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TRANS 1,2-FUNCTIONALIZATION OF CYCLOALKENES USING SELENIUM INTERMEDIATES

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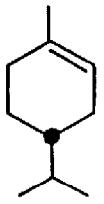
Abstract: The reaction of excess phenylselenenyl halides with trisubstituted cyclic olefins in aqueous acetonitrile is regio- and stereospecific and affords trans halohydrins in excellent yields. The reaction proceeds through the formation of a β-hydroxyalkyl phenyl selenide which evolves to halohydrin presumably via an epoxy-intermediate.

The reaction of phenylselenenyl halides in hydroxylated solvents with double bond represents an efficient route to trans β-hydroxyselenides,[1] which are valuable intermediates in organic synthesis.[2] We now report that the reaction of trisubstituted olefins in cyclic systems with excess phenylselenenyl chloride (PhSeCl) in aqueous acetonitrile, produces trans β-hydroxyselenides which are transformed in situ into trans chlorohydrins in a completely regio- and stereospecific fashion.

As one might expect from the course of hydroxyselenation of olefins[1] the interaction of PhSeCl (1 eq) with (+)-p-menthene 1 gives the hydroxyselenide 2a as one diastereomer in 90% yield [^{1}H NMR ($CDCl_3$) δ 0.79, 0.85 (d, 3 each, J = 6 Hz, H_3-9 and H_3-10), 1.39 (s, 3, H-7), 3.40 (m, 1, H-2), 7.20 - 7.65 (m, 5, aromatic H); ^{13}C NMR ($CDCl_3$) δ 19.8 (C-9 or C-10), 19.9 (C-10 or C-9), 24.7 (C-5), 29.2 (C-7), 30.8 (C-8), 32.4 (C-3), 35.2 (C-6), 39.0 (C-4), 54.8 (C-2), 72.6 (C-1), 127.2, 128.9, 130.7, 134.2 (aromatic C)]; similarly, the methyl-decalone 3[3] is converted into the compound **4a** (87%) [^{1}H NMR ($CDCl_3$) 1.39 (s, 3, methyl), 3.36 (m, 1, H-7), 7.10-7.70 (m, 5, aromatic H); ^{13}C NMR ($CDCl_3$) δ 26.4 (C-3), 27.3 (C-8), 30.9 (methyl), 32.2 (C-4), 39.3 (C-4a), 41.7 (C-2), 42.6 (C-5), 49.9 (C-8a), 53.5 (C-7), 72.5 (C-6), 127.5, 129.2, 130.3, 134.0 (aromatic C), 211.8 (C-1)].



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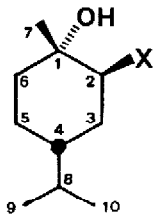
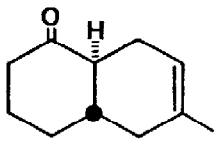


2a X = SePh 2b X = Cl



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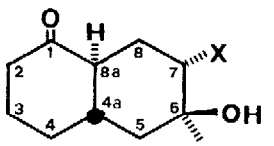
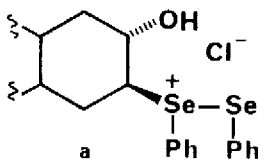


4a X = SePh 4b X = Cl

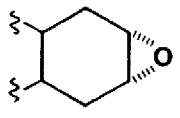
Treatment of selenides 2a and 4a with excess PhSeCl (4 eq) at room temperature leads to the trans chlorohydrins 2b (78%) [^{1}H NMR ($CDCl_3$) δ 0.77 (d, 6, J = 6 Hz, H_3-9 and H_3-10), 1.21 (s, 3, H-7), 3.86 (m, 1, H-2), ^{13}C NMR ($CDCl_3$) δ 19.7 (C-9 or C-10), 19.9 (C-10 or C-9), 24.0 (C-5), 28.1 (C-7), 31.3 (C-4), 32.9 (C-3 or C-6), 33.5 (C-6 or C-3), 36.3 (C-8), 65.8 (C-2), 71.7 (C-1)] and 4b (72%) [^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3, methyl), 3.97 (dd, 1, J = 3, 4 Hz, H-7), ^{13}C NMR ($CDCl_3$) δ 26.3 (C-3), 28.8 (methyl), 29.0 (C-8), 32.0 (C-4), 38.9 (C-4a), 39.9 (C-5), 41.6(C-2), 47.8 (C-8a), 64.5 (C-7), 71.7 (C-6), 211.6 (C-1)]. The same chlorohydrins are also obtained, one pot and in higher yields (92 and 88% respectively), by interaction of 1 and 3 with excess PhSeCl (5 eq).[4]

