

Molecules **2001**, *6*, M274**(4a*S*,6*R*,8a*S*)-4a,5,9,10,11,12-Hexahydro-6*H*-benzofuro[3a,3,2-ef][2]benzazepine-3,6-diol (Norsanguinine)****Matthias Treu and Ulrich Jordis***[Institute of Organic Chemistry](#), VUT, A-1060 Vienna, Getreidemarkt 9, Austria
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Norsanguinine (**2**) is an alkaloid isolated from the bulbs of *L. sanguinea* [1] and synthesized as racemate by Kita [2]. We report the first synthesis of chiral norsanguinine starting from N-norgalanthamine (**1**) [3] by O-demethylation using L-Selectride® [4]. To a solution of norgalanthamine (1.0 g, 3.66 mmol) in dry THF (40 mL) L-Selectride (17.0 mL, 17.0 mmol, 1 M in THF) was added and refluxed for 24 h. The solution was cooled to ambient temperature, then EtOAc (20 mL) and distilled water (100 mL) were added. The layers were separated, and the organic layer was extracted with distilled water (4 x 20 mL). The combined aqueous layers were washed with EtOAc (2 x 20 mL) and concentrated *in vacuo*. The residue was purified by column chromatography (100 g SiO₂, CHCl₃ : MeOH : conc. NH₃ = 90 : 9 : 1) and triturated with acetone (5 mL). Yield: colorless crystals (0.78 g, 82%).

Mp. 142 - 144 °C (lit [1] 141 – 142 °C).

TLC: CHCl₃: MeOH : conc. NH₃ = 89 : 10 : 1, R_f = 0.15.[α]_D²⁰ = -54° (c 0.1, MeOH) (lit [1] [α]_D²⁰ = -14° (c 0.1, CHCl₃)) [5].

¹H NMR (DMSO-*d*₆): δ 6.40 (d, *J* = 8.3 Hz, 1H), 6.49 (d, *J* = 8.3 Hz, 1H), 6.02 (d, *J* = 11.2 Hz, 1H), 5.79 (dd, *J* = 11.2 Hz, *J* = 5.4 Hz, 1H), 4.43 (s, 1H), 4.08 (s, 1H), 3.90 (d, *J* = 15.9 Hz, 1H), 3.71 (d, *J* = 15.9 Hz, 1H), 3.19 - 2.92 (m, 2H), 2.31 (d, *J* = 15.9 Hz, 1H), 2.12 - 1.94 (m, 1H), 1.79 - 1.56 (m, 2H).

¹³C NMR (DMSO-*d*₆): δ 145.6 (s), 140.4 (s), 133.0 (s), 132.3 (s), 127.7 (d), 127.6 (d), 119.6 (d), 114.8 (d), 86.5 (d), 60.1 (d), 53.1 (t), 48.3 (s), 46.6 (t), 40.2 (t), 30.8 (t).

Anal. Calcd for C₁₅H₁₇NO₃: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.26; H, 6.84; N, 5.38.**References and Notes:**

1. Abdallah, O. M. *Phytochemistry* **1995**, *39*, 477-478.
2. Kita, Y.; Arisawa, M.; Gyoten, M.; Nakajima, M.; Hamada, R.; Tohma, H.; Takada, T. *J. Org. Chem.*

1998, *63*, 6625-6633.

3. Thal, C.; Guillou, C.; Mary, A.; Renko, D.; Potier, P.; Christen, Y. Preparation and pharmaceutical compositions of galanthamine derivatives. WO 9703987, **1997** [*Chem. Abstr.*: 126:212284].
4. Coop, A.; Janetka, J. W.; Lewis, J. W.; Rice, K. C. *J. Org. Chem.* **1998**, *63*, 4392-4396.
5. Pure **2** was found to be almost insoluble in CHCl₃.

Sample Availability: Available from the author and from MDPI.

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