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WALLACH'S ANOMALOUS BENZYLIDENE DERIVATIVES

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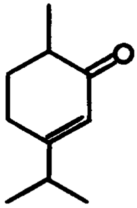
In his classic work on monoterpenes, Wallach[1] obtained several anomalous 'benzylidene' derivatives whose structure did not contain an active methylene group. The structures of these compounds have not been investigated. We now report on one of them, 'dibenzylidene carvenone hydrochloride', formed by condensing carvenone[2] (1) with benzaldehyde in the presence of hydrogen chloride at 0°, to which we assign structure (2). The compound, $C_{24}H_{27}ClO_2$, m.p. 195-196°, had $\nu_{max.}$ 1720 cm.$^{-1}$, $\lambda_{max.}$ (dioxan) 290 (1.93) and 297 (1.90) mμ and was dehydrochlorinated with lithium chloride-dimethylformamide to ketone (3), m.p. 170°, $\nu_{max.}$ 1665 cm.$^{-1}$ $\lambda_{max.}$ 249 (4.28) mμ. Refluxing compound (2) with glacial acetic acid regenerated carvenone and benzaldehyde (ratio 1 :2, g.l.c. and i.r.).



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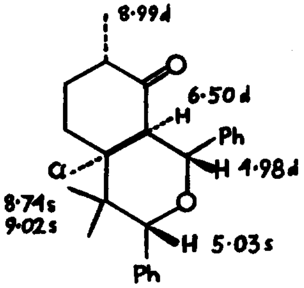

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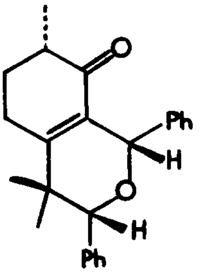
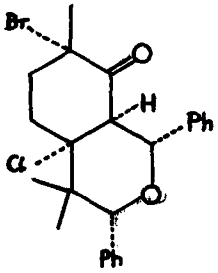


(3)

Bromination of compound (2) with phenyltrimethylammonium perbromide gave the monobromoketone (4) m.p. 144-146°, which on treatment with 10% alcoholic potassium hydroxide yielded the unsaturated alcohol (5), m.p. 200-202°, $\nu_{max.}$ 3,535, 1665, 1620 cm.$^{-1}$, $\lambda_{max.}$ 243 (4.11) mμ. Attempted acetylation was accompanied by aromatisation to give the acetate (6; R = Ac), m.p. 207-208°, $\nu_{max.}$ 1758 cm.$^{-1}$, which was hydrolysed to the phenol (6; R = H), m.p. 151-152°, $C_{24}H_{24}O_2$, $\nu_{max.}$ 3,626, 1620 w cm.$^{-1}$, $\lambda_{max.}$ 275 (3.34), 281 (3.38), $\lambda_{max.}$ (N/100 alkali) 247 (3.82) and 299.5 (3.65)mμ, τ 2.62 s (5H, aromatic), 2.76s (5H, aromatic), 3.03s (2H, aromatic), 4.19s (1H), 5.45s (1H), 5.97s (1H, hydroxylic), 7.98 s (aromatic methyl), 8.79s and 8.84s (gem-dimethyl), giving a



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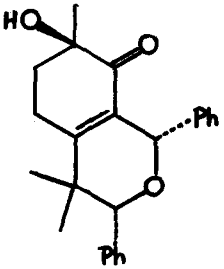

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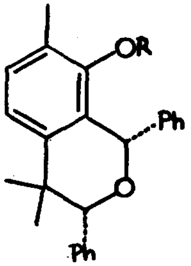

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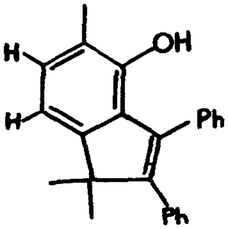
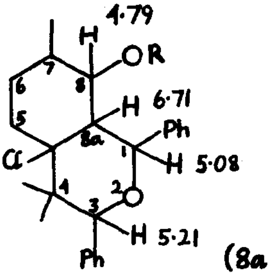


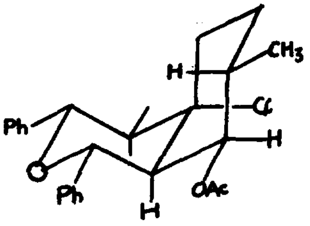
(7)

positive Gibb's test. Treatment with boron trichloride at -80° for 1 hr. gave the indene (7), m.p. 146-147°, $C_{24}H_{22}O$, $\nu_{max.}$ 3550, 1603 $cm.^{-1}$, $\lambda_{max.}$ 281 (3.80), 302 (3.70), 314 (3.53) mμ, $\lambda_{max.}$ (N/100 alkali) 341 (3.32) mμ. The n.m.r. spectrum showed 3 methyl singlets (τ 8.34, 8.43 and 7.89), 2 phenyl multiplets (τ 2.53, 2.86), a hydroxylic proton (τ 5.26), and a pair of o-aromatic protons (AB, τ 3.34, J = 7 c/s). This sequence of aromatisation, and Wittig-type



$J_{8,8a} = 5$ c/s
$J_{1,8a} = 11$ c/s
$J_{7,8} = 11$ c/s

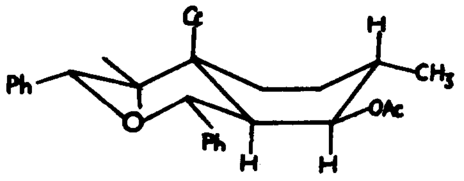
(8a, R = H)
(8b, R = Ac)



(9)

rearrangement of the tetrahydropyran ring, together with the substitution pattern of the indene (7) defines the constitution (2) (without stereochemistry) for 'dibenzylidene carvenone hydrochloride'. N.m.r. assignments are shown in cipher (2).

