EFFICIENT SYNTHESIS OF STEROIDAL 1,2,3-TRIAZOLES

Nana Barbakadze[1], Nanuli Nadaraia[1], Meri Kakhabrishvili[1]

[1]Tbilisi State Medical University Iovel Kutateladze Institute of Pharmacochemistry, Tbilisi, Georgia
n.barbakadze@tsmu.edu

Steroids play an important role in the physiological processes of living organisms and are widely used in medical practice. Purposeful chemical modification of steroidal substances obtained from plant raw materials, leading to changes in biological activity, is essential for the development of new pharmaceuticals. The majority of synthetic steroidal compounds, including nitrogen-containing derivatives, are biologically potent substances [1]–[3]. It has been established that steroidal azoles can interact with certain enzymes, exhibiting strong inhibitory properties, and are considered promising antitumor agents [4]. To obtain potentially biologically active compounds, new steroidal 1,2,3-triazoles were synthesized using a triazolization methodology [5], [6], which significantly reduced the number of synthetic steps required. The structures of the synthesized compounds were confirmed by ^{1}H and ^{13}C NMR spectroscopy. Evaluation of the agonistic and antagonistic properties of the synthesized steroidal 1,2,3-triazoles showed that several compounds reduced androgen receptor activity by 40%. Screening nitrogen-containing steroids for biological activity enables the creation of new libraries of potential therapeutic agents and facilitates the identification of lead compounds for the development of new drug precursors.

[1] R. Singh, S. Thota, and R. Bansal, “Studies on 16,17-pyrazoline substituted heterosteroids as anti-Alzheimer and anti-Parkinsonian agents using LPS-induced neuroinflammation models of mice and rats,” ACS Chem. Neurosci., vol. 9, no. 2, pp. 272–283, 2018.
[2] A. H. Banday, S. A. Shameem, and S. Jeelani, “Steroidal pyrazolines and pyrazoles as potential 5α-reductase inhibitors: Synthesis and biological evaluation,” Steroids, vol. 92, pp. 13–19, 2014.
[3] J. Cui et al., “Synthesis, characterization and antitumor activities of some steroidal derivatives with side chain of 17-hydrazone aromatic heterocycle,” Steroids, vol. 95, pp. 32–38, 2015.
[4] A. S. Latysheva and A. Yu. Misharin, “Steroidal inhibitors of CYP17A1—the template for novel anti-cancer agents development,” Biomed. Chem.: Res. Methods, vol. 1, no. 2, p. e00020, 2018.
[5] J. Thomas et al., “A single-step acid catalyzed reaction for rapid assembly of NH-1,2,3-triazoles,” Chem. Commun., vol. 52, no. 59, pp. 9236–9239, 2016.
[6] J. Thomas et al., “A general metal-free route towards the synthesis of 1,2,3-triazoles from readily available primary amines and ketones,” Chem. Commun., vol. 52, no. 14, pp. 2885–2888, 2016.