Synthesis of (+)-14-Hibaone

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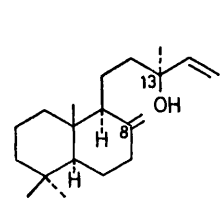
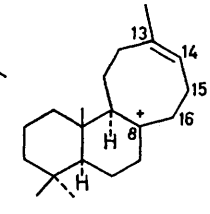
Summary Acetolysis of the tetracyclic epimeric alcohols, precursors of the biogenetic intermediate postulated by Edwards, which were prepared from $\Delta^{8(14)}$-podocarpen-13-one *via* a photochemical adduct with dichloroethylene, leads to (+)-14α-hibyl acetate, ultimately converted into (+)-14α-hibaone.

CYCLIZATION of mano-ol (**1**) into 14α-hibyl formate (**2a**) has been shown conclusively to proceed through a cyclo-octenyl cation (**3**).[1] It was suggested that (**3**) might lead to a tetracyclic intermediate (**4a**), which would ultimately rearrange into the hibyl cation (**2b**). We report a direct conversion of the synthetic alcohols (**4b**) and (**4c**), precursors of (**4a**), into 14α-hibyl acetate (**2c**).

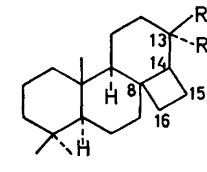
The tricyclic αβ-unsaturated ketone (**5**),[2] when irradiated in *trans*-dichloroethylene (Hanau lamp, high pressure) at 0 °C, under argon, undergoes cycloaddition to give a complex mixture of tetracyclic dichloroketones (40%). This mixture was directly refluxed in benzene with ethylene glycol and a small amount of toluene-*p*-sulphonic acid, and then dehalogenated (Na–NH_3),[3] whereby two olefinic ethylene acetals were formed which were separated by t.l.c. (silica gel–$AgNO_3$). The major compound {360 mg from 1 g of (**5**), m.p. 78–80°; $[\alpha]_D$ ($CHCl_3$) +48°; n.m.r.: 2 olefinic H, part of an ABX system, J_{AB} 3 Hz, indicative of a cyclobutene ring[4]† }, was suspected to be isomer (**6**) on the basis of Scott and Wrixon's rule.[5]



(1)

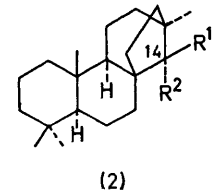


(3)



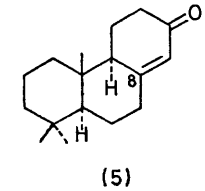
(4)

a; R^1 = Me; R^2 = +
b; R^1 = Me; R^2 = OH
c; R^1 = OH; R^2 = Me



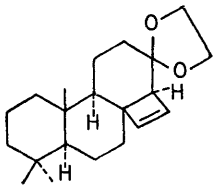
(2)

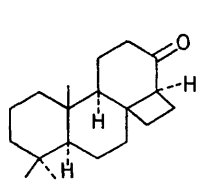
a; R^1 = H; R^2 = OCHO
b; R^1 = H; R^2 = +
c; R^1 = H; R^2 = OAc
d; R^1 = H; R^2 = OH

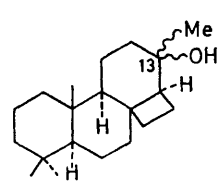


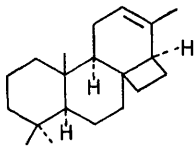
(5)

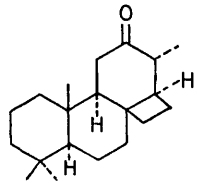
† Satisfactory microanalytical data were obtained throughout.

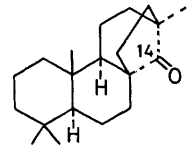

(6)


(7)


(A) and (B)


(8)


(10)


(9)

Catalytic hydrogenation of (**6**), and hydrolysis of the acetal group led to the ketone (**7**), m.p. 67—68° $[\alpha]_D$ ($CHCl_3$) +30°. The latter exhibits a positive Cotton effect, associated with an $n \rightarrow \pi^*$ transition, as predicted by the octant rule for (**7**), thus confirming the β-orientation of the cyclobutane ring.

MeMgI reacts with (**7**) to give a mixture of two tertiary alcohols (A) (60%), m.p. 135—137° $[\alpha]_D$ ($CHCl_3$) + 46°, and (B) (40%), m.p. 93—95° $[\alpha]_D$ ($CHCl_3$) +22°. Their stereochemistry is still unknown. When heated individually in AcOH–NaOc, both (A) and (B) afford essentially two compounds, one of which is 14α-hibyl acetate (**2c**) [30% from both (A) and (B)], m.p. 84—85°, which was identified by its n.m.r. spectrum and its conversion into 14-hibaone (**9**), m.p. 103—105°, $[\alpha]_D$ ($CHCl_3$) + 9°, $\Delta\epsilon$ −1·4 (λ_{max} 300 nm) *via* 14α-hibol (**2c**), m.p. 112—113°, $[\alpha]_D$ ($CHCl_3$) − 6°. Direct comparison of our compounds with authentic samples of 14-hibaone and 14α-hibyl acetate proved their identity.‡

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‡ The major product of the acetolysis of either (A) or (B) is the olefin (**8**), m.p. 49—50°, $\Delta\epsilon$ +0·125 (λ_{max} 207 nm) (predicted +ve); δ 1·55 (d, 2·2 Hz) p.p.m., merges into a singlet upon double irradiation of the olefinic multiplet at δ 5·32 p.p.m. Hydroboration and oxidation gave ketone (**10**), m.p. 118—120°, $[\alpha]_D$ ($CHCl_3$) + 247°, which also exhibits the expected positive Cotton effect thus providing further evidence for the β-orientation of the cyclobutane ring in (**6**) and its derivatives.

[1] O. E. Edwards and R. S. Rosich, *Canad. J. Chem.*, 1968, **46**, 1113; O. E. Edwards and B. S. Mooto, *ibid.*, 1969, **47**, 1189; E. Wenkert and Z. Kumazawa, *Chem. Comm.*, 1968, 140; J. L. Fourrey, J. Polonsky, and E. Wenkert, *ibid.*, 1969, 714; S. F. Hall and A. C. Oehschlager, *ibid.*, p. 1157.
[2] P. K. Grant and R. Hodges, *J. Chem. Soc.*, 1960, 5274.
[3] H. O. House and T. H. Cronin, *J. Org. Chem.*, 1965, **30**, 1061.
[4] P. Laszlo and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1962, **85**, 2017.
[5] A. I. Scott and A. D. Wrixon, *Chem. Comm.*, 1969, 1182, 1970, **43**.