In these processes, the displacement of phenylseleno group occurs with retention of configuration. It is well known that the displacement of the phenylseleno moiety in β-haloselenides leads to cis-dihaloalkanes, by an S_N2 process.[5]

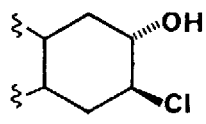
The observed stereochemistry in 2b and 4b may be explained by assuming the participation of neighbouring group in the displacement of the selenonium chloride (a)[6]: the process most likely generates an epoxide (b) which is converted into the corresponding chlorohydrin (c), by interaction with a chloride anion.



a

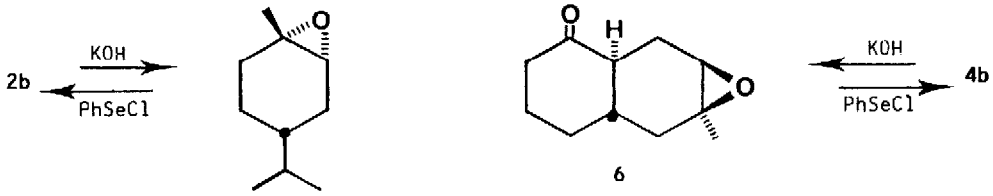


b



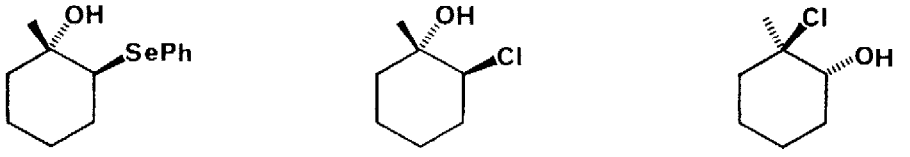
c

Evidence for such a proposed mechanism is provided by the conversion of epoxides 5[7] and 6 [^{1}H NMR ($CDCl_3$) δ 1.27 (s, 3, methyl), 2.97 (d, 1, J = 4 Hz, H-7), ^{13}C NMR ($CDCl_3$) δ 22.6 (methyl), 23.3 (C-8), 25.7 (C-3), 32.1 (C-4), 36.7 (C-4a), 38.5 (C-5), 41.7 (C-2), 49.0 (C-8a), 57.4 (C-6), 58.3(C-7), 210.4 (C-1)], obtained respectively by alkaline treatment of **2b** and **4b**, into the corresponding chlorohydrins 2b (60%) and **4b** (63%), upon reaction with PhSeCl.[9]



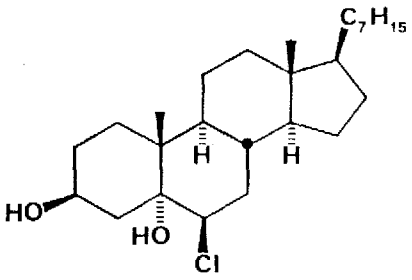
5 6

In addition, the reaction of methylcyclohexene with PhSeCl generates the adduct 7[1] which is converted into the mixture (3:1) of halohydrins **8** and **9**.[9] The formation of the mixture of halohydrins from 7 strongly supports the intermediancy of an epoxide.[10] In contrast to the behaviour of the hydroxyselenides 2a and **4a**, 7 displaces the phenylseleno group only at a higher temperature; this is not surprising considering the trans-diequatorial orientation of the hydroxy and phenylseleno groups in 7. Treatment of methylcyclohexane-1,2-oxide with excess PhSeCl produces the same mixture of halohydrins **8** and **9**.



7 8 9

It is known that the epoxidation of cholesterol with peracids always produces a mixture of α-and β-epoxides,[11] that are difficult to separate. By our procedure cholesterol has been selectively transformed into the corresponding α-epoxide (11). Cholesterol failes to react with 1 eq of PhSeCl,[12] but using an excess of reagent the chlorohydrin 10 is obtained as the only reaction product. This compound is easily converted into the corresponding α-epoxide (11), by SiO_2 exposure (63% overall yield).



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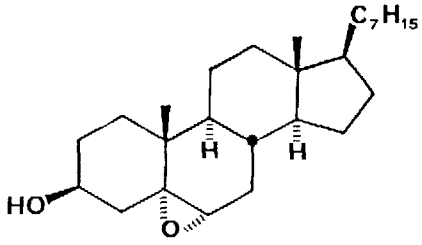

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