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TRICYCLO[3,3,0,$0^{2,8}$]OCTANONES AS BUILDING BLOCKS IN NATURAL PRODUCTS SYNTHESIS (I). --THE SYNTHESIS OF CHRYSOMELIDIAL--

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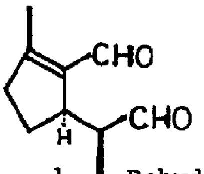
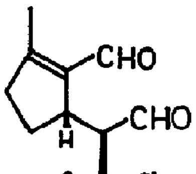
Summary : The stereocontrolled synthesis of chrysomelidial from 4-methyl-tricyclo[3,3,0,$0^{2,8}$]octan-3-one is described.

The increasing number of cyclopentanoid natural products and their interesting biological activity has stirred considerable interest into synthesis of such compounds. We have emberked upon the synthesis of cyclopentanoid natural products via same intermediate which is easily obtained from ordinary starting material. We selected tricyclo[3,3,0,$0^{2,8}$]octanone as the varsatile intermediate. Tricyclo[3,3,0,$0^{2,8}$]octanone, obtained from photolysis1) of bicyclo[2,2,2]octanone or decomposition2) of 2-cyclopenten-1-yldiazomethylketone with cupric sulfate, was transformed with formic acid or p-toluenesulfonic acid into functionalized bicyclo[3,3,0]octanone, which has a distinguishable functional group in the each five membered ring and can be led into cyclopentanoid natural products via the selective conversion of the functional group. We have applied this versatile intermediate, tricyclo[3,3,0,$0^{2,8}$]octanone, towards one of the cyclopentanoid monoterpenes.

Recently a new monoterpene dial, dehydroiridodial (1), was isolated as a principle of the pungency of *Actinidia polygama* Miq., and it was synthesized by K. Yoshihara et al..3) On the other hand, chrysomelidial (2), the stereoisomer of dehydroiridodial, was isolated from the larval defensive secretion of a chrysomelide beetle (*Plagiodera versicolora*) in 1977, and it was synthesized in 1978 by J. Meinwald et al..4) Both syntheses were non-stereospecific syntheses involving tedious separation steps.

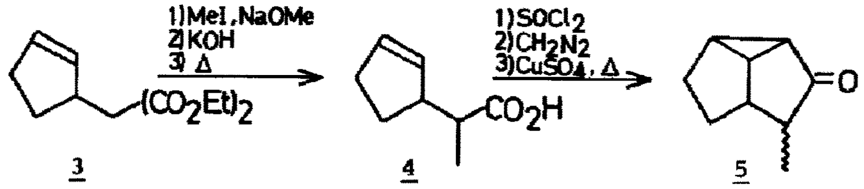


1 Dehydroiridodial

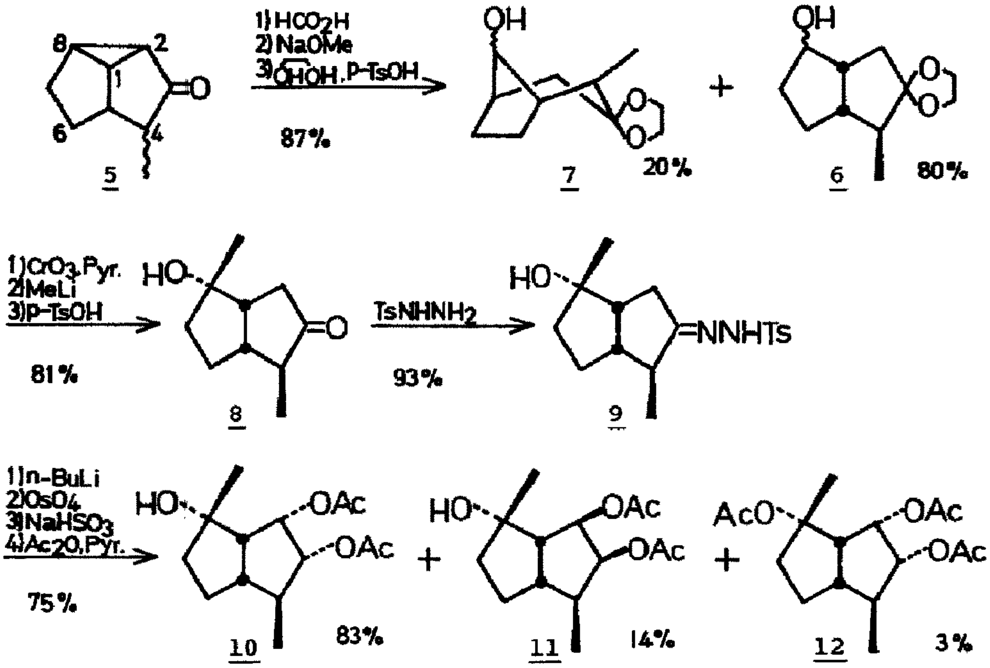


2 Chrysomelidial

We wish to report the stereocontrolled synthesis of chrysomelidial from 4-methyl-tricyclo[3,3,0,0^{2,8}]octan-3-one (5)5)which was prepared from diethyl 2-cyclopenten-1-ylmalonate (3)6)by the general method of Doering7). Methylatio of 3 with methyl iodide followed by hydrolysis and decarboxylation afforded 2- cyclopenten-1-yl)propionic acid (4) [bp.129-131°C/19mmHg] in 79 % yield. Conve sion of 4 into its acid chloride, followed by treatment with ethereal diazomethane, furnished the diazo ketone, and the decomposion of the latter with cupric sulfate in refluxing cyclohexane yielded 4-methyl-tricyclo[3,3,0,0^{2,8}]oct 3-one (5) [bp.85-87°C/10mmHg] in 83 % overall yield from 4.

