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Hydroxyselenation of Acetoxycyclohex-2-ene

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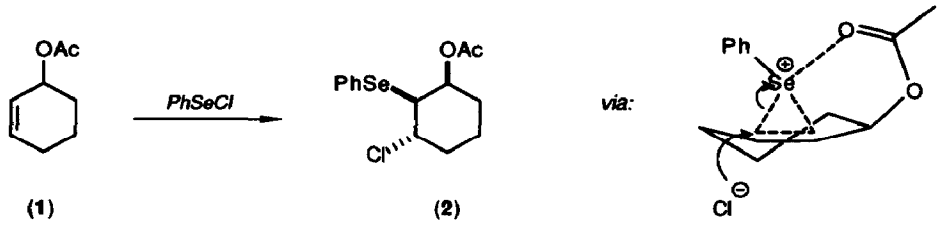
Abstract: *The reaction of acetoxycyclohexene with N-phenylselenophthalimide in the presence of water is non-regiospecific, in contrast to the previously reported chloroselenation reaction.*

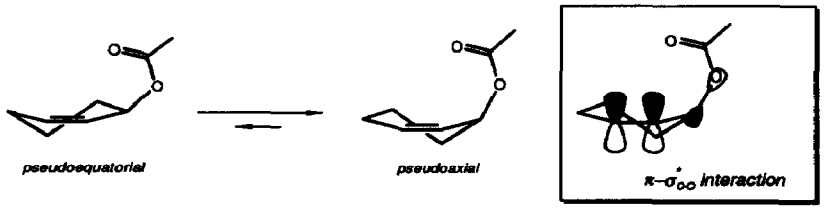
The reaction of 1-acetoxycyclohex-2-ene (1) with phenylselenyl chloride is regiospecific: 1,2-*trans*-1,6-*cis*-6-acetoxy-2-chloro-1-phenylselenenylcyclohexane (2) is the only product observed (scheme 1). The neighbouring group stabilization of the intermediate selenonium ion by the pseudoequatorially oriented acetate group of a half-chair-conformed cyclohexene has been proposed to explain regiospecificity in electrophilic selenations of such systems.[1]



(1) (2)

SCHEME 1

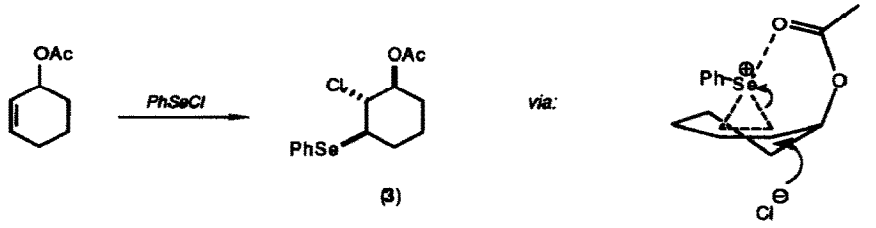
However, a subsequent report offered data to suggest that acetoxycyclohexene exists almost exclusively as the *pseudoaxial* conformer, due to an anomeric effect (scheme 2).[2]



SCHEME 2

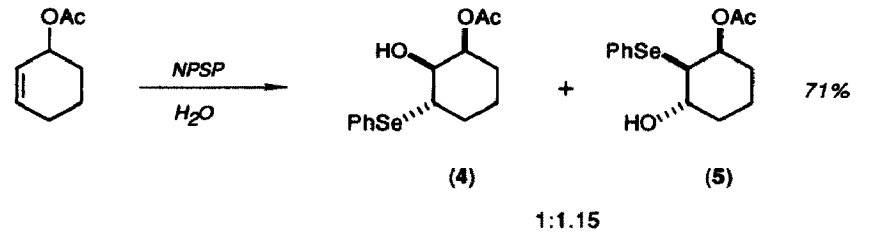
If this is the case then the anchimeric assistance offered in the course of the above reaction would promote formation of 1,2-*trans*-2,3-*trans*-3-acetoxy-2-hydroxy-1-

phenylselenylcyclohexane (3), assuming the reaction proceeds through a *trans*-diaxial ring opening of a selenonium ion (scheme 3).



