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A NEW, FACILE SYNTHESIS OF THE 3-METHYL-2(5H)-FURANOID STRUCTURAL UNIT FROM KETONES

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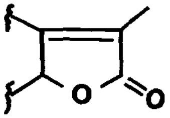
The 3-methyl-2(5H)-furanoid structural unit is prepared from ketones via 1,4-rearrangement of siloxyalkenes on peroxidation and via oxetene rearrangement of 1-diethylaminopropyne in 53-58% overall yield.

The synthesis of the title unit (1) from α-epoxyketones has been reported from this laboratory.[1] Because the moiety 1 together with its readily accessible derivatives 2[2] and 3[3,4] occur frequently in natural products (especially sesquiterpenes), the method can be used as a part of total synthesis of e.g. eremophilenolide[5].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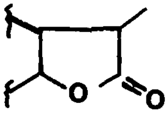
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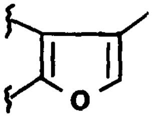
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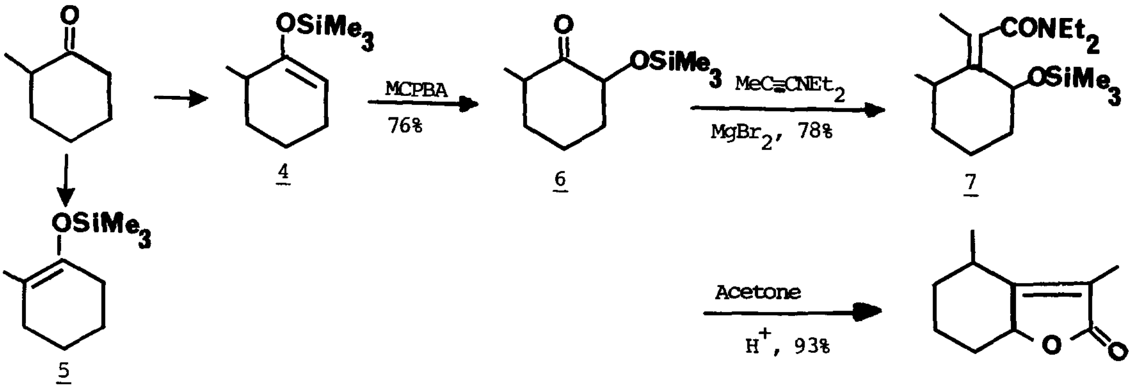
The usual intermediates in the syntheses of sesquiterpenes are various kinds of cyclohexanone systems[5] which may be transformed to the corresponding α-epoxyketones via phenylselenenylation, selenoxide fragmentation[6] and alkaline hydrogen peroxide oxidation. It appeared probable that α-siloxyketones (from 1,4-rearrangement of siloxyalkenes on peroxidation[7], e.g., 4 to 6 in 76% yield) might be more convenient intermediates than α-epoxyketones, especially since siloxyalkenes are readily prepared from ketones in high yields under kinetically (97%) or thermodynamically (84%) controlled conditions[8] (e.g. 4 or 5).



8, overall 56%

The treatment of siloxyketone 6 with 1-diethylaminopropyne[9] and dry $MgBr_2$ in dry ether[1] gave after oxetene rearrangement the siloxyamide 7 in 78% yield which upon acidic treatment in acetone underwent ring closure giving the lactone 8 in 93% yield.

The advantage of this procedure for preparing the unit 1 is its simplicity and the fact that all the reaction steps starting from a ketone can be performed successively without purification of the intermediates (this may decrease the overall yield). Thus, this method appears highly convenient for the conversion of ketones into compounds 1 (overall yields): 2-methylcyclohexanone → 1 (i.e. 8), 56% : cyclohexanone → 1, 58% : 2-octalone (cis/trans) → 1, 53%.

A typical procedure (without isolation of intermediates)[10]:

2-Methylcyclohexanone (300 mg) was silylated with the Me_3SiCl / LDA / THF system.[8] Dry hexane was added into the reaction mixture and the precipitated LiCl was filtered. The solvent was evaporated and the remaining viscous oil was dissolved in dry CH_2Cl_2 (10 ml). The peroxidation with MCPBA (560 mg ; 1.2 x equiv.) was performed at 0°C.[7] After addition of dry hexane (40 ml; to precipitate acidic compounds) the solution was filtered through neutral alumina and the solvent was evaporated. Dry ether (10 ml) was added together with 500 µl (ca 1.3 x equiv.) of 1-diethylaminopropyne. Then 700 mg (ca 1.3 x equiv.) of dry $MgBr_2$ was added into vigorously stirred mixture under argon. The stirring was continued at ambient temperature for 2 hr during which time a very viscous sirup developed on the wall of the reaction flask. Saturated $NaHCO_3$ solution was added and the ethereal layer was separated and evaporated. The residue was dissolved in 20 ml of acetone. A few drops of dil. H_2SO_4 or cons. HCl was added and the mixture was first stirred at room temperature for 2 hr and then refluxed for 3-4 hr. After cooling $NaHCO_3$ (200 - 300 mg) was added, the solids filtered and acetone evaporated. The residue was chromatographed on preparative silica gel TLC-plates (1:9 EtoAc/$CHCl_3$ as eluant) yielding the furanone 8 in 56% overall yield from 2-methylcyclohexanone.

REFERENCES AND FOOTNOTES

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10. In an other run all the intermediates (all viscous oils) were purified and identified by spectral data. Yields are unoptimized.

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