Solvolytic Rearrangement of 1β-Tosyloxy-4α, 8aβ-dimethyldecalin Derivatives; a Synthesis of (±)-Bulnesol

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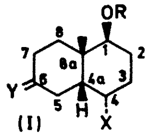
Summary Solvolytic rearrangement of the title compounds has been examined and (±)-bulnesol synthesised.

IN connection with the synthesis of some guaiane-type sesquiterpenoids, we have examined solvolytic rearrangement of 1β-tosyloxy-4α,8aβ-dimethyl-*cis*-decalin (Ia) derivatives functionalised at C-6. The α-methyl group of (Ia) at C-4 was expected to contribute, in conformational equilibrium, to predominant distribution of the steroidal conformation, which is favourable for the rearrangement of (Ia) and its derivatives into hydroazulenes.

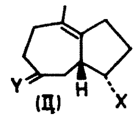
Recently, Heathcock and Ratchiffe[1] have reported solvolytic rearrangement of (Ib), and obtained the hydroazulenic ketone (IIa) and the hydronaphthalenic ketones (IIIa) and (IIIb) in yields of 9, 74, and 13%, respectively. They have attributed this result to predominancy of the non-steroidal conformation in (Ib).

A dioxan solution of the acetoxy-ketone[2] (IVa), triethyl orthoformate, and a catalytic amount of toluene-*p*-sulphonic acid was allowed to stand for overnight at room temperature, giving the enol ether (Va), ν_{max} 1735, 1650, 1625 cm^{-1}, δ 5·00 (overlapped 2H). Reaction of (Va) with the Vilsmeier reagent, prepared from dimethylformamide and phosgene, gave the iminium salt (Vb) after evaporation of the solvent, and (Vb), without further purification, was treated with lithium aluminium hydride to give the amine (Vc), ν_{max} 3400 (OH), 2830, 2752, 2700 cm^{-1} (NMe_2), δ 2·17 (s., 6H), 2·80 (s., 2H), 5·60 (s., 1H). The quaternary ammonium salt (Vd), m.p. 200° (decomp.), was obtained from (Vc) as an ethanol-insoluble solid in the usual manner, and its overall yield was 78% on the basis of (IVa). Compound (Vd) was heated under reflux in ethanol with freshly prepared Raney nickel (10 times its weight) affording the hydrogenolysis product (Ve), ν_{max} 1645, 1620, 817 cm^{-1}, δ 1·58 (s., 3H), which was then hydrolysed with sulphuric acid in aqueous methanol to the hydroxy-ketone (IVb), ν_{max} 3400, 1655 cm^{-1}, δ 1·07 (d., 3H, *J* 6·2 Hz), 3·45 (q., 1H, *J* 9 and 6 Hz), 5·81 (d., 1H, *J* 1·8 Hz), in quantitative overall yield from (Vd). The long-range coupling constant of the olefinic proton of (IVb) in the n.m.r. definitely indicated



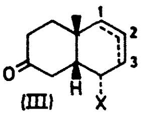
(I)

(a) X = Me, Y = H_2, R = Ts
(b) X = H, Y = O, R = Ts
(c) X = Me, Y = O, R = H
(d) X = Me, Y = O, R = Ac
(e) X = Me, Y = O, R = Ts



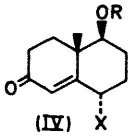
(II)

(a) X = H Y = O
(b) X = Me, Y = O
(c) X = Me, Y = H_2



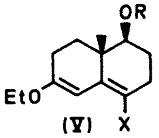
(III)

(a) $\Delta^{1(2)}$, X = H
(b) $\Delta^{2(3)}$, X = H
(c) $\Delta^{1(2)}$, X = Me



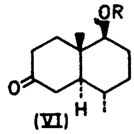
(IV)

(a) X = H, R = Ac
(b) X = Me, R = H
(c) X = Me, R = Ac



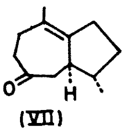
(V)

(a) X = H, R = Ac
(b) X = $CH{:}NMe_2^+Cl^-$, R = Ac
(c) X = CH_2NMe_2, R = H
(d) X = $CH_2NMe_3^+I^-$, R = H
(e) X = Me, R = H

