SYNTHESIS OF (±)-ELAEOKANINE E AND (±)-12-EPIELAEOKANINE D

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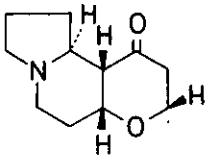
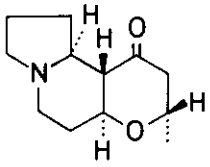
Summary --- The synthesis of (±)-elaeokanine E (1) and (±)-12-epielaeokanine D (8) has been achieved by the stereoselective Birch reduction of epimeric dihydro-γ-pyrone derivatives (6) and (7).

Elaeokanines E (1) and D (2), isolated from Elaeocarpus kaniensis Schltr. by Johns et al.,[1] are epimers with respect to C-7 and have both the characteristic trans-indolizidine and tetrahydro-γ-pyrone ring system. In connection with our synthetic studies on Elaeocarpus alkaloids,[2] we wish to report here the first total synthesis of (±)-elaeokanine E (1) and (±)-12-epielaeokanine D (8).

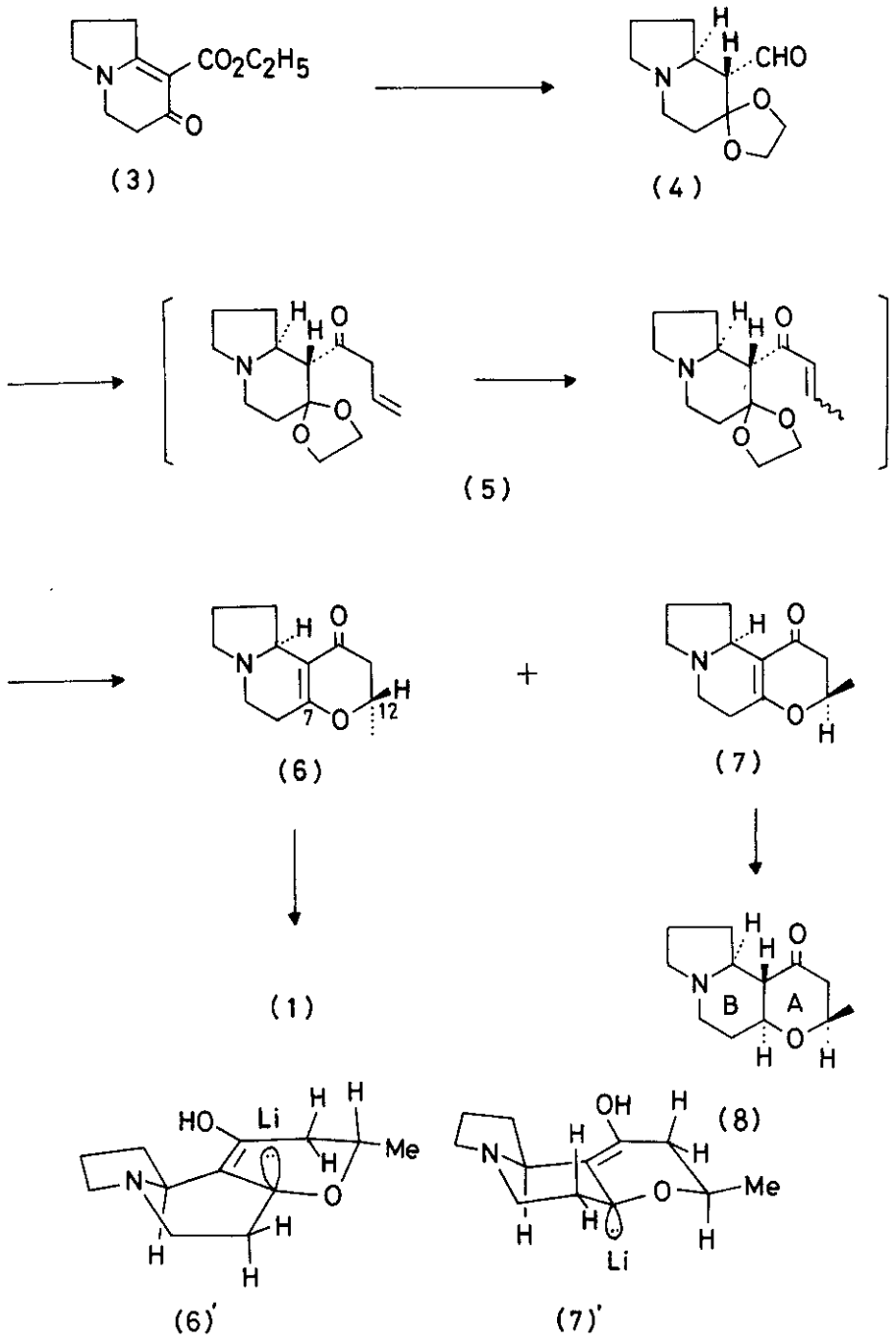


elaeokanine E (1)



elaeokanine D (2)

