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# THE CYCLOPROPANATION OF CYCLOALKENONE SILYL ENOL ETHERS. THE ORIENTED α- OR α'-MONOMETHYLATION OF CYCLOALKENONES.

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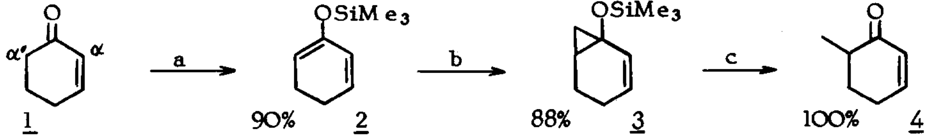
It has been reported that the cyclopropanation of trimethylsilyl enol ethers of saturated aldehydes and ketones, using a recent, improved modification of the Simmons-Smith reaction (Zn/Ag couple is used instead of Zn/Cu couple and the product is isolated, not by classical acidic hydrolysis, but by pyridine work-up (1)) is a good route to siloxycyclopropanes (2). The methanolysis of the latter leads to cyclopropanols and acidic or (better) alkaline hydrolysis to the α-monomethylation product of the starting carbonyl compounds (2). All these reactions have a real synthetic interest (see also (3)).

The purpose of the present communication is to show firstly that 2-trimethylsiloxy-cycloalka-1,3-dienes, easily prepared from α-cycloalkenones, undergo monocyclopropanation almost exclusively in the 1,2-position by reaction with the modified Simmons-Smith reagent. Subsequent methanolysis gives the corresponding cyclopropanol and alkaline or acidic hydrolysis leads to the α'-methylation product of the cycloalkenone.



For instance, a) cyclohexenone 1 treated by lithium diisopropylamide (4), then ClSiMe$_3$ in THF + Et$_2$O (50/50) at 0° following House's method (5), gives exclusively 2-siloxy-cyclohexa-1,3-diene 2 b.p. 33 - 37°/10$^{-2}$mm Y : 90% ; b) the reaction of 2, with 1.1 equivalents of CH$_2$I$_2$, Zn/Ag in boiling ether, for 18 hrs, followed by the addition of 2,2 equivalents of pyridine, filtration of the zinc complex so formed and distillation, leads to the vinylsiloxycyclopropane 3 b.p. 40 - 42°/ 3x10$^{-2}$mm Y: 88% ; c) by refluxing for 8 or 10 hours in M/10 methanolic NaOH 3 is quantitatively converted into 6-methyl-cyclohex-2-ene-1 one 4 b.p. 74- 75 °/24 mm. Analogous results (i.e. α'-methylation) have been obtained from cyclohexenones 5, 6, 7, 8. Cyclic siloxydienes like 2 are as easily prepared from ketones 5, 6 and 7 as from ketone 1, even though these three compounds are well known to undergo very facile enolisation towards the α carbon atom with exo migration of the double bond. Ketone 8 can be converted into its silyl enol ether by using NEt$_3$ and ClSiMe$_3$ ; but the LiN(C$_3$H$_7$)$_2$ method is better. In the case of 6 steric hindrance by the gem-dimethyl group does not prevent cyclopropanation and a second α'-methylation of the product is possible in the same manner without difficulty.

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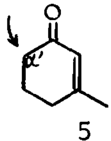

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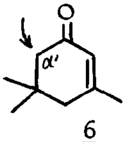

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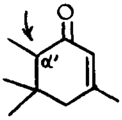

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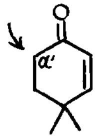

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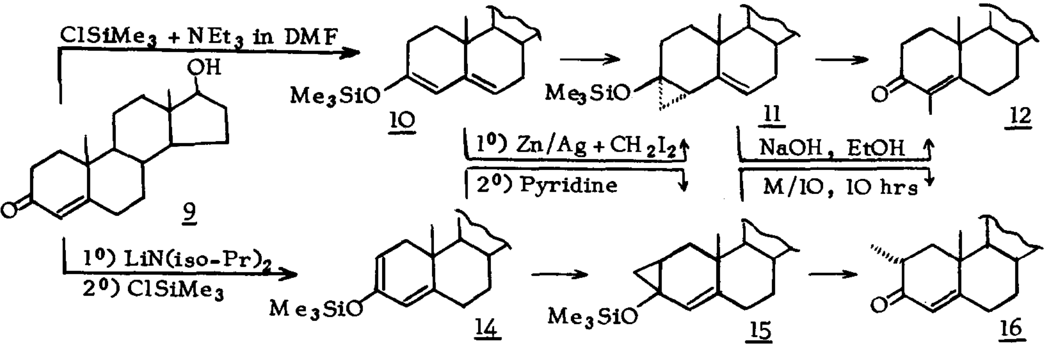
Secondly, an example chosen in the steroid field, shows that either α-methylation or α'-methylation of a cycloalkenone can be carried out as required by using such a sequence. It is more specific than the direct methylation of cross-conjugated dienolates formed with lithium $2^0$-amide bases (4) and leads exclusively to the mono-methylated ketone.

Indeed we recently published that 4-methyl-testosterone 12 can be easily prepared from testosterone 9 via the 3-siloxy-3,5-diene 10 (formed from thermodynamic enolate of 9) by cyclopropanation with $CH_2I_2$ + Zn/Ag and pyridine work-up, followed by alkaline hydrolysis of the product 11, whereas methanolysis of 11 leads to the corresponding cyclopropanol.

From 9, a sequence of reactions analogous to 1 → 2 → 3 → 4 may be carried out leading initially to 3-siloxy-2,4 diene (formed from kinetic enolate of 9) : 14 a liquid (Y : 90%) ; the latter with 1.5 or 2 equivalents of $CH_2I_2$ + Zn/Ag (reflux for 18 hrs in ether) and then pyridine work-up, only gives the cyclopropanation product in the 2,3 position : 15 Y : 85% as an approximately 50 : 50 mixture of α and β epimers. Treatment of 15 for 48 hrs in boiling 1 M alcoholic NaOH leads exclusively to the 2α-methyl-testosterone m.p. 152$^0$ (lit. (7) 151 - 153$^0$) also identified by its spectra (16).



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