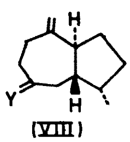


(VI)

(a) R = H
(b) R = Ac
(c) R = Ts

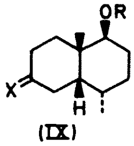


(VII)



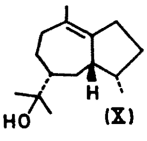
(VIII)

(a) Y = O
(b) Y = H_2



(IX)

(a) X = α-OH, R = THP
(b) X = β-CN, R = THP
(c) X = α-CO_2Me, R = H



(X)

equatorial orientation of the secondary methyl group at C-4.[3]

The *cis*- and *trans*-fused saturated hydroxy-ketones (Ic) and (VIa) were prepared as follows: hydrogenation of (IVb) on 5% palladium–strontium carbonate resulted in formation of a mixture consisting of three parts of (Ic), ν_{max} 1702 cm^{-1}, δ 4·08 (q., 1H, *J* 6 and 10 Hz), and of one part of (VIa), m.p. 84—84·5°, ν_{max} 1708 cm^{-1}, δ 3·30 (q., 1H, *J* 6 and 10 Hz). An authentic sample of the latter was obtained from (IVb) on lithium–liquid ammonia reduction. On the other hand, the acetoxy-ketone (IVc), m.p. 64·5—65·5°, λ_{max} 235 nm (log ϵ 4·18), obtained from (IVb) on acetylation, was hydrogenated on the same catalyst as above to the *cis*-acetate (Id) contaminated with only a trace of the *trans*-acetate (VIb). After separation, (Id) and (VIb) were hydrolysed with alkali to the corresponding hydroxy-ketones (Ic) and (VIa), respectively.

The *trans*-tosylate (VIc), m.p. 149—151°, underwent solvolysis in refluxing glacial acetic acid containing potassium acetate, yielding the rearrangement product (VII), ν_{max} 1708 cm^{-1}, δ 1·05 (d., 3H, *J* 5 Hz), 1·65 (br. s., 3H) in 85% yield, while the *cis*-tosylate (Ie), m.p. 126—127°, under similar reaction conditions, gave (IIIc) (46%), ν_{max} 1715, 730 cm^{-1}, δ 5·43 (d., 1H, *J* 10·5 Hz), 5·73 (br. d., 1H, *J* 10·5 Hz), (IIb + VIIIa) (an inseparable mixture; 38%) and other three minor unidentified products. Wolff–Kishner reduction of the mixture of (IIb) and (VIIIa) gave a mixture of the olefins (IIc and VIIIb; in the ratio 3·7 : 1), from which (IIc) was separated by preparative g.l.c. Compound (IIc) was identified by a comparison of the i.r. and n.m.r. spectra with those of the authentic specimen.[4] Thus, the yield of the rearrangement products obviously increased as expected.

On lithium aluminium hydride reduction, the tetrahydropyranyl ether of (Ic) exclusively afforded the equatorial alcohol (IXa), ν_{max} 3370 cm^{-1}, δ 3·3—4·1 (4H), 4·67 (br. s., 1H), whose tosylate, without purification, was treated with sodium cyanide in dimethylsulphoxide–t-butyl alcohol providing the axial nitrile (IXb), m.p. 117—118°, ν_{max} 2220 cm^{-1}, δ 2·91 (br. s., 1H, $W_{\frac{1}{2}}$ 11 Hz) in 40% yield from (IXa). The cyanide (IXb) was hydrolysed with potassium hydroxide in hot ethylene glycol, following by removal of the tetrahydropyranyl ether group with mineral acid and by subsequent esterification with diazomethane. The resulted hydroxy-ester (IXc) (93% yield), m.p. 66—67°, ν_{max} 1730 cm^{-1}, δ 2·20 (br. s., 1H), 3·90 (q., *J* 10 and 5·6 Hz), was treated under similar solvolysis conditions, and the product was allowed to react with methyl-lithium. From the crude methylation product, (±)-bulnesol [5](X), m.p. 78—80°, was separated by preparative g.l.c., and identified by a comparison of the i.r., n.m.r., and retention time with those of natural bulnesol.

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