

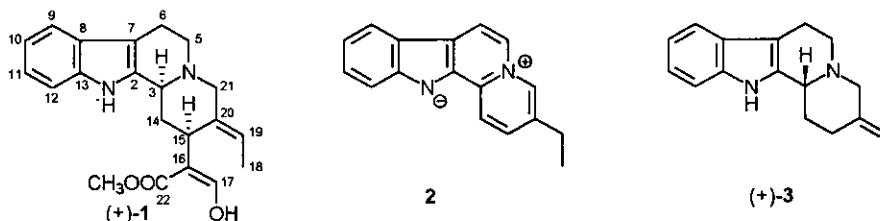
SHORT SYNTHESIS OF 14,15-DIDEHYDRO-*E*-DEPLANCHEINE, PRESUMED BIOSYNTHETIC INTERMEDIATE IN THE FORMATION FROM GEISSOSCHIZINE, OF *CORYNANTHÉ* ALKALOIDS MISSING THE THREE-CARBON UNIT AT C-15

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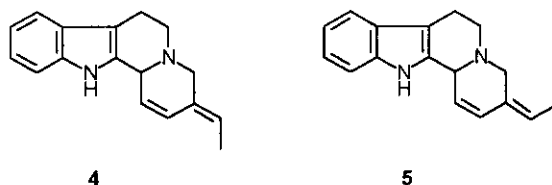
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Abstract- A short synthesis of 14,15-didehydro-*E*-deplancheine (4) and its *Z*-analogue (5) is described.

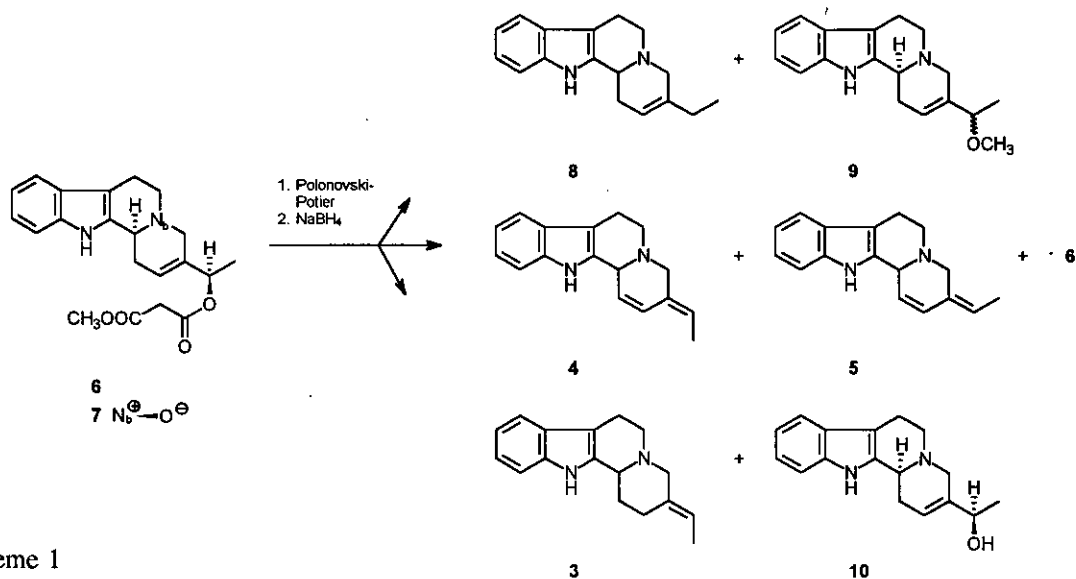
The carbon skeleton of the indole alkaloids of the *Corynanthé* group, *e.g.* (+)-geissoschizine [(+)-1] (biogenetic numbering¹) usually bears a three-carbon unit (C-16, C-17, and C-22) at the C-15 position. However, in some of these alkaloids {*e.g.* flavopereirine (2), (+)-deplancheine [(+)-3]} the three-carbon unit is missing.²



In the present paper we describe a short route to 14,15-didehydro-*E*-deplancheine (4) and 14,15-didehydro-*Z*-deplancheine (5). The former is presumed to be the biosynthetic intermediate in the formation from geissoschizine (1), of *Corynanthé* alkaloids missing the three-carbon unit at C-15.^{3,4}

