International Conference on Natural Products and Physiologically Active Substances (ICNPAS-2004)
September 12-17, 2004, Novosibirsk, Russia
Invited Lecture

Advances in the Syntheses of Bioactive Fused 1,2,3-Triazoles and 1,2,3-Thiadiazoles

Vasiliy A. Bakulev

TOSLab, 28 Mira, Urals State Technical University, Ekaterinburg, 620002, Russia
Fax: +7-3433754135
E-mail: bakulev@toslab.com

The fused 1,2,3-thiadiazoles and 1,2,3-triazoles are special interest of medicinal chemistry because of their structural similarity to purines and because benzothiadiazoles have been recently identified by scientists from Novartis as a class of chemical plant activators.[1] Furthermore, mesoionic fused 1,2,3-triazoles have been recently patented by Furber and coworkers (AstraZeneca Pharmaceuticals) for wide spectrum of biological activity.[2]

The systematic study for alkylation of 5-hydroxy-1,2,3-triazoles allowed us to find a new approach to 1,2,3-triazoles fused to six- and seven-membered rings.[3] On the other hand, the rearrangements of 1,2,3-thiadiazoles discovered in TOSLab gave us a background of a novel approach to 1,2,3-triazoles condensed with six- and seven- and eight-membered rings.[1]

We have developed a novel approach to 1,2,3-thiadiazolo[4,5-c]pyrimidines using the nucleophilic substitution reaction of 5-chloro-1,2,3-thiadiazoles with malonic acid derivatives. Subsequent intramolecular condensation of the initially formed derivatives of 2-(1,2,3-thiadiazol-5-yl) acetic acid was used to prepare a variety of 1,2,3-thiadiazolo[4,5-c]pyrimidin-4(5H)-ones and pyrano[3,4-d][1,2,3]thiadiazole.[1] To prepare 1,2,3-thiadiazolo[5,4-d]pyrimidines we have used three component synthesis starting from ethyl 5-amino-1,2,3-thiadiazole-4-carboxylate, orthoester and a series of aliphatic amines.[1] Indeed a few small libraries of fused 1,2,3-triazoles and 1,2,3-thiadiazoles have been synthesized and screened for antiviral activity.

References:

1. V.A.Bakulev, W.Dehaen. The Chemistry of 1,2,3-Thiadiazoles. E.C.Taylor, P.Wipf. Ed.; Willey, Interscience, USA. **2004**, 241 pp.
2. P.A.Abbot, R.V.Bonnert, M.V.Caffrey, P.A.Cage, A.J.Cooke, D.Donald, M.Furber, S.Hill, Withnall, Tetrahedron **2002**, *58*, 3158.
3. E.A.Savel'eva, Yu.A.Rozin, M.I. Kodess, L.Van Meervelt, W.Dehaen, Yu.Yu.Rozin, V.A.Bakulev, Tetrahedron **2004**, *60*, 5367.