Reduction of the chloro ketone (2) with lithium aluminium hydride, followed by acetylation, gave the chloro-acetate (8b), m.p. 167-168°, for which n.m.r. assignments are shown. Assuming the validity of the Karplus relation in this system, only two structures, (9) and (10), are possible. These are differentiated by the ring junction stereochemistry, on which information was obtained as follows. The chloro ketone (2) was treated with pyridine/D_2O



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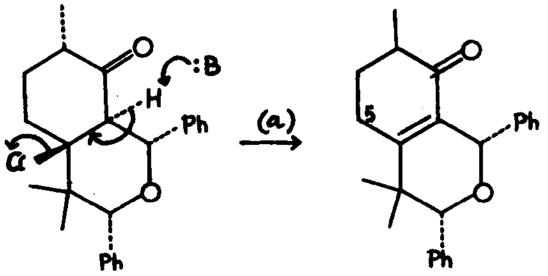
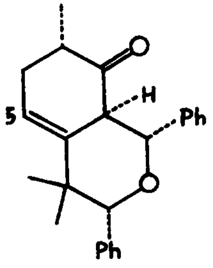


to give the unsaturated ketone (3) shown (mass and n.m.r. spectra) to have incorporated deuterium at C-5 (some dideuterated product was formed). Ketone (3) is not deuterated in pyridine/D_2O. Thus dehydrochlorination proceeds via a mechanism in which deuterium is abstracted from the medium. Concerted elimination, from a trans-ketone, as in route (a) is unacceptable: on the other hand elimination using the cis 4a-8a ketone, proceeding via the β,γ-unsaturated ketone (11) and followed by isomerisation to the α,β-unsaturated ketone (3) with incorporation of deuterium at C-5, provides a satisfactory explanation of the observation. Thus chloro alcohol (8a) has stereochemistry (9), and the stereochemistry of 'dibenzylidene carvenone hydrochloride' follows.



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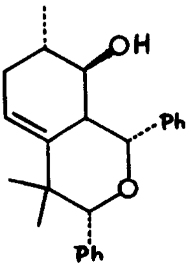

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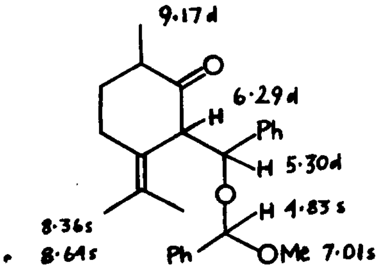

(13)

Dehydrochlorination with lithium chloride of alcohol (8a) gave the unsaturated alcohol (12), m.p. 163-165°, τ 4.44 (1H, olefinic), oxidised by chromium trioxide to the β,γ-unsaturated ketone (11), m.p. 167-168°, $\nu_{max.}$ 1715 $cm.^{-1}$, τ 4.26. The latter readily isomerises in pyridine/D_2O to ketone (3) deuterated at C-5 (mass and n.m.r. spectra).

Reduction of 'dibenzylidene carvenone hydrochloride' with zinc in methanol gave an unexpected product (13), $C_{25}H_{30}O_3$, $\nu_{max.}$ 1709 $cm.^{-1}$, with the n.m.r. assignments shown. This ketone affords acetone on ozonolysis, and decomposes in air, via acetal hydrolysis and retro-aldol, to carvenone and benzaldehyde (g.l.c., i.r.). Borohydride reduction is accompanied by acetal hydrolysis, and the diol (14), m.p. 158-159° is obtained, forming a diacetate m.p. 69-70°. Formation of ketone (13) is more readily explained by methoxide attack at C-3 of ketone (2) than by reduction with zinc metal. In agreement the transformation (2) → (13) is effected by a solution of zinc in methanol, and by magnesium methoxide. In contrast, sodium ethoxide dehydrochlorinates ketone (2). A likely explanation for this unusual reaction lies in co-ordination of the ether oxygen to essentially undissociated 'zinc methoxide' followed by nucleophilic displacement as shown in cipher (15).

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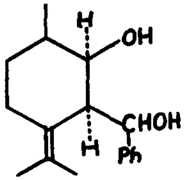

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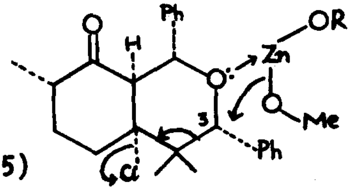

Satisfactory analytical data has been obtained for all compounds mentioned above.

REFERENCES

1. O. Wallach, Annalen, 1899, 305, 261.

2. O. Wallach, Annalen, 1900, 314, 376.