

Studies in terpenoids. Part 43*: Synthesis of (\pm)-2,6-dimethyl-10-(*p*-tolyl) undeca-2,6 (E)-diene, the diterpene of *Salvia dorisiana***

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Abstract. (\pm)-2, 6-Dimethyl-10-(*p*-tolyl) undeca-2,6(E)-diene (1a), a diterpene hydrocarbon from the essential oil of *Salvia dorisiana* has been synthesised by two methods. One pot reaction of *p*-tolylmagnesium bromide with geranylacetone (5) and hydrogenolysis of the resulting benzylic alcohol (1b) without isolation furnished the natural product (1a). In the other method citrylidene-*p*-methylacetophenone (6a) was used as the starting material. The trienone (6a) was reduced to the corresponding alcohol (6b) which was hydrogenated to (6c) and oxidised to the dienone (6d). Reaction of the dienone (6d) with methylmagnesium iodide, followed by dehydration of the carbinol and reduction with lithium in liquid ammonia furnished the diterpene (1a).

Keywords. Diterpene; *Salvia dorisiana*; synthesis by one pot reaction; geranylacetone; citrylidene-*p*-methylacetophenone.

1. Introduction

A new monocyclic diterpene has been isolated recently from the leaf oil of *Salvia dorisiana* and its structure has been established as 2,6-dimethyl-10-(*p*-tolyl) undeca-2, 6(E)-diene (1a) on the basis of spectral evidence (Halim and Collins 1975). The hydrocarbon (1a), which can be regarded as an isoprenologue of α -curcumene (2), is theoretically capable of cyclisation involving the aromatic ring and the 6, 7-double bond along the possible paths 'a' or 'b' to generate the bicyclic diterpenes (3 or 4) which can be regarded as the isoprenologues of dehydrocadinane and dehydrohimalchalone respectively. The synthesis of (1a) was therefore considered to be of interest, (i) for confirmation of the structure of the natural product and (ii) for providing an easy access to the hydrocarbon (1a) for the cyclisation experiments.

2. Results and discussion

2.1. Synthesis via geranylacetone (5) by a one-pot reaction

The synthesis of the diterpene (1a) was accomplished by adoption of Hall's one-pot technique (Hall *et al* 1975). Thus the reaction of *p*-tolylmagnesium bromide with

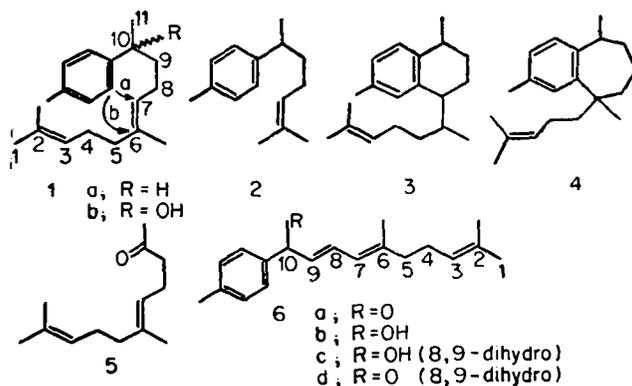
*Part 42, Anantha Reddy P and Krishna Rao G S. *J. Chem. Soc. (Perkin D)*, in press.

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geranylacetone (5) (Dicker and Whiting 1958) and hydrogenolysis of the resulting benzylic alcohol (1b) without isolation, followed by column chromatography, furnished the diterpene (1a) in excellent purity with spectra (IR and PMR) and mass spectral fragmentation pattern identical in all respects as reported in literature (Halim and Collins 1975).

2.2. Synthesis via citrylidene-*p*-methylacetophenone (6a)

In another variation citrylidene-*p*-methylacetophenone (6a) (Sy 1956) was reduced by lithium aluminium hydride to give the corresponding trienol (6b). On hydrogenation (6b) gave the 8, 9-dihydroalcohol (6c) which was oxidised (Collins *et al* 1968) to the 8, 9-dihydroketone (6d). Successive steps of Grignard reaction with methylmagnesium iodide, dehydration and metal-ammonia reduction on the 8, 9-dihydroketone (6d) gave the diterpene (1a), identical (IR and PMR) with the one obtained from the one-pot reaction described above.



3. Experimental

All melting and boiling points reported are uncorrected. The IR spectra were recorded on Perkin-Elmer model 700 or model 137 and the PMR spectra on Varian HA-100D or T-60 spectrometers. Light petrol refers to petroleum ether fraction, b.p. 40-60°. b.t. refers to bath temperature in short path distillations. The solvent extracts were appropriately washed and dried over anhydrous sodium sulphate before removal of solvents during work-up of reactions.

3.1. (\pm)-2, 6-Dimethyl-10-(*p*-tolyl) undeca-2, 6(*E*)-diene (1a)

3.1.1. By one-pot reaction from geranylacetone (5)-*p*-tolylmagnesium bromide was prepared from *p*-bromotoluene (1.14 g) and magnesium (0.16 g) in dry ether (20 ml). When all the magnesium reacted, dry tetrahydrofuran (25 ml) was added, followed by the dropwise addition of geranylacetone (5) (1.3g) in tetrahydrofuran (10 ml). The reaction mixture was stirred for 5 hr and left overnight. Ether was distilled off and the residual mixture was refluxed for 4 hr and cooled to room temperature. Liquid

