Conference abstract PO-15

Antitrypanosomal Activity of 4-Aminobicyclo[2.2.2]octane Derivatives

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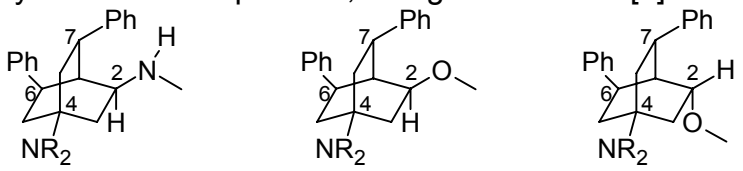
Every year about half a million people are infected with Human African Trypanosomiasis (HAT) and more than 40.000 people die from this disease [1]. Infections with *Trypanosoma brucei rhodesiense*, which is the more virulent of the two causative organisms, can only be treated with two drugs, suramin and melarsoprol, which can cause severe side effects and which have to be administered by painful injections. Moreover, exclusively the arsenic compound melarsoprol is able to cure CNS infections of *T. b. rhodesiense*. which elicits an encephalopathy in 10% of the patients, killing half of them [2].



The (2-*exo*)-4-aminobicyclo[2.2.2]octan-2-ols exhibit activity against this organism [3]. Recently, their (2-*endo*)-isomers were prepared showing similar biological properties [4]. We synthesized several of their ester and ether derivatives as well as 2-amino analogues with improved activity and selectivity (IC_{50} cytotoxicity / IC_{50} activity). The most active of the new compounds, a bicyclo-octyl ω-aminopropionate, is 40 times as potent as the lead compounds.

[1] WHO Report 2004, Statistical Annex, page 120.

[2] Kennedy PGE. Diagnostic and neuropathogenesis issues in human African trypanosomiasis. Int J Parasitol. 2006; 36: 505–512. doi:10.1016/j.ijpara.2006.01.012

[3] Weis R, Brun R, Saf R, Seebacher W. 4-Aminobicyclo[2.2.2]octanone Derivatives with Antiprotozoal Activities. Monatsh Chem 2003; 134: 1019–1026. doi:10.1007/s00706-003-0011-7

[4] Schlapper C, Seebacher W, Kaiser M, Brun R, Saf R, Weis R. Epimers of bicyclo[2.2.2]octan-2-ol derivatives with antiprotozoal activity. Eur J Med Chem. 2008; 43: 800–807. doi:10.1016/j.ejmech.2007.06.007

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