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ABOUT THE MECHANISM OF THE REARRANGEMENT OF β-HYDROXYALKYLSELENIDES TO KETONES

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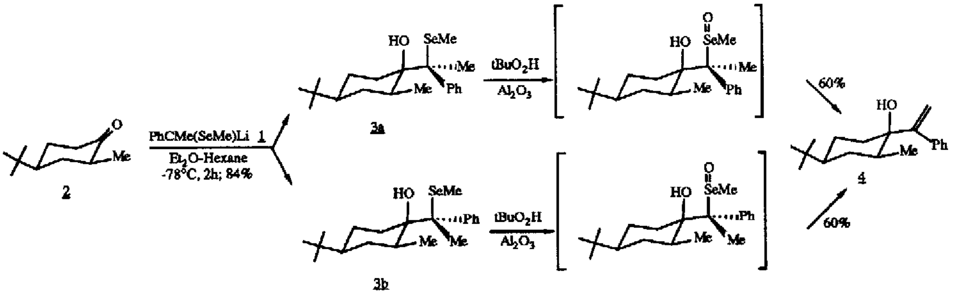
The regio and stereochemistry of the ring enlargement of β-hydroxyalkyl methylselenides derived from cyclic ketones is disclosed and sheds some light on the intimate mechanism of the rearrangement.

We recently described that β-hydroxyalkylselenides bearing two alkyl groups on the carbon linked to the selenium atom react with silver tetrafluoroborate [1,2c] or with dichlorocarbene [2] to produce ketones resulting from their rearrangement.We now report our results concerning the intimate mechanism of such reactions.

We have for that purpose carefully studied the stereochemical features of these transformations on the two stereoisomeric β-hydroxyalkylselenides 3a and 3b. These have been obtained as a one to one mixture on reaction of 1-methylseleno-1-phenyl-ethyllithium [3,4] 1 with cis-2-methyl-4-tert-butyl-cyclohexanone [5] 2 (ether-hexane : -78°C, 2h; 84 % yield; TLC SiO_2, ether-pentane 5-95, 3a rf 0.36; 3b rf 0.44) and have been separated by preparative layer chromatography. The structure of 3b (mp 73°C, pentane) has been unambiguously ascertained by X-ray crystallography and results from the equatorial attack [6] of the organometallic on 2. That 3a is the diastereoisomer of 3b which also results from the equatorial attack on 2 has been deduced from the chemical correlation shown in the Scheme 1. We have for that purpose destroyed the chiral center which makes the difference between the two compounds using the well established selenoxide elimination reaction ($tBuO_2H$-Al_2O_3, THF, 55°C, 3.5h; 60 % yield; TLC SiO_2, ether-pentane 10-90, rf 0.46) and we have confirmed (^1H, ^{13}C NMR, IR, TLC) the identity of the allyl alcohol 4 from both origins.

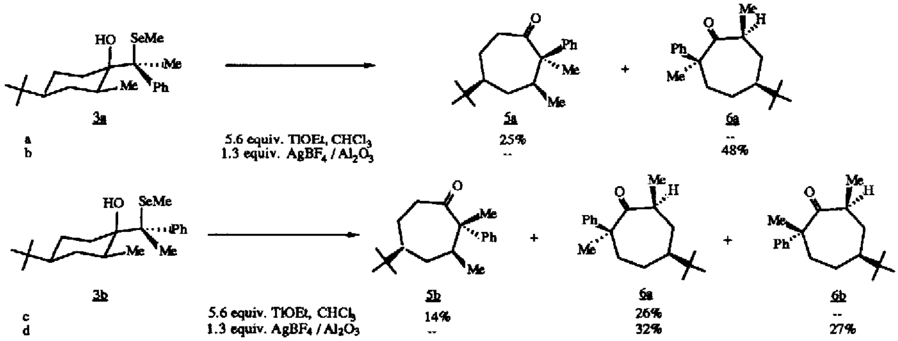
Scheme 1



We expected to get on these models, some information about the stereochemical outcome of the rearrangement both at the migrating carbon and at the migration terminus. For that purpose each of these β-hydroxyalkylselenides have been subjected to the reaction of dichlorocarbene (5.6 equiv. TlOEt, 0.25 M in 3, $CHCl_3$, 20°C, 8h) and of silver tetrafluoroborate supported on basic alumina (1.3 equiv. AgBF, 8 equiv. Al_2O_3 Woelm, 0.25 M in 3, $CHCl_3$, 20°C, 4h). Cycloheptanones 5 or 6 resulting respectively from the migration of the more and the least substituted carbon have been isolated [7] as pure products and their structure determined by X-ray crystallography (5a mp 66°C, pentane; 6b mp 97°C, pentane) or deduced from their mass spectra and from NMR experiments (5b and 6a) which includes comparisons with those of related structure (5a and 6b) as well as experiences involving proton-proton and long range proton-carbon 2D correlations (6a). This was not possible on 5b due to the small amount of compound we had in hand. We however found that the coupling constants obtained experimentally fully agree with those obtained by calculation [8] on the more stable conformer (pseudo chair with equatorial tert-butyl and methyl groups).

Thus it appears from the results reported above and assembled in Scheme 2 that this rearrangement proceeds with retention of the configuration at the migrating carbon whatever are the stereoisomer of β-hydroxyalkylselenide (3a or 3b) and the experimental conditions used (CCl_2 or $AgBF_4$). On the other hand the regiochemistry of the resulting cycloheptanone and the stereochemistry at the migration terminus proved to be completely dependent upon both the stereochemistry of the starting material and nature of the reagent used. Thus the β-hydroxylalkylselenide 3a reacts with dichlorocarbene and regio- and stereoselectively leads to the cycloheptanone 5a resulting from the migration of the most substituted carbon. Its diastereoisomer 3b produces, under similar conditions, a mixture of regioisomers 5b and 6a, in which the latter, arising from the migration of the least substituted carbon prevails. Particularly interesting is the observation that inversion of configuration occurs in all the cases at the migration terminus suggesting that a concerted process is taking place (Scheme 2, entries a and c).

Scheme 2



The reaction takes another course when silver salts are instead used since both the regio- and the stereochemical outcomes are different from those disclosed above. Not only the least substituted carbon now migrates but also the ring enlargement proceeds with almost complete racemization from 3b and with apparent complete retention of configuration from 3a. The latter might be the result of two consecutive inversions involving the intermediate formation of an epoxide which remains to be confirmed.

We cannot propose at the present time an unified theory which explains all the results reported herein but it is obvious that the mechanisms of the two ring enlargement reactions differ markedly. We assume from the stereochemical results disclosed above that the dichlorocarbene mediated rearrangement occurs in a concerted fashion on an antiperiplanar conformation whereas the one involving silver tetrafluoroborate takes place stepwise. As far as the regiochemistry is concerned it is clear that "the inherent migratory aptitude scales" [9] which have been often used to predict or to explain the ability of groups to migrate in related rearrangements is no longer valid in our case and therefore other criteria such as the relative conformation in the transition states might play a crucial role.

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7) We isolated, beside the expected cycloheptanones 5 and / or 6 resulting from the ring expansion reaction, the allyl alcohol 4 (14 % from 3a, 11 % from 3b) and cis-2-methyl 4-tert-butyl cyclohexanone 2a (25 % from 3a, 18 % from 3b) resulting respectively from the elimination of methylselenodichloromethane or from the C,C bond cleavage on the betaine intermediate. If the reaction is instead performed with silver tetrafluoroborate olefins 7a and 7b resulting from the anti elimination of the hydroxyl and selenenyl moieties are also produced 1 (23 % from 3a, 13 % from 3b).

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