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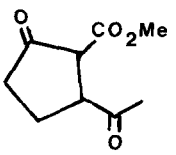
SYNTHESIS OF A HIGHLY FUNCTIONALISED BICYCLO[3.3.0]OCTANE

Alan T. Hewson* and David T. MacPherson, Department of Chemistry, Sheffield City Polytechnic, Pond Street, Sheffield, S1 1WB.

Summary: The bicyclo[3.3.0]octanes 4 and 5 are prepared by making use of vinyl phosphonium salts, and 4 is used in formal total syntheses of chrysomelidial and loganin.

There has been a surge of interest in recent years in the area of cyclopentane chemistry. This interest, prompted largely by work on prostaglandins, has now been extended to polyquinanes. A recent review has discussed developments in the latter area.[1]

We have previously described syntheses of the diketoester 1 [2] and the vinyl phosphonium salts 2 and 3 [3]. We now report the use of these compounds in the synthesis of a bicyclo[3.3.0]octane which is highly functionalised in a way promising great potential for the synthesis of natural products.



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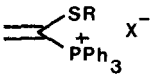
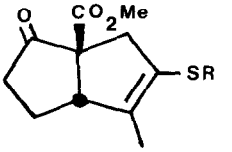


2 ; R = Me , X = Cl
3 ; R = Ph , X = I

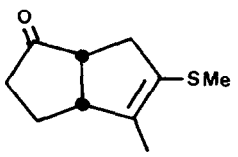


4 ; R = Me
5 ; R = Ph

Treatment of a THF solution of 1 with sodium hydride, followed by addition of the phosphonium salt 2 gave the bicyclo[3.3.0]octane 4 (97%; oil; IR (neat) 1740, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.7, m, 3H; 2.1-2.3, m, 4H; 2.2, s, 3H; 3.0-3.2, m, 2H; 3.5-3.7, m, 1H; 3.7, s, 3H). Similarly, use of phosphonium salt 3 gave 5 (82%, m. 79-81 °C). Decarbomethyoxylation of 4 was readily achieved by use of sodium cyanide in HMPA[4] affording 6 (82%; oil; IR (neat) 1730, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.72, s, 3H; 2.1, m, 4H; 2.2, s, 3H; 2.75, m, 3H, 3.4, broad unresolved signal 1H).

Treatment of 6 with methyl lithium in ether gave stereospecifically the alcohol 7 (75%; oil; IR (neat) 3430 cm^{-1}) whose hydrolysis ($HgCl_2/CH_3CN/H_2O$) gave the keto alcohol 8 (69%; m. 57.5-58.5 °C; lit. [5]m. 58.5-59.0 °C). This latter compound has previously been converted to chrysomelidial, 9, the defence secretion of a chrysomelide beetle.[5]

The approach to loganin also began with the bicyclo[3.3.0]octane 6. Cyanohydrin formation (NaCN/EtOH/AcOH), followed by dehydration ($POCl_3$/pyridine) gave the unsaturated nitrile 10 69%; m.67-69°; IR (KBr) 2220 cm^{-1}) which afforded the unsaturated ketoester 11 (48%; oil; IR (neat) 1740, 1720 cm^{-1}) with MeOH/c. H_2SO_4.



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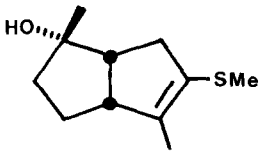

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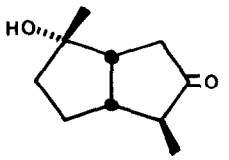

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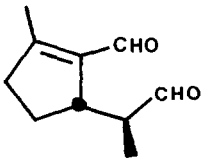

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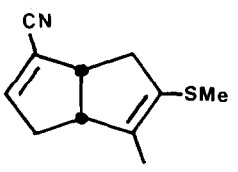
Stereospecific reduction of 11 with $NaBH_4$ gave the alcohol 12 (82%; IR (neat) 3450, 1710, 1630 cm^{-1}). Inversion of stereochemistry at the hydroxyl bearing carbon was then achieved via mesylation (MsCl/pyridine) followed by S_N2 displacement (Bu_4NOAc) to give the acetate 13 (74%; oil; IR (neat) 1740, 1720, 1640 cm^{-1}; ^1H NMR δ 6.6, m, 1H; 1.5-2.8, m, 6H; 2.05, s, 3H; 1.0, d, 3H).



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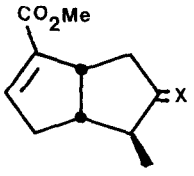
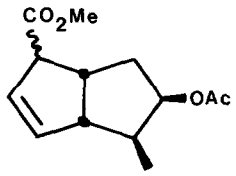


11 ; X= O

12 ; X= H, OH

13 ; X= OAc, H



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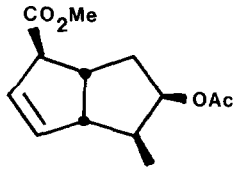

15

Deconjugation of the α,β-unsaturated ester was achieved[6] by treatment of 13 with four equivalents of LDA in THF/HMPA at -78°, and quenching of the anion with methanol. The product 14 (39%) appeared from its NMR spectrum to be a single compound, although the stereochemistry of the carbomethoxy group is not definitely known. However, the IR and ^1H NMR spectra of 14 were identical with those of 15 prepared by a different route.[7] In terms of the conversion of 14 to loganin the stereochemistry of the carbomethoxyl bearing carbon is of no consequence since that centre becomes sp^2 hybridised.[7]

Acknowledgements

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