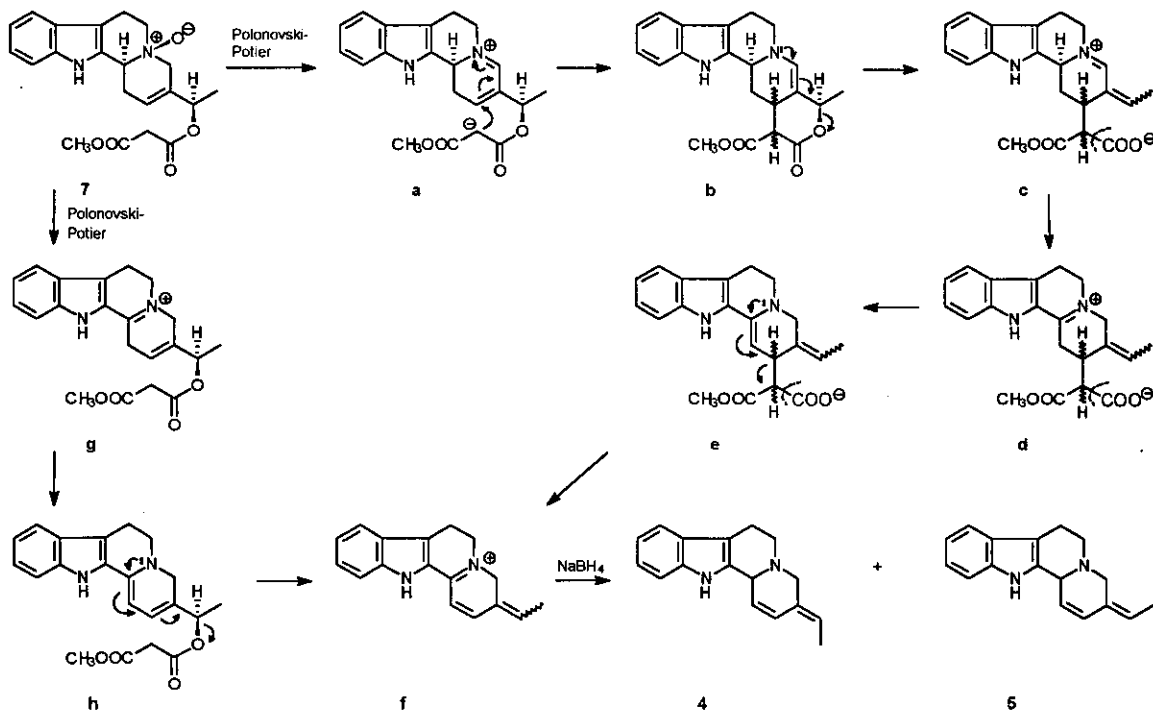


*N*_b-Oxide (7),⁵ prepared with *m*-CPBA from our recently described monomalonate of allylic alcohol (6),⁶ was allowed to react with TFAA under Polonovski-Potier conditions. The mixture obtained was treated with NaBH₄. After normal work-up, compounds (4, 5), [(6) (deoxygenated starting material)], (8, 9), [(3) (traces)], and (10) were isolated and purified by tlc (Scheme 1).⁷



Scheme 1

The formation of the major compounds (**4**) and (**5**) can be presented in two manners: The Polonovski-Potier reaction of N_6 -oxide (**7**) leads to the conjugated iminium ion (**a**). An intramolecular nucleophilic attack takes place and affords the pentacycle (**b**). A *retro*-Mannich reaction follows and yields the iminium ion (**c**). Isomerization of the iminium ion (**c**) to the new iminium ion (**d**),⁸ followed by proton



Scheme 2

cleavage, leads to the enamine (e), from which a second *retro*-Mannich reaction affords the conjugated iminium ion (f). Alternatively, and more likely, the direct formation of the iminium ion (g) from N_b-oxide (7), followed by proton cleavage, leads to the enamine (h), from which a conjugated *retro*-Mannich reaction affords the iminium ion (f). NaBH₄ reduction completes the formation of compounds (4) and (5) (Scheme 2).

When the same reaction was carried out using NaBD₄ instead of NaBH₄, deuterium was exclusively found in the C-3 position of compounds (4) and (5) (compounds 4-3-d₁ and 5-3-d₁), in agreement with the proposed mechanisms.

The spectral data (*cf.* References and Notes, and Figure 1) and earlier results⁹ are in full accord with the proposed structures.

