HETEROCYCLES, Vol 16, No 1, 1981

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

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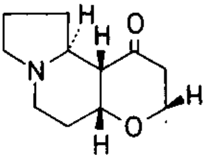
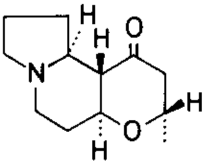
Summary --- The synthesis of (±)-elaeokanine E (1) and (±)-12-epielaeokanine D (8) has been achieved by the stereoselective Birch reduction of epimeric dihydro-γ-pyrone derivatives (6) and (7).

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).

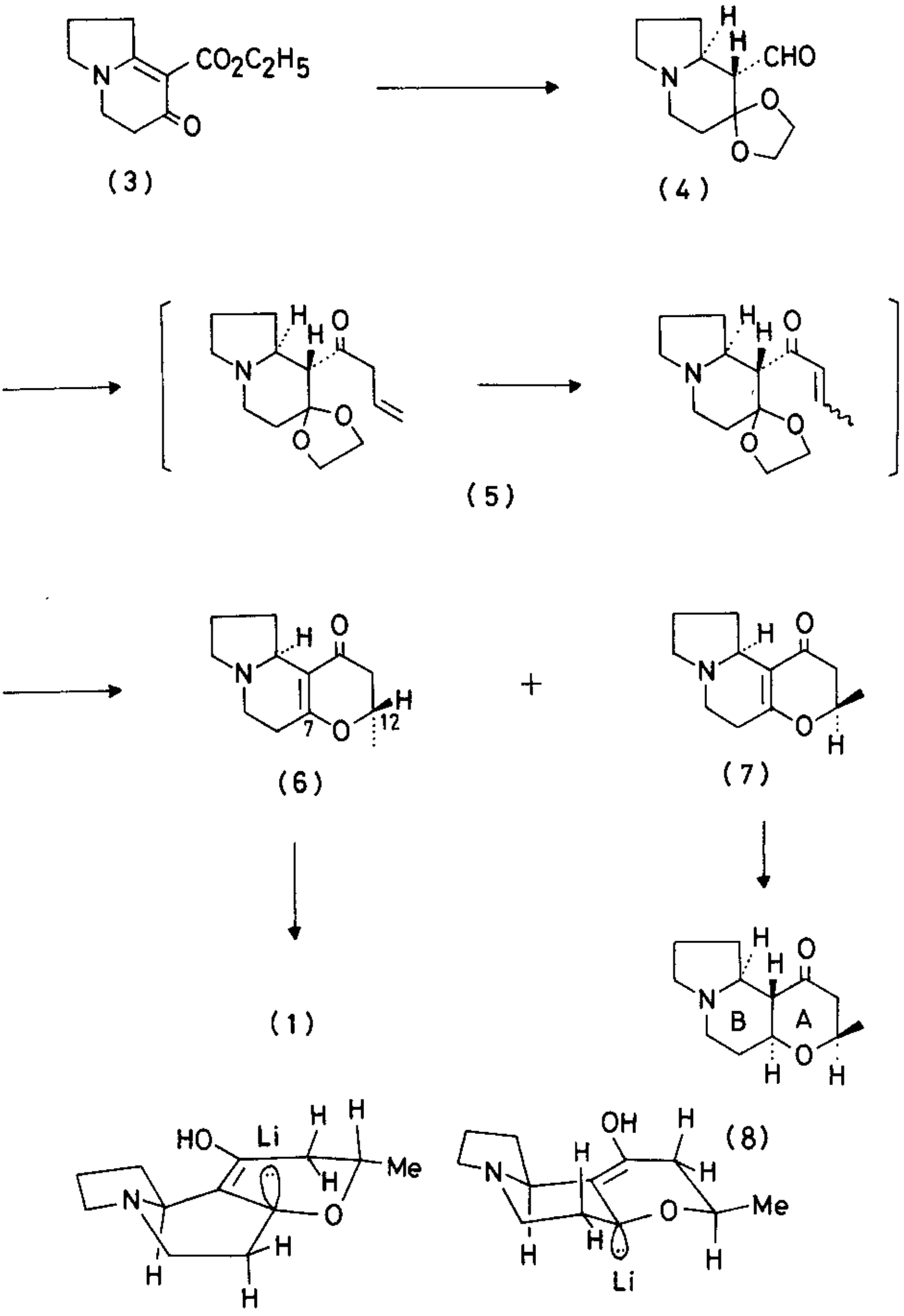


elaeokanine E (1)



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$_2$O, -70° (ii) (CH$_2$OH)$_2$/TsOH/C$_6$H$_6$ (iii) LiAlH$_4$/THF-Et$_2$O, reflux (iv) NCS-DMS/toluene-CH$_2$Cl$_2$], by refluxing with allylmagnesium bromide in THF-Et$_2$O 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$_2$SO$_4$, 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
12
+
(7)
(1)
B
A
(8)
HO
Li
Me
(6)'
OH
Li
Me
(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.

Acknowledgment We are indebted to Dr. J.A. Lamberton (CSIRO, Melbourne) for the gift of the N.M.R. spectrum of natural elaeokanine E.

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).

Received, 13th September, 1980