sebris, A.; Turks, M. *Chem. Heterocycl. Compd.* **2019**, *55*, 1041–1043. b) Tišler, M. *Synthesis* **1973**, *1973*, 123–136. c) Leškovskis, K.; Mishnev, A.; Novosjolova, I.; Turks, M. *J. Mol. Struct.* **2022**, *1269*, 133784. d) Cmoch, P.; Korczak, H.; Stefaniak, L.; Webb, G.A. *J. Phys. Org. Chem.* **1999**, *12*, 470–478. e) Thomann, A.; Zapp, J.; Hutter, M.; Empting, M.; Hartmann, R.W. *Org. Biomol. Chem.* **2015**, *13*, 10620–10630.

[2] Bräse Stefan, K.B. *Organic Azides: Syntheses and Applications*; Bärse, S., Banert, K., Eds.; John Wiley & Sons, Ltd.: Chichester, UK, **2009**, ISBN 9780470682517.

[3] Leškovskis, K.; Mishnev, A.; Novosjolova, I.; Turks, M. *Molecules* **2022**, *27*, 7675.