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SPIROVETIVANES FROM SILYLATED 1-HYDROXYCYCLOPROPANECARBOXALDEHYDE.

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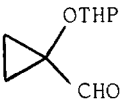
SUMMARY : The spiro[4.5]decan-2-one and a spirovetivane, key intermediates of the [4.5] spirobicyclic sesquiterpenes, have been prepared from silylated 1-vinylcyclopropanols. A selective desilylation of enol ethers is featured.

In the preceding communication a convenient synthesis of the 1-hydroxycyclopropanecarboxaldehyde tetrahydropyranyl ether 1, efficient precursor of 1-vinylcyclopropanol derivatives, which undergo readily either specific four or five ring annulations has been reported (1).



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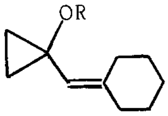
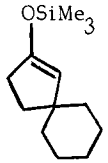


2a R = THP
b = H
c = $SiMe_3$



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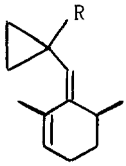
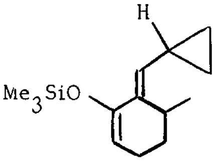
This attractive synthon appears to be also a partner of choice for five-membered ring spiro-annulation. So, Wittig reaction of aldehyde 1 with cyclohexylidenephosphorane prepared from the corresponding phosphonium iodide and potassium t-butoxide in THF gave the vinylcyclopropane 2a in 78% yield. Removal of the THP group of 2a by means of pyridinium p-toluenesulfonate (PPTS) (2) in ethanol at 55°C, within 3 hours as monitored by TLC, provided the 1-vinylcyclopropanol 2b, which can be then silylated (3) to give the 1-trimethylsiloxy 1-vinylcyclopropane 2c, in 95% yield from 2a. On flash thermolysis at 650°C for 10 ms 2c underwent $C_3 \longrightarrow C_5$ spiroannulation into the regiospecific enol silyl ether of the spiro[4.5]decan-2-one 3 (4), a basic carbone framework found in sesquiterpenes of the spirovetivane or acorane class (5), which has been the target of many syntheses (6).

As a matter of fact, the thermal ring enlargement of the vinylcyclopropane systems 4 (7) and 5 (8) has been recently used to prepare some spirovetivanes.



4a R = $SiMe_3$
b = $-C(CH_3)_2OCH_3$



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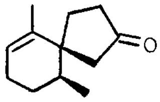

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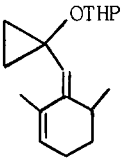
However, the great advantage offered by the thermal ring expansion of 1-siloxyvinylcyclopropanes such as 2c is to provide directly a spiroketone with the carbonyl group in the proper position found in the spirovetivane 6, a constituent of Vetiver oil, which plays a significant role in the reconstitution of this essential oil (9) and constitutes particularly the key intermediate for the synthesis of biogenetically related spirovetivanes of economic importance, such as (±) α-vetispirene (10), (±) β-vetivone (11), (±) hinesol (12), agarospirol (12) .... Moreover, driving substituent effect (13-15) and stereoselectivity (8), due to the presence of a siloxy group on the cyclopropane ring, can be expected for the thermal vinylcyclopropane - cyclopentene rearrangement. Taking into account these considerations, we have initiated an investigation aimed at the total stereoselective synthesis of the natural spiroketone 6 from the aldehyde 1.



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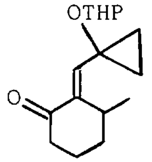

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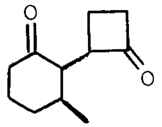

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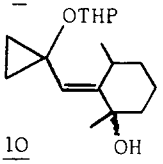
Our approach began with the direct olefination of the aldehyde 1 but, in spite of many attempts, for example coupling of 2,6-dimethyl-2-cyclohexen-1 one with 1 in the presence of Ti(o) (7), we have not obtained the expected diene 7. On the other hand, trapping of the enolate anion resulting from the cuprous iodide-catalyzed addition of methylmagnesium iodide to 2-cyclohexen-1-one with 1 afforded the corresponding ketol ; which, underwent dehydration into the enone 8 (75% yield from 1) upon successive treatment with acetic anhydride and 1,5-diazabicyclo [4.3.0]non-5-ene following the procedure used by Piers et al., to obtain 5 from cyclopropanecarboxaldehyde (8). Unfortunately, attempts to remove the THP group of the enone 8 in mild acidic conditions, so upon heating in ethanol at 40°C in the presence of (10 mol. %) of PPTS (2) led exclusively, within 100 mn as monitored by TLC, to the cyclobutanone 9.



