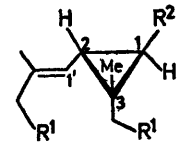
Synthesis of Prephytoene Alcohol

By L. CROMBIE,* D. A. R. FINDLEY, and D. A. WHITING*
(*Department of Chemistry, The University, Nottingham* NG7 2RD)

Summary Synthesis of C_{40} prenylogues of presqualene alcohol is described; the former are of interest in carotenoid biosynthesis.

PRESQUALENE alcohol (**1**; R^1 = geranyl, R^2 = CH_2OH),[1] which has been synthesised,[2] plays an important role in the biosynthesis of squalene from farnesyl units.[1,3] Carotenoid biosynthesis involves tail-tail coupling of two C_{20} molecules in a related way, although the mechanism involves proton loss to form phytoene (**2**; R = farnesyl) rather than hydride reduction to lycopersene (**3**; R = farnesyl).[4] Involvement of prephytoene pyrophosphate (**1**; R^1 = farnesyl, R^2 = $CH_2O{\cdot}P_2O_6H_3$) might be expected and an unambiguous synthesis of the alcohol was undertaken. This report is prompted by the recent findings of Altman, Rilling, *et. al*[5] that a product having this structure can be prepared by zinc-catalysed reaction of geranylgeraniol with an appropriate diazoalkene. The pyrophosphate of their compound cochromatographs with a product of incubation of a *Mycobacteria* sp. Both natural and synthetic compounds were converted into carotenoids on incubation with *Mycobacteria*.[5]

We have used a now well tried[2a,6] addition–elimination approach, in which all-*trans*-farnesylacetone (**4**; R = farnesyl) was converted into geranylgeranoate ester (**5**) with diethylmethyl- or triethyl-phosphonacetates. Reduction to geranylgeraniol and reaction of the corresponding bromide with sodium benzenesulphinate afforded the *all-trans* sulphone (**6**; R = farnesyl) (60%), purified by p.l.c., $M^+(C_{26}H_{38}O_2S)$, τ 1·95—2·50 (5H, ArH), 4·95 (4H, olefinic), 6·18 (2H, d), 8·0 (12H), 8·32, 8·39, and 8·65 (15H, 5-Me). Condensation of the sulphone with ester (**5**; R^1 = farnesyl, R^2 = Me) in dimethyl formamide–KOBu^t gave the cyclopropane ester. Two stereoisomers (**1**) (low R_f) and (**7**) (high R_f) (R^1 = farnesyl, R^2 = CO_2Me) were separated by p.l.c. (silica gel HF254, diethyl ether–light petroleum, 19:1). The former had M^+ $C_{41}H_{66}O_2$, ν_{max} 1720 cm^{-1}, and τ 4·86 (6H, olefinic), 5·07 (1H, d, J 8·5 Hz, 1′-H), 7·99 (24H), 8·32 and 8·41 (27H, vinyl-Me), 8·57 (1H, d, $J_{1,2}$ 5·2 Hz, 1-H), and 8·74 (3H, 3-Me). The high R_f isomer was spectroscopically very similar, but had τ 5·06 (1H, d, J 8·5 Hz, 1′-H), 8·60 (1H, d, $J_{1,2}$ 5·2 Hz, 1-H), and 8·86 (3H, 3-Me). Both esters have the *trans*-1,2 stereochemistry, from the magnitude of $J_{1,2}$; the geometry of the 1,3-relationship follows from comparison of the 3-Me chemical shifts with those of the methyl



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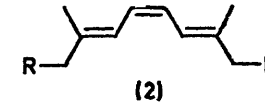

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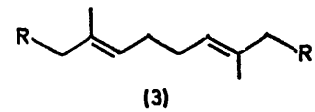

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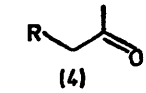

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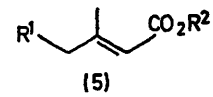

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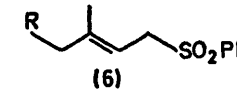

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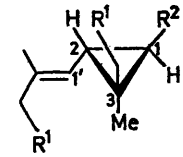

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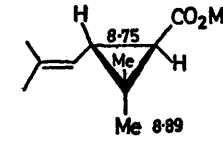

(8)

signals in methyl chrysanthemate[7] (**8**) and relatives. Hydrogenation ($7H_2$) gave the expected saturated ester (M^+).

Reduction ($LiAlH_4$) of the cyclopropane esters gave the corresponding prephytoene alcohols (**1**) (low R_f) and (**7**) (high R_f), (R^1 = farnesyl, $R^2 = CH_2OH$). The former, with stereochemistry parallel to that of presqualene alcohol, had M^+ $C_{40}H_{66}O$, τ 4·90 (6H, olefinic), 5·10 (1H, d, 1′-H), 6·31 (2H, CH_2.OH), 7·99 (24H), 8·32 and 8·41 (27H, vinyl-Me), and 8·90 (3H, 3-Me). The high R_f isomer had a similar spectrum but with τ 8·98 (3H, 3-Me). On hydrogenation, 6·5 mol. equiv. of hydrogen were absorbed, giving the corresponding saturated alcohol. (M^+ $C_{40}H_{80}O$). Tritiated prephytoene alcohols have been prepared ($LiAlT_4$), and study of their role in carotenoid biosynthesis is in progress.

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† G.l.c. for esters: 50 ft OV225 SCOT column and 5 ft 5% **SE30 on Chr**omosorb W, 210°.

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