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HOMO-1,4-ADDITION OF GRIGNARD REAGENTS TO β-OXO THIOCARBONYL COMPOUNDS CIS CYCLOPROPANE RING CLOSURE.

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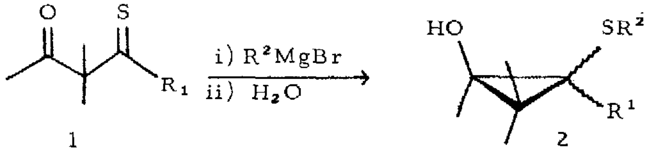
We have recently reported (1) that thiophilic addition of Grignard reagents to the β-oxo thioketone 1 ($R^1 = CH_3$) yielded 2-alkylthiocyclopropanols 2. Only one stereoisomer was obtained, whose configuration was presumed to be cis. In another field, thiophilic addition of Grignard reagents to dithioesters (2) is also reported. This prompted us to study the behaviour of dithioesters bearing a β-carbonyl group such as 1 (R^1= S alkyl) (3) toward Grignard reagents. At room temperature, these dithioesters react with organomagnesium bromides in tetrahydrofuran. They give a ring closure and yield in each case one stereoisomer of 2,2- bis (alkylthio) 1,3, 3-trimethylcyclopropanols 2 (R^1= SMe-R^2= Et, tBu ; R^1= SEt-R^2= Et) Yields= 45-65 % - NMR (CCl_4)δ_{OH}= 2,8-3,2 ppm disappearing after treatment with D_2O - IR (CCl_4)ν_{OH}= 3425-3440 cm^{-1} (4).

To gain further information about the mechanism, we ran the reaction with convenient substituents to attempt to prepare a couple of stereoisomers. When treated by iPrMgBr, dithioester 1a gives the cyclopropanol 2a (yield= 70 %) and dithioester 1b the cyclopropanol 2b (yield= 55%) when treated by EtMgBr. Compounds 2a and 2b are diastereoisomers and this demonstrates that the reaction is again stereospecific.



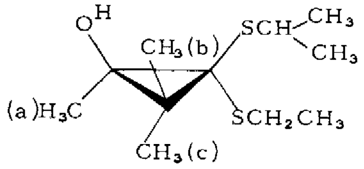
1 2

$$1a\ (R^1 = SEt) \xrightarrow{isoPrMgBr} 2a$$

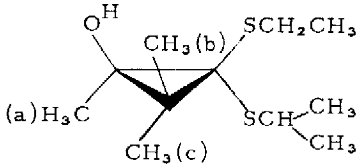
$$1b\ (R^1 = SisoPr) \xrightarrow{EtMgBr} 2b$$

The configurations of isomers 2a and 2b were assigned using a proton NMR shift reagent. We chose tris(2,2-dimethyl-6,6,7,7,8,8,8-heptafluoro-3,5-octanedionato) europium. Interesting proton shifts are observed. They will be expressed vs mol ratio $[Eu(FOD)_3/substrate]$. In the range of ratios used (0,10 to 0,35) experimental plots align. For the two compounds, the hydroxyl proton signal undergoes the largest shift followed by the (a) methyl protons (slopes 2a= 14,1 ; 2b= 13,0); it shows, as expected (5,6), that the metal is coordinated with the oxygen atom but not with the sulfur atoms. Shifts of the (b) and (c) methyl protons respectively for compounds 2a (sl. : 6,1-5,2) and 2b (6,4-4,5) are similar. This indicates the nearly identical geometry of the two complexes. For configuration attribution the most significant shifts are those of methine and methylene. For compound 2a δ_{CH} increases more rapidly than δ_{CH} for compound 2b while increasing $[Eu(FOD)_3/substrate]$ ratios. Inversely, CH_2 signal for cyclopropanol 2a is shifted more slowly than that of compound 2b (7). More over the spectra of compound 2a exhibit two methyl doublets (iPr. group), the separationof which increases with the ratio $\left[\mathrm{Eu(FOD)_3/cyclopropanol}\right]$ (up to$\Delta\delta$= 1,07 ppm for ratio= 0,34). For compound 2b, in spite of this magnetic non equivalence, the separation of the two doublets is not significantly observed. All of these findings provide good evidence for the conclusion that in compound 2a the iPr group is located closer to the metal than the iPr group of 2b and inversely for the Et group. This leads us to conclude that the compounds 2a and 2b have the following configurations and that they both result from cis addition.

2a

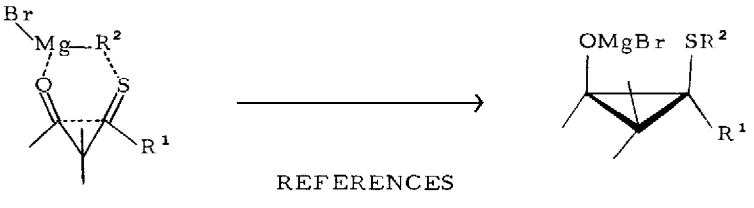


2b



The preceding method of configurational assignment allows us to use it to determine the structure of the stereoisomer 2 obtained by reaction of thioketone 1(R^1= CH_3) with iPrMgBr (1). After addition of Eu(FOD)$_3$, shifts observed for the hydroxyl proton and the (a),(b),(c)methyl proton types (sl= 13,1 - 7,5-4,7)are closely comparable with preceding ones ; analogous complex geometry may be assumed. Once more, we observed a large separation of the doublets of isopropyl's methyls, due to the magnetic non equivalence of these groups (up to 0,65 ppm for ratio= 0,21). This leads us again to attribute a cis geometry to the compound 2 (R^1= CH_3).

So we assume that all cyclopropanols 2 are products of cis-addition of Grignard reagents upon thiocarbonyl compounds 1. As indicated below, a concerted homo-1,4-addition can explain the specific cis-addition. The assistance of a neighbouring group stiffens the positive character of the thiocarbonyl's sulfur atom ; such a mechanism might also explain an other exclusive thiophilic addition that we observed recently with an α carbonyl group (8).



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7 - All slopes, have been calculated according to the least squares method ; the correlation coefficients are $\geqslant$ 0,990.
Compound 2a : slope CH_2= 3,7 ; slope CH= 5,6 - Compound 2b : the slopes are undetermined for, in the range of ratios used, the signals of the two protons overlap.
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