An Efficient Approach To Novel Tetrahydropyridoazepines. Expansion Of Azepines’ Drug-like Chemical Space

S. Ryabukhin, D. Volochnyuk, O. Grygorenko, A. Subota

**Introduction and Aim**

The quest for lead-oriented synthesis proposed by medicinal chemistry in early 2010s have prompted the design and study of low-molecular-weight, hydrophilic, conformationally restricted and sp³-enriched molecular scaffolds. Fused azepanes are promising chemistry in early 2010s have prompted the design and study of 6,7,8,9-tetrahydro-5H-pyrido[3,2-c]azepines (1), which contain fused azepane and pyridine rings, were evaluated as cannabinoid (CB2) receptor modulators (2), H1-antihistamines (3), or serotonin (5HT2c) receptor agonists (4).

Herein, we report an alternative approach to 5-substituted 6,7,8,9-tetrahydro-5H-pyrido[3,2-c]azepines, which also relies on the formation of imines as the key step.

**Synthesis**

(i) LDA (1.2 eq), THF, –78 °C, 90 min; (i) (1.13 eq), THF, –78 °C, 80 min; (ii) CrO3 (3 eq), acetone, rt, 18 h; (iii) NaBH4 (3 eq), MeOH, 0 °C to rt, 8 h; (iv) PMe3 (1.5 eq), DIAD (1.5 eq), PPh3 (1.5 eq), Ph, rt, 6 h; (v) NaBH4 (3 eq), MeOH, 0 °C to rt, 8 h; (vi) sat. HCl in Et2O, rt

**Results**

**Contact**

Sergey Ryabukhin, PhD
s.v.ryabukhin@gmail.com
Enamine Ltd, www.enamine.net
78 Chervonotkatska St, 02660 Kyiv, Ukraine

**References**