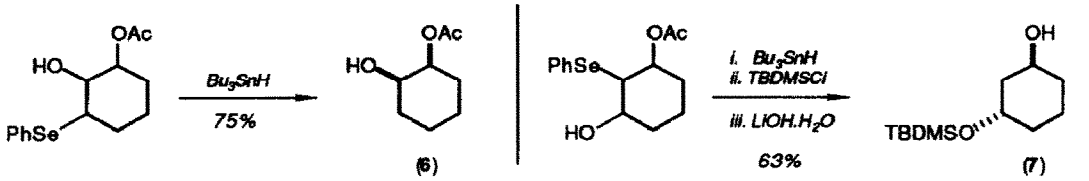
SCHEME 3

We have studied a reaction related to that shown in scheme 1, *viz.* reaction of acetoxycyclohexene with *N*-phenylselenophthalimide[3] in the presence of water[4] and found the reaction to be completely regiocatholic (scheme 4). Hydroxyselenation of (1) is previously unreported, but proceeds at room temperature to give approximately equal amounts of both possible regioisomeric hydroxyselenides, (4) and (5) in 71% isolated yield; these isomers are separable by flash chromatography and were tentatively assigned the structures shown from interpretation of their ^{1}H nmr spectra.[5] The ^{13}C nmr spectra of these compounds suggested that the regioisomers were each produced as



SCHEME 4

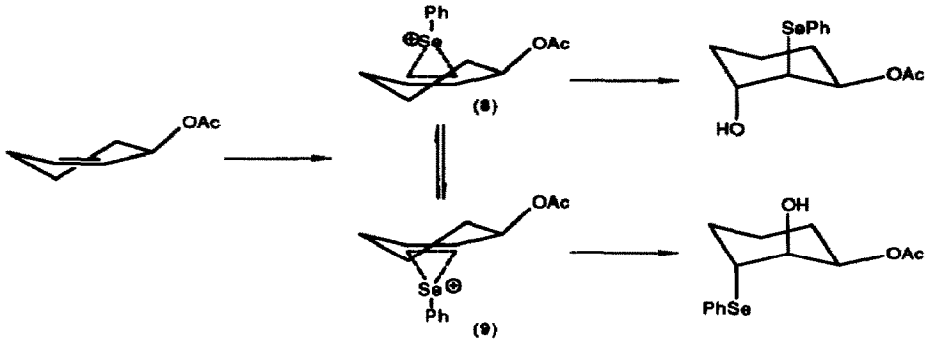
single diastereomers, and this surmise was confirmed by chemical correlation. Thus, reduction of 3-acetoxy-2-hydroxy-1-phenylselenenylcyclohexane (4) with tributylstannane gave 2-hydroxyacetoxycyclohexane (6) in 75% yield (scheme 5). The spectral properties of the compound matched that of the previously reported *cis*-isomer.[6]



SCHEME 5

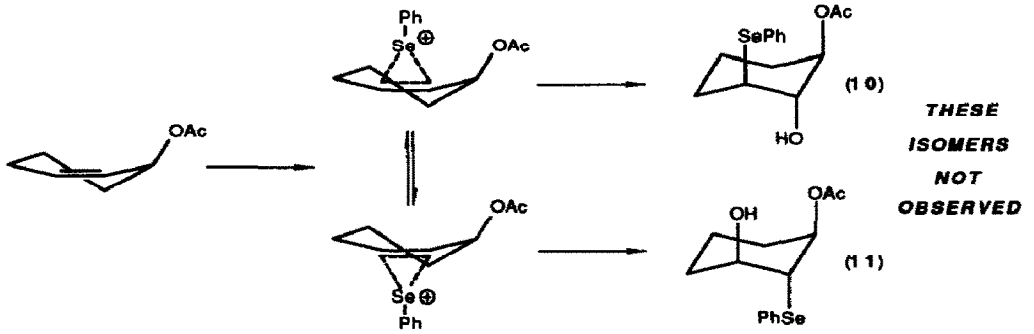
2-acetoxy-6-hydroxy-1-phenylselenenylcyclohexane (5) was reduced in similar fashion, silyl protected and saponified to give 1-^{t}butyldimethylsilyloxy-3-hydroxycyclohexane (7) in 63% yield for the sequence. This was seen to be the *trans*-isomer when compared with the spectral data of the unambiguously prepared material.[7]

These observation imply that there is *no neighbouring group participation by acetate* under the conditions for hydroxyselenation and that, therefore, selenonium ions (8) and (9) are equally likely to be involved (scheme 6).[8] However, our results show that, despite the postulated pseudoaxial conformational preference because of the generalised anomeric effect, acetoxycyclohex-2-ene reacts *via* the pseudoequatorial conformer, as suggested by Liotta. Presumably, if the axial-type conformer is more populated, a Curtin-Hammett effect may be invoked to rationalise this discrepancy.



