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OXIDATION STUDIES USING PYRIDINIUM CHLOROCHROMATE ON (+)-3-CARENE DERIVATIVES

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MATSUI et al.\(^1\) reported that rethronyl esters of (±) cis- and (±) trans-2,2,3-trimethylcyclopropanecarboxylic acids exhibit high insecticidal activity. Therefore, it was expected that the pure optically active isomers of 2,2,3-trimethylcyclopropanecarboxylates, with the 1R-cis configuration should show enhanced insecticidal activity. For obtaining such esters, the hydroxaldehyde viz. 2,2-dimethyl-1-(2-methyl-2-hydroxypropyl)-1-formylcyclopropane (II) was considered as the suitable starting material.

Pyridinium chlorochromate\(^2\) (PCC) is considered as one of the best mild oxidizing agents for selective oxidation of primary alcohols to aldehydes in high yields. The diol (III) obtained from (+)-3-carene (I) was subjected to PCC oxidation in the hope of getting the desired hydroxaldehyde (II). Contrary to our expectation a mixture of two lactones was obtained as the major product of the reaction.

These have been separated by column chromatography over silicic acid. Fractions eluted with petroleum ether containing 65% chloroform gave a solid, purified by crystallization from petroleum ether (36%), m.p. 82–83\(^\circ\). [\(\alpha\)]\(^{20}_D\) = 78\(^\circ\) (C, 2.0, CHCl\(_3\)) identified as (−) cis-dihydroxysanthemolactone (V) by comparison of spectral properties with those reported in the literature\(^3\).

Elution of column with chloroform containing 20% ethyl acetate furnished a TLC pure liquid (18%) identified as the hydroxylactone (VII), \(\text{C}_{10}\text{H}_{16}\text{O}_{3}\), M\(^+\) 186, [\(\alpha\)]\(^{20}_D\) = 48\(^\circ\) (C, 1.7. CHCl\(_3\)) by spectral properties described below: \(\text{IR: 3521 (OH), 1752 (\(\gamma\)-lactone) PMR: 1.26 (9H, s, methyls of hydroxyisopropyl and one of the methyls at C\(_4\)), 1.4 (5H, s, overlapping a multiplet, another methyl at C\(_4\) and CH\(_2\) at C\(_5\)), 2.2–2.5 (3H, m, CH\(_2\) at C\(_2\) and methine proton at C\(_3\)), 3.06 (1H, brs, exchangeable with D\(_2\)O, OH proton).}

The assignment of structure to hydroxylactone (VII) was further confirmed by its conversion to the known (−) pyrocine\(^4\). Thus, dehydration of hydroxylactone (VII) by PTS in refluxing benzene afforded a crystalline solid (85%), \(\text{C}_{10}\text{H}_{16}\text{O}_{2}\), M\(^+\) 168, m.p. 84–85\(^\circ\); [\(\alpha\)]\(^{20}_D\) = 69\(^\circ\) (C, 1.8. CHCl\(_3\)) identified as (−) pyrocine (VIII) on the basis of following spectral data: \(\text{IR: 1770 (\(\gamma\)-lactone), 840 (CH=CH=C=)}\); \(\text{PMR: 1.21, 1.36 (3H each, s each, methyls at C}\(_4\)), 1.7, 1.76 (3H each, s each, vinyl methyls), 2.26, 2.43 (1H each, d each, J = 5 Hz each, methylene protons at C\(_3\)), 2.96 (1H, m, methine proton at C\(_3\)) and 5.0 (1H, d, J = 9 Hz, olefinic proton).

