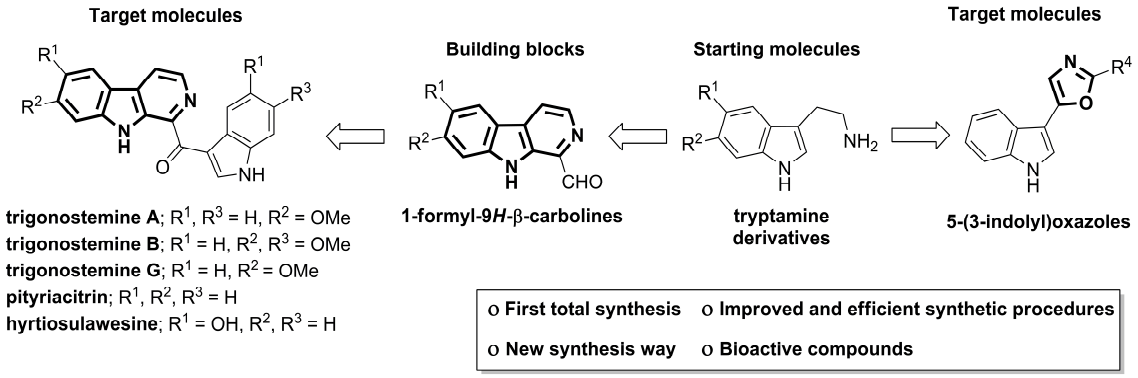
TOTAL SYNTHESIS OF INDOLE ALKALOIDS

Tímea Szabó[a,b], Balázs Volk[a] and Mátyás Milen[a]

[a] Egis Pharmaceuticals Plc., Directorate of Drug Substance Development,
1475 Budapest, P.O.B. 100, Hungary
[b] Budapest University of Technology and Economics,
Department of Organic Chemistry and Technology, Hungary

Indole alkaloids are widely distributed in many natural sources mainly plants, microorganisms or marine creatures and several representatives of this family show wide range of biological effect. The fantastic diversity of structures and medicinal potential inherent in them encourage researchers to accomplish the synthesis of natural products and its synthetic derivatives.

β-Carboline alkaloids are major representatives of indole containing natural products.[1] Both natural and synthetic derivatives exhibit a broad spectrum of biological and pharmacological activities. In our researches the first total synthesis of bioactive natural products trigonostemine A, B, G and a new synthesis of pityriacitrin, and hyrtiosulawesine were described through key intermediates, variously substituted 1-formyl-β-carbolines, which were prepared in an improved and efficient synthetic approach.



Remarkable members of natural products containing the 5-(3-indolyl)oxazole motif show interesting pharmaceutical activity have been isolated or synthesized in the recent decade.[2] In the present work, an alternative protocol has been developed for the preparation of natural and unnatural substituted-5-(3-indolyl)oxazoles via the T3P® assisted Robinson−Gabriel cyclization of N-acyl-β-oxotryptamines. The work-up and purification are convenient, there is no need for halogenated or strongly acidic additives and the target molecules are obtained in good to excellent yields.

[1] Devi N, Kumar S, Pandey SK, Singh V, *Asian J. Org. Chem*. **2018**, 7, 6–36.

[2] Ibrar A, Khan I, Abbas N, Farooq U, Khan A, *RSC Adv*. **2016**, 6, 93016–93047.