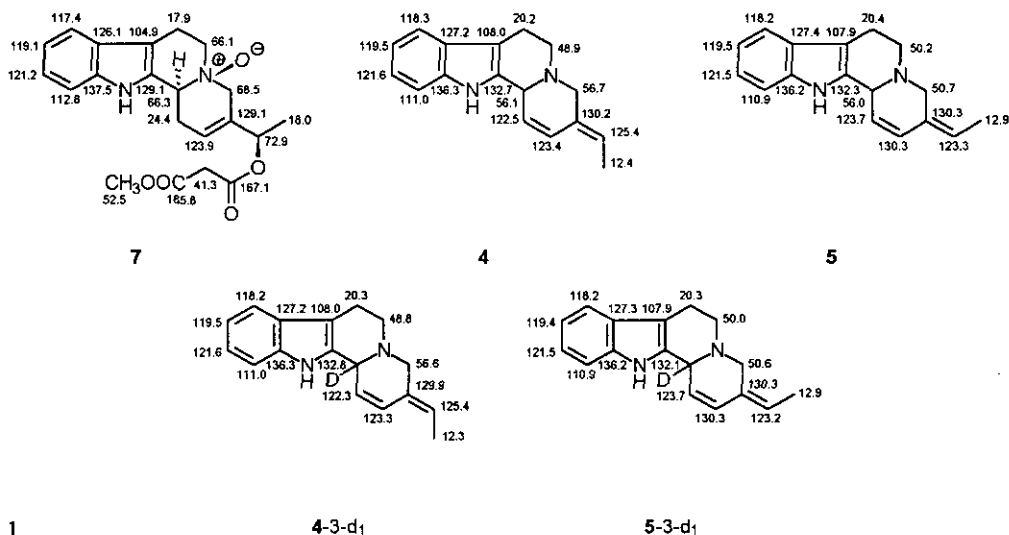


Figure 1

The choice between the C-20 ethylene side chain configurations (*E*- versus *Z*-) of compounds (4) and (5) was confirmed by NOE measurements, which gave the following results (Figure 2).

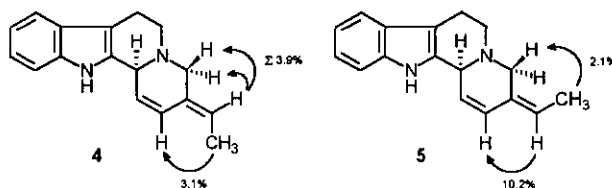


Figure 2.

REFERENCES AND NOTES

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2. M. Lounasmaa and A. Tolvanen, "The Monoterpenoid Indole Alkaloids", ed. by J.E. Saxton, 2nd Edition, Wiley, New York, 1994, pp. 57-159.
3. A.I. Scott, *Bioorg. Chem.*, 1974, **3**, 398. See also, C. Kan-Fan and H.-P. Husson, *Tetrahedron Lett.*, 1980, **21**, 4265.
4. Although naturally occurring (+)-geissoschizine [(+)-1] and (+)-deplancheine [(+)-3] have turned out to have opposite configurations at C-3,¹⁰ the mechanism proposed by Scott³ is still applicable for the formation of deplancheine from geissoschizine.