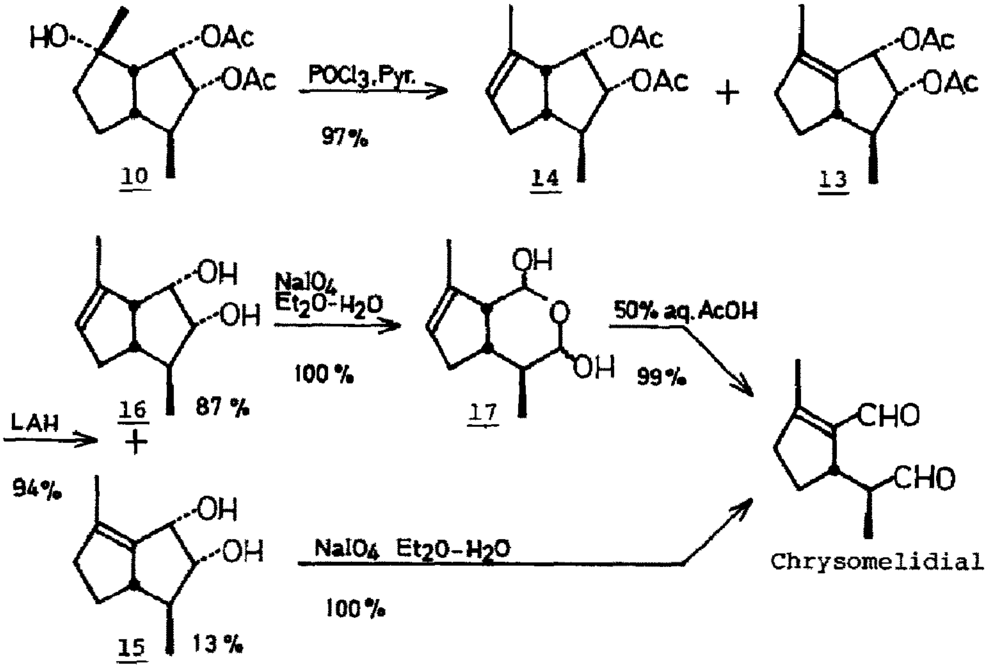


Ring cleavage of 5 with 99 % formic acid at 70-80°C for 30 min followed b methanolysis and ketalization in usual manner gave in 87 % yield a mixture of t desired ketal (6) [2-8 bond cleavage] and its structural isomer (7) [1-2 bond cleavage] in ratio 4:1 by pmr, and the two isomers were easily separated with column chromatography. 6 was oxidized with chromium trioxide-pyridine complex i methylene chloride to give the corresponding ketone which, upon alkylation with



methyl lithium in ether at -78°C followed by treatment with p-toluenesulfonic acid in aqueous THF, afforded ketoalcohol (8) [mp.58.5-59.0°C] in 81 % yield. Refluxing of 8 with p-toluenesulfonyl hydrazine in methanol for 30 min produced the corresponding hydrazone (9) [mp.139-141°C] in 93 % yield. Treatment of 9 with excess n-butyl lithium in THF, followed by oxidation with osmium tetraoxide in ether, and acetylation gave in 75 % yield diacetate (10), (11) and triacetate (12) in ratio 83:14:3[8].

10 was treated with phosphoryl chloride in pyridine at 50°C for 3 hr to form in 97 % yield a mixture of the desired tetra-substituted olefin (13) and tri-substituted olefin (14) in ratio ca. 15:85 by pmr. Reduction of the mixture of 13 and 14 with lithium aluminium hydride in ether gave diol (15) and (16) in ratio 13:87 in 94 % yield. Oxidation of 15 with sodium periodate in ether-water [1:1] at 4°C for 24 hr afforded chrysomelidial in 100 % yield. Same oxidation of 16 produced the hydrate of dial (17), which was transformed into chrysomelidial by refluxing in 50 % aqueous acetic acid for 15 min in 99 % overall yield from 16. Diacetate (11) was also converted to chrysomelidial by the same procedure.



The pmr and ir spectrum, and mass fragmentation of the synthetic chrysomelidial were consistent with those of the natural chrysomelidial[4].

References and Footnotes

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4. J. Meinwald, T. H. Jones, T. Eisner and K. Hicks, Proc. Nat. Acad. Sci. USA 74, 2189 (1977) ; J. Meinwald and T. H. Jones, J. Amer. Chem. Soc., 100, 18 (1978)
5. We are currently utilizing this useful intermediate in the synthesis of loganin, elenolic acid, xylomollin, brefeldin A and prostaglandin.
6. Org. Synth., Coll. Vol. 4, 291
7. W. von E. Doering, E. T. Fosser and R. L. Kaye, Tetrahedron, 21, 25 (1965)
8. The stereochemistry of diacetate (10) and (11) was determined by the rate o acyl rearrangement : Diacetate (10) was treated with excess acetic anhydrid in pyridine at 25°C for 72 hr afforded the triacetate (12), however diaceta (11) was not transformed to the corresponding triacetate in the same experimental condition. We considered that the olefin derived from 9 was preferentially oxidized with osumium tetraoxide from the surface of hinder side by influence on the hydroxy group, which took the form a complex-like with osumium tetraoxide.

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