The Grignard reaction of the aldehyde (4),[2] prepared from the keto ester (3) via 4 steps [(i) $LiAlH_4$/THF-Et_2O, -70° (ii) $(CH_2OH)_2$/TsOH/C_6H_6 (iii) $LiAlH_4$/THF-Et_2O, reflux (iv) NCS-DMS/toluene-CH_2Cl_2], by refluxing with allylmagnesium bromide in THF-Et_2O for 3 hr, followed by the Jones oxidation gave the ketone (5). This ketone (5) exhibits its carbonyl absorption at 1715 cm^{-1}, which changes to that at 1690 and 1670 cm^{-1} owing to the double bond migration on standing at room temperature. Deketalization of (5) under various acidic conditions (47% aq. HBr, 10 hr; cond. HCl, 2 days; 50% H_2SO_4, 2 days) accompanied by the cyclisation gave two dihydro-γ-pyrone derivatives (6)[3] and (7)[4] in the ratio of 3.5:1 in 30% total yield from (4). Reduction of the pyrone (6) in liquid ammonia-absolute EtOH with lithium at -80° afforded only one product, (±)-elaeokanine E (1), whose spectral data [I.R. (CCl_4): 1710 cm^{-1}; Mass m/e: 209 (M^+), 208, 192, 166, 122, 97; N.M.R. ($CDCl_3$): δ 1.33 (3H, d, J=6 Hz, CH_3), 3.75 (1H, m, H-12), 3.83 (1H,


CO2C2H5
(3)
CHO
(4)
(5)
(6)
(7)
(1)
HO
Li
Me
(6)'
OH
(8)
(7)'

narrow m, H-7)] were identical with those of the natural alkaloid, in 80% yield. Catalytic hydrogenation of the acetate salt of (6) with PtO_2 in absolute EtOH also gave (±)-(1) in 30% yield. From these results, we concluded that the methyl configurations at C-12 in (6) and (7) were α and β, respectively. In the metal reduction of α,β-unsaturated ketones, the stereochemical outcome at the β-carbon will be determined by the organometallic intermediate adopting the conformation of lowest energy prior to protonation, and the configuration at the α-carbon, which is controlled by the nature of the protonation of the intermediate enol, is usually less important.[5] In the Birch reduction of pyrones (6) and (7), conformers (6)' and (7)' would be more stable allylic anion intermediates, respectively. The former could furnish cis A/B ring junction, and the latter would result trans A/B ring junction. In fact, the product (8) obtained in 80% yield, showed no narrow maltiplet signal for H-7 in cis A/B ring[1] and the spectral data[6] were not identical with those of natural elaeokanine D (2).[1] Therefore the compound (8) was identified as (±)-12-epielaeokanine D.

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References and Notes

1. N.K. Hart, S.R. Johns, and J.A. Lamberton, Chem. Commun., 1971, 460; Idem., Aust. J. Chem., 1972, 25, 817.
2. T. Watanabe, Y. Nakashita, S. Katayama, and M. Yamauchi, Heterocycles, 1980, 14, 1433.
3. I.R. (CCl_4): 2800-2600, 1670, 1610 cm^{-1}; Mass m/e: 207 (M^+); N.M.R. ($CDCl_3$): δ 1.44 (3H, d, J=6.4 Hz, CH_3), 4.23-4.64 (1H, m, H-12).
4. I.R. (CCl_4): 2800-2600, 1670, 1620 cm^{-1}; Mass m/e: 207 (M^+); N.M.R. ($CDCl_3$): δ 1.43 (3H, d, J=6.4 Hz, CH_3), 4.23-4.65 (1H, m, H-12).
5. H.O. House, "Modern Synthetic Reactions" 2nd ed., W.A. Benjamin, Inc., California, 1972, pp 173-205.
6. I.R. (CCl_4): 1710 cm^{-1}; Mass m/e: 209 (M^+), 208, 192, 166, 122, 97; N.M.R. ($CDCl_3$): δ 1.34 (3H, d, CH_3), 3.75 (1H, m, H-12).

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