5. **Preparation of the *trans*-N₅-oxide (7).** A solution of compound (6)⁶ (215.7 mg, 0.59 mmol) and *m*-CPBA (110.7 mg, 0.64 mmol, 1.1 equiv.) in dry CH₂Cl₂ (20 ml) was stirred for 4 h at room temperature (Ar atm). The solvent was evaporated and the crude product was purified by column chromatography (alumina, CH₂Cl₂/MeOH; 99/1, CH₂Cl₂/MeOH; 98/2) to give compound (7). Yield: 118.2 mg (53%) (amorphous material). Ir: 1730 cm⁻¹ (C=O). ¹H-Nmr: δ 1.25 (3H, d, J=6 Hz, -OCHCH₃), 3.35 (2H, s, OCCH₂CO), 3.73 (3H, s, -OCH₃), 5.32 (1H, q, J=6 Hz, -OCHCH₃), 6.80 (1H, br, H-15), 7.0-7.1 (2H, m, H-10, H-11), 7.44 (2H, d, J=8 Hz, H-9, H-12), 11.20 (1H, s, NH). For the ¹³C-nmr data, see Figure 1. Ms: 384 (M⁺), 368, 268, 251, 170 (100%). Anal. Calcd for C₂₁H₂₄N₂O₅: C, 65.61; H, 6.29; N, 7.29. Found C, 65.42; H, 6.10; N, 7.14.
6. M. Lounasmaa, P. Hanhinen, and R. Jokela, *Tetrahedron*, 1995, **51**, 8623.
7. **Behaviour of compound (7) in the Polonovski-Potier reaction conditions and in NaBH₄ treatment.** A solution of *trans*-N-oxide (7) (79.7 mg, 0.21 mmol) in dry CH₂Cl₂ (7.0 ml) was cooled to -15 °C and trifluoroacetic anhydride (TFAA) (80 μl, 2.5 equiv.) was added in portions (Ar atm). The reaction mixture was stirred for 2 h at room temperature. The solvent was evaporated and the residue dissolved in MeOH/HCl_{aq} [7.0 ml MeOH + 10 μl HCl (16%)]. The mixture was stirred for 2 h at room temperature. NaBH₄ (47.5 mg, 1.25 mmol, 6 equiv.) was added to the mixture in small portions at -2 °C during 15 min (Ar atm). The mixture was stirred at room temperature overnight. H₂O (12 ml) was added, MeOH evaporated, and the mixture extracted with CH₂Cl₂. The crude product (68.7 mg) was fractionated by plc (silica gel, CH₂Cl₂/MeOH; 95/5).
- Compound (6). Yield: 2.0 mg (3%). For analytical data, see ref. 6.
- Compound (8). Yield: 5.1 mg (10%). For analytical data, see ref. 9.
- Compound (9). Yield: 4.4 mg (8%). For analytical data, see ref. 9.
- Compound (5). Yield: 14.8 mg (29%) (amorphous material). ¹H-Nmr: δ 1.71 (3H, d, J=7 Hz, =CHCH₃), 3.43 (1H, d, J=14 Hz, H-21α), 3.76 (1H, d, J=14 Hz, H-21β), 4.51 (1H, br s, H-3), 5.47 (1H, q, J=7 Hz, =CHCH₃), 5.82 (1H, br d, J=10 Hz, H-14), 6.21 (1H, dd, J₁=10, J₂=1 Hz, H-15), 7.09 (1H, t, J=7 Hz, H-10), 7.12 (1H, t, J=7 Hz, H-11), 7.30 (1H, d, J=7 Hz, H-12), 7.47 (1H, d, J=7 Hz, H-9), 8.07 (1H, br s, NH). For the ¹³C-nmr data, see Figure 1. Ms: 250 (M⁺, 100%), 249, 235, 170, 169. Anal. Calcd for C₁₇H₁₈N₂: C, 81.56; H, 7.25; N, 11.19. Found C, 81.32; H, 7.18; N, 11.02.
- Compound (4). Yield: 6.5 mg (13%) (amorphous material). ¹H-Nmr: δ 1.72 (3H, d, J=7 Hz, =CHCH₃), 3.49 (2H, def., H-21α, H-21β), 4.65 (1H, br s, H-3), 5.37 (1H, q, J=7 Hz, =CHCH₃), 5.92 (1H, br d, J=10 Hz, H-14), 6.58 (1H, dd, J₁=10 Hz, J₂=1 Hz, H-15), 7.06 (1H, t, J=7 Hz, H-10), 7.10 (1H, t, J=7 Hz, H-11), 7.30 (1H, d, J=7 Hz, H-12), 7.45 (1H, d, J=7 Hz, H-9), 8.17 (1H, br s, NH). For the ¹³C-nmr data, see Figure 1. Ms: 250 (M⁺, 100%), 249, 235, 170, 169. Anal. Calcd for C₁₇H₁₈N₂: C, 81.56; H, 7.25; N, 11.19. Found C, 81.34; H, 7.12; N, 10.98.
- Compound (3). Yield: Traces. For analytical data, see ref. 9.
- Compound (10). Yield: 3.9 mg (7%). For analytical data, see ref. 9.
- Replacement of NaBH₄ with NaBD₄ in the above procedure:**
- Compound (5-3-d₁). Yield: 14.1 mg (28%) (amorphous material). ¹H-Nmr: As for compound (5) (δ 4.51 was absent). For the ¹³C-nmr data, see Figure 1. Ms: 251 (M⁺, 100%), 250, 249, 236, 235, 171, 170, 169. HRms: Found: 251.1527. Calcd for C₁₇H₁₇DN₂: 251.1532.
- Compound (4-3-d₁). Yield: 7.0 mg (14%) (amorphous material). ¹H-Nmr: As for compound (4) (δ 4.65 was absent). For the ¹³C-nmr data, see Figure 1. Ms: 251 (M⁺, 100%), 250, 249, 236, 235, 171, 170, 169. HRms: Found: 251.1537. Calcd for C₁₇H₁₇DN₂: 251.1532.
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9. R. Jokela, A. Juntunen, and M. Lounasmaa, *Planta Med.*, 1987, **53**, 386.
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