ammonia (100 ml), distilled over sodium, was directly let into the flask containing the reaction mixture. Thin slices of lithium (0.25g) were added in small lots with stirring. After the addition was complete the reaction mixture was stirred for 30 min and ammonium chloride (2g) was added carefully till the colour was discharged. The ammonia was allowed to evaporate off and water (100 ml) was added to the residue. The hydrocarbon was extracted with light petrol. Removal of the solvent from the extract, followed by column chromatography (silicagel-hexane) gave the diterpene (1a) (1.6g). Shortpath distillation furnished an analytically pure sample, b.t. 140–145°/2mm Hg; MS: (m/e) 270 (M⁺, 50%), 227, (52%), 159 (32%), 145 (72%), 132 (88%), 119 (100%), 105 (52%), 91 (33%) and 69 (55%); ν_{\max} (neat): 1517, 1458, 1375, 1108 and 816 cm⁻¹; PMR: δ (C Cl₄) 1.2 (3H, d, $J=8$ Hz, CH-CH₃), 1.5–1.7 (9H, m, vinyl-Me), 1.97 (8H, m, CH₂), 2.3 (3H, s, Ar-Me), 2.67 (1H, m, C₁₀-H), 5.13 (2H, m, vinyl-H) and 7.05 (4H, s, Ar-H) (Found: C, 88.72; H, 10.96. C₂₀H₃₀ requires C, 88.82; H, 11.18%).

3.1.2. From citrylidene-*p*-methylacetophenone (6a).—Citrylidene-*p*-methylacetophenone (6a) (Sy 1956) prepared by condensation of freshly distilled citral (7.6 g) with *p*-methylacetophenone (6.7 g) in the presence of aqueous sodium hydroxide (10.5 ml, 30%) at room temperature for 60 hr and b.p. 180°/3mm Hg (9 g); ν_{\max} (neat): 1670–1660, 1600 and 1580 cm⁻¹; PMR: δ (CCl₄) 1.60 (9H, bs, vinyl-Me), 1.86 (2H, m, C₄-H₂), 2.13 (2H, m, C₅-H₂), 2.33 (3H, s, Ar-Me), 5.0, (1H, m, vinyl-H), 5.80–7.60 (3H, vinyl-H), 7.03 (2H, d, $J=8$ Hz, Ar-H *ortho* to Me) and 7.66 (2H, d, $J=8$ Hz, Ar-H *ortho* to C=O).

A solution of the foregoing trienone (6a) (1.34 g) in dry ether (10 ml) was added dropwise to a suspension of lithium aluminium hydride (0.15g) in dry ether (20ml) and stirred for 4 hr. Usual work-up furnished the trienol (6b) in quantitative yield; ν_{\max} (neat): 3375, 1660, and 1610 cm⁻¹; PMR: δ (CCl₄) 1.46–1.86 (9H, 3s, vinyl-Me), 2.1 (1H, bs, OH, exchanges with D₂O), 4.8–7.26 5H, vinyl-H and CH-OH) and 7.03 (4H, s, Ar-H).

The above trienol (6b) in ethanol (25 ml) was shaken at atmospheric pressure with hydrogen in the presence of palladium-carbon (10%, 0.1 g) at 30° till the rapid absorption of hydrogen (105 ml at 30° at atmospheric pressure) ceased. On work-up, the dienol (6c) was obtained (1.1 g); ν_{\max} (neat): 3375, 1670 and 1620 cm⁻¹; PMR: δ (CCl₄) 1.43–1.83 (9H, 3 merged s, vinyl Me), 1.83–2.2 (8H, m, CH₂), 2.36 (3H, s, Ar-Me), 4.3–5.4 (3H, m, 2 vinyl-H and CHOH) and 7.06 (4H, s, Ar-H).

A solution of the above dienol (6c) (4.12 g) in methylene chloride (30 ml) was treated with chromium trioxide-pyridine complex [prepared from CrO₃ (9.6 g) and dry pyridine (90 ml) in CH₂Cl₂ (100 ml)] at room temperature for 30 min. The usual work-up furnished the dienone (6d) (3.8 g); ν_{\max} (neat): 1680 and 1600 cm⁻¹; PMR: δ (CCl₄) 1.46–1.83 (9H, bs, vinyl-Me), 1.83–2.26 (6H, m, allylic CH₂) 2.43 (3H, s, Ar-Me), 2.80 (2H, t, COCH₂), 4.6–5.6 (2H, vinyl-H), 7.2 (2H, d, $J=8$ Hz, Ar-H *ortho* to Me) and 7.83 (2H, d, $J=8$ Hz, Ar-H *ortho* to C=O).

A solution of the dienone (6d) (1.3 g) in dry ether (20 ml) was added to a solution of methylmagnesium iodide in ether (20 ml) [prepared from magnesium (0.12 g) and methyl iodide (1.42 g)]. The reaction mixture was stirred for 5 hr and left overnight. It was poured into saturated aqueous ammonium chloride (200 ml) and the product was extracted with ether (50 ml \times 4). Distillation of the solvent gave the crude carbinol (1b) which was treated with *p*-toluenesulphonic acid (0.05 g) in a solution of

benzene (50 ml) for 12 hr at room temperature. The dehydrated product was taken up in ether (5 ml) and the solution added to liquid ammonia (100 ml; distilled over sodium). Thinly cut lithium (0.2 g) pieces were added in lots to the liquid ammonia solution with stirring. After 30 min ammonium chloride (2 g) was added. The ammonia was allowed to evaporate off. Water (100 ml) was added and the product was extracted with light petrol. Removal of the solvent followed by column chromatography (silica gel-hexane) furnished the pure diterpene (1 g), identical (IR and PMR) with the one obtained by the one-pot technique.

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References

- Collins J C, Hess W W and Frank F J 1968 *Tetrahedron Lett.* 3363
Dicker D W and Whiting M C 1958 *J. Chem. Soc.* 1994
Halim A F and Collins R P 1975 *J. Agric. Food. Chem.* **23** 506
Hall S S, McEnroe F J and Shue H J 1975 *J. Org. Chem.* **40** 3306
Sy M M 1956 *Compt. Rend.* **243** 1772