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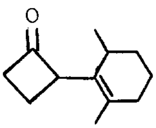

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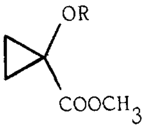
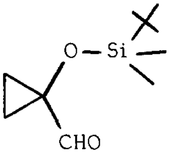
Addition of one equivalent of methyllithium to the enone 8 gave the tertiary cyclohexanol 10 which, in the same conditions (EtOH, PPTS, 40°) underwent rearrangement into the 2-vinylcyclobutanone 11. (For examples of such a ready $C_3 \rightarrow C_4$ ring expansion, see ref. 1).



12a R = H

b = $SitBu(CH_3)_2$



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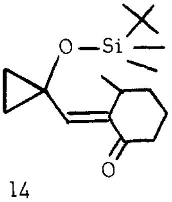

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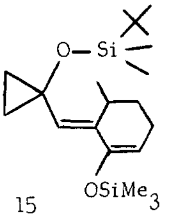
To achieve the synthesis of the target molecule 6 we have prepared the 1-(t-butyldimethylsiloxy) cyclopropanecarboxaldehyde 13. Thus, treatment of the readily available hydroxyester 12a (1) with $ClSiMe_2t.Bu$ in DMF in the presence of 2 equiv. of imidazole (16) gave the silylated cyclopropanol 12b. Then, reduction of 12b with DIBAH in toluene at -70°C, followed by oxidation of the resulting cyclopropylcarbinol by means of oxalyl chloride activated dimethylsulfoxide (17) provided the aldehyde 13 in 94% overall yield from 12a. Application of the Piers procedure (8) which allowed the preparation of enone 8 from 1 led to the siloxy enone 14 in 73% overall yield from the aldehyde 13.



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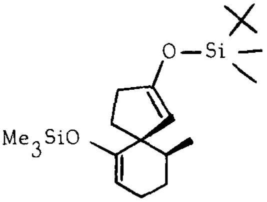

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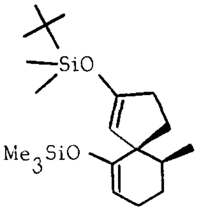

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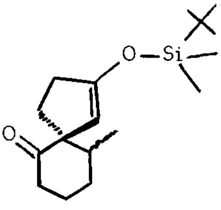
The enone 14 was then converted (LDA, $ClSiMe_3$, Ether) into the corresponding enol trimethyl ether 15. Flash thermolysis at 600°C of this compound gave a mixture of the spiro disilylated enol ethers 17 and 18 in a ratio of 78/22, as shown by capillary GC. The presence of the enol silyl ether of five- and six-membered ketones is consistent with the spectroscopic data : two vinylic protons at δ 4.25 (s) and 4.55 (t) ppm in NMR and two double bond stretching frequencies in IR at 1645 and 1655 cm^{-1}, respectively. As previously shown, conjugation of the vinylic bond such as in 15, facilitates the thermal rearrangement by lowering the required activation energy (15). On the other hand, flash thermolysis of enone 14 produced an important amount of desilylated derivative of 17 (ν C=O : 1710 and 1750 cm^{-1}).

Then, highly selective desilylation of 17 (containing 22% of 18) into the epimeric cyclohexanones 19 (ν C=O : 1710 cm^{-1}) was obtained upon treatment with 0.1 M triethylamine in methanol (19) at 30°C for 48 hr ; while for instance, addition of $ClSiMe_3$ (1 μl) to a methanolic solution of 17 (25 μl) and after 2 mn at 10°C, quenching with NEt_3, of the so formed HCl, gave the dione 20. (νC=O : 1710 and 1750 cm^{-1}).



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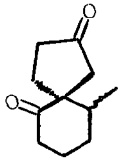

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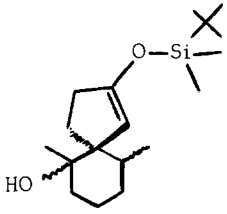

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Finally, addition of $IMgCH_3$ to 19 in ether gave the epimeric alcohols 21 which underwent dehydration and desilylation on treatment with p-toluenesulfonic acid in refluxing benzene to provide in 90% yield, a mixture of spiroenones, from which the major compound 6, isolated by liquid chromatography on silica gel, exhibited IR and NMR spectra identical with those published for this enone (8,10). (We are very grateful to Professor G. Buchi for copies of spectra of enone 6).

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