However, PCC oxidation of diol (III) under buffer conditions (2 equivalents of sodium acetate) afforded in addition to the above two lactones (V and VII) the expected hydroxaldehyde (II) but in low yield (13%) as a thick liquid, \(\text{C}_{10}\text{H}_{16}\text{O}_{2}\), M\(^+\) 170, identified by spectral data: \(\text{IR: 3509 (OH), 2740, 1695 (CHO) PMR: 0.75 (1H, m, C}\(_3\) cyclopropane proton), 1.0, 1.1 \{3H each, s each, gem-dimethyl), 1.2 (8H, brs, methyls of hydroxy isopropyl and CH\(_2\) at C\(_3\)), 1.6 \{1H, m, C\(_4\) cyclopropane proton), 2.96 (1H, brs, exchangeable with D\(_2\)O, OH proton) and 9.3 \(\{1H, d, J = 6 Hz, aldehyde proton).\}

The tertiary alcohol (XIV) was considered as a suitable intermediate, since it was expected to give, on dehydration followed by oxidation of the resulting olefin, the required 2,2,3-trimethylcyclopropanecarboxylic acid. However, the Huang-Minlon reduction of (II) to (XIV) did not proceed satisfactorily.

* Satisfactory elemental analysis have been obtained for all the compounds reported.
** IR bands expressed in \(\nu\) (cm\(^{-1}\)) and PMR chemical shifts in \(\delta\) (ppm) scale with TMS as internal standard.
Dehydration of hydroxyacetate viz. 3-(acetoxy-methyl)-2,2-dimethyl-cis-1-(2-hydroxy-2-methylpropyl) cyclopropane (IX) by POCl₃/pyridine at 0° is known to yield a mixture of two isomeric unsaturated acetates (X and XI) in 60:40 ratio. Acetate (X) has been successfully converted into methyl (+)-cis-chrysanthemate by Bhat et al. The isomeric unsaturated acetate (XI) which is a by-product, has now been converted into (+) cis-dihydrochrysanthemolactone (VI).

Thus in another sequence of reactions, acetate (XI) on epoxidation with perbenzoic acid (PBA, 2N) gave the epoxyacetate (XII, 92%), C₁₂H₁₅O₃, M⁺ 212, [α]ᵢ²⁰⁻¹⁸.₂⁰ (C, 2, CHCl₃); 1R: 1730, 1240 (-OCOCH₃); PMR (CDCl₃): 0.60, 0.80 (1H each, m, C₁ and C₃ cyclopropane protons), 1.06, 1.16 (3H each, s each, gem-dimethyl), 1.33 (3H, s, tertiary methyl in the side chain), 1.56 (2H, brm, CH₂ at C₃), 2.03 (3H, s, acetate methyl), 2.48 (2H, m, methylene protons attached to carbon bearing the epoxide function) and 4.0 (2H, m, CH₂ at C₃).

Lithium aluminium hydride reduction of epoxyacetate (XII) in ether at 0° followed by usual work-up afforded the crystalline diol (IV, 92.5%), C₁₆H₃₀O₂; m.p. 72–73°, M⁺ 172, identified by the spectral data: IR: 3320, 1020 (OH); PMR (CDCl₃): 0.7 (2H, m, C₁ and C₃ cyclopropane protons), 1.12 (3H each, s each, gem-dimethyl), 1.32 (6H, s, hydroxy-isopropylmethyls), 1.54 (2H, m, CH₂ at C₁), 3.34–3.94 (2H, m, CH₂OH protons) and 4.76 (2H, s, exchangeable with D₂O, OH protons).

Jones chronic acid oxidation of the diol (IV) under controlled conditions gave a mixture of products, separated into acidic (19%) and neutral (70%) parts. The neutral part was purified by column chromatography over silicic acid and identified as (+)-cis-dihydrodihydranthemolactone (VI). C₁₈H₂₆O₂, m.p. 82–83° (petroleum ether). M⁺ 168 [α]ᵢ²⁰⁺⁺ 50° (C, 1.5, CHCl₃) by comparison of spectral properties with those reported earlier. The acidic part was esterified with an ethereal solution of diazo methane and characterized as the known hydroxyster (XIII).

(+)-cis and (-)-cis-dihydrodihydranthemolactones are important intermediates in the synthesis of (+) 1R-cis and (+) 1R-trans chrysanthemic acids, which give rise to active insecticidal esters.

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