Stereoselective Total Synthesis of (±)-Seychellene

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Summary The described stereoselective total synthesis of racemic seychellene fully confirms the structure and stereochemistry assigned to this novel natural product.

THE structure and absolute stereochemistry of the novel sesquiterpene seychellene, isolated[1,2] from *Pogostemon patchouli* Pallet *var. suavis* Hook, have been assigned[2] as shown in (I). We report here the total synthesis of (±)-seychellene, *via* a highly stereoselective route which fully corroborates the structure and stereochemistry suggested.

Reaction of the known[3] tetrahydropyranyl ether derivative (II) with lithium dimethylcuprate[4] in ether, followed by trapping of the intermediate enolate anion with acetyl chloride,[5] gave, in 78% yield the enol acetate (III).† Epoxidation of the latter with *m*-chloroperbenzoic acid in benzene, followed by thermal rearrangement[6] of the resulting epoxide (IV), afforded the crystalline keto-acetate (V), m.p. 120—123°,‡ in 74% yield.

Reaction of (V) with methylenetriphenylphosphoran in dimethyl sulphoxide[7] gave the olefinic acetate (VI), contaminated with a small amount of the corresponding alcohol (VII). Successive subjection of the former [or the mixture of (VI) and (VII)] to hydrogenation [tris(triphenylphosphine)chlororhodium[8] in benzene], hydrolysis (potassium hydroxide in methanol), and oxidation (chromium trioxide in pyridine) afforded, in 50% overall yield from the keto-acetate (V), the crystalline ketone (VIII), m.p. 96—98°. The latter was recovered unchanged when subjected to basic epimerizing conditions. Ketone (VIII) was reacted with methyl-lithium in ether and the resulting

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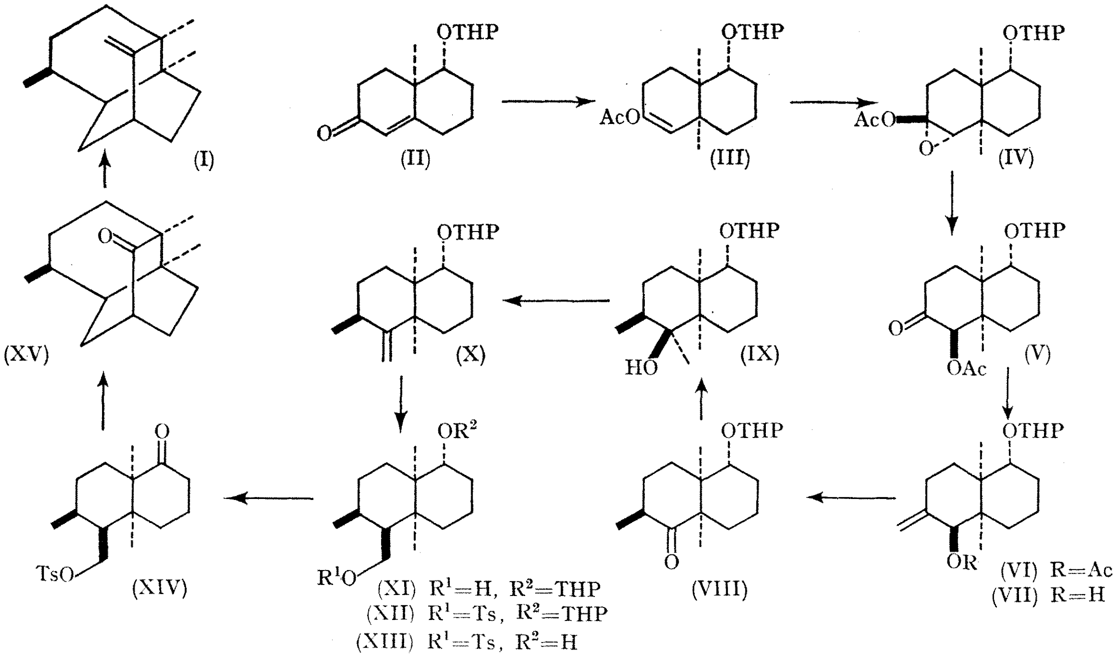
† The stereochemical assignments of all synthetic intermediates were based upon recorded analogy and/or upon conformational analysis. Details will be given in the full paper. Furthermore, all new compounds described gave satisfactory analytical data and showed spectral properties in complete accordance with the structures assigned.

‡ Subsequent removal of the tetrahydropyranyl protecting group from this compound gave the corresponding alcohol, m.p. 195—195·5°, which was clearly shown to be stereochemically homogeneous.



tertiary alcohol (IX) (67% yield, m.p. 96—98°) was dehydrated by means of thionyl chloride in benzene–pyridine at 0°, to give, in quantitative yield, the exocyclic olefin (X). Hydroboration of the latter in tetrahydrofuran gave a near quantitative yield of the primary alcohol (XI) which, upon treatment with toluene-*p*-sulphonyl chloride in dry pyridine, afforded the corresponding tosylate (XII), m.p. 117—117·5°, in 73% yield. Removal of the tetrahydropyranyl protecting group was achieved by heating a solution of compound (XII) in methanol containing a catalytic amount of toluene-*p*-sulphonic acid. The product (XIII), m.p. 117—118°, was oxidized with chromium trioxide in pyridine to give [75% yield from (XI)] the crucial synthetic intermediate, keto-tosylate (XIV), m.p. 108—108.5°.

When the keto-tosylate (XIV) was treated with an excess of methylsulphinyl carbanion in dimethyl sulphoxide[9] at 75° for 2 hr., the tricyclic ketone (XV) [b.p. 120° (bath temperature)/0·2 mm.] was obtained in 90% yield. Treatment of the latter with ethereal methyl-lithium, followed by dehydration of the resulting crude tertiary alcohol with thionyl chloride in benzene–pyridine gave, in 85% yield, (±)-seychellene (I). The latter synthetic material exhibited an i.r. spectrum and g.l.c. retention times identical with those of authentic seychellene.

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