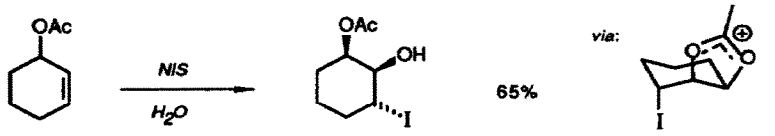
SCHEME 6

If the pseudoaxial conformer was involved in the reaction, 1,2-*trans*-2,3-*trans*-3-acetoxy-2-hydroxy-1-phenylselenenylcyclohexane (10) and 1,2-*trans*-1,6-*trans*-2-acetoxy-6-hydroxy-1-phenylselenylcyclohexane (11) would be produced (scheme 7). The complete absence of these substances from the product mixtures indicates preference for pseudoequatorial orientation.



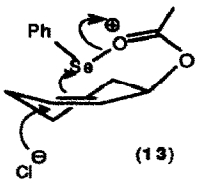
SCHEME 7

The lack of control in these hydroxyselenations is not due to the presence of water, as confirmed when water is added to the reaction of acetoxycyclohexene with phenylselenenyl chloride: (2) is again the only product of the reaction. These results are in stark contrast to the reaction of (1) with *N*-iodosuccinimide in the presence of water, when regio- and diasterospecific reaction occurs to give 1,2-*trans*-2,3-*cis*-3-acetoxy-2-hydroxycyclohexenyl iodide (12) (scheme 8).[9]



(12)

SCHEME 8



(13)

We suggest that the diasterospecific reaction seen by Liotta *et al* may be due to the formation of a seleno-oxonium ion (13) which constrains delivery of selenium from the same face as the oxygenated substituent; there is clearly no inherent face selectivity in the direct formation of selenonium ion, as shown by the reaction of the imide-based selenating reagent. In the latter situation the much inferior leaving-group ability of the source of selenonium ion precludes formation of species such as (13), thereby preventing intramolecular delivery of selenium and leading to both possible selenonium ions and, therefore, equal proportions of regioisomers upon reaction with water. The factors affecting this reaction are currently under investigation in our laboratory.

Acknowledgement
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5. Data for (4):δ_H (270MHz; $CDCl_3$) 1.38-2.20 (6H, m, 3 x CH_2), 2.11 (3H, s, Me), 2.76 (1H, brs, OH), 3.38 (1H, dt, J 9.7 and 3.67, C<u>H</u>SePh), 3.52 (1H, dd, J 9.53 and 2.75, C<u>H</u>OH), 5.28-5.34 (1H, m, C<u>H</u>OC(O)Me), 7.24-7.38 (3H, m, Ph), 7.58-7.64 (2H, m, Ph); δ_C (67.5MHz; $CDCl_3$) 170.66, 136.15, 134.24, 129.02, 128.23, 72.29, 71.81, 46.28, 31.36, 28.24, 21.24, 20.92; m/z 314 (M^+, 23.7%), 157 (67.7), 147 (60.1), 104 (31.7), 97 (77.6), 43 (100). Data for (5):δ_H (270MHz; $(CD_3)_2CO$) 1.40-2.00 (6H, m, 3 x CH_2), 1.90 (3H, s, Me), 3.47 (1H, dd, J 7.7 and 3.3, C<u>H</u>SePh), 3.97-4.06 (1H, m, C<u>H</u>OH), 5.25-5.32 (1H, m, C<u>H</u>OC(O)Me), 7.23-7.28 (3H, m, Ph), 7.57-7.62 (2H, m, Ph); δ_C (67.5MHz; $(CD_3)_2CO$) 170.12, 135.00, 134.69, 129.81, 123.73, 73.60, 70.80, 55.61, 33.07, 20.83, 19.69; m/z 314 (M^+, 22.1%), 158 (10.7), 147 (100), 104 (64.2), 97 (41.6), 76 (60.5), 50 (23.5), 43 (60.2).
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