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REGIO- AND STEREOSELECTIVE ELECTROPHILIC ADDITIONS TO <u>EXO</u> AND <u>ENDO</u>-2-HYDROXY-2-METHYL-7-OXABICYCLO[2.2.1]HEPT-5-ENE

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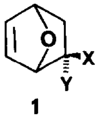
Summary. The regio- and stereoselectivity of electrophilic additions of PhSeCl and PhSCl to isomeric 2-hydroxy-2-methyl-7-oxabicyclo[2.2.1]hept-5-enes is highly dependent upon the relative stereochemistry of the substrate.

The regioselectivity of electrophilic additions to the endocyclic double bond of 7-oxanorbornenic systems, 1, is controlled by the remote substituents at C-2[1], and leads to important synthetic intermediates[2]. In this report, we shall address how the stereochemistry of the substituents at C-2 may influence the outcome of this highly stereoselective process. In the preceeding paper[3], we described the preparation of methyl carbinols 2 and 3, readily available by stereoselective alkylation of 7-oxabicyclo[2.2.1]hept-5-en-2-one (1, X,Y = O). Our initial results focus on the electrophilic additions of benzeneselenenyl chloride and benzenesulfenyl chloride to the C=C double bond of bicyclic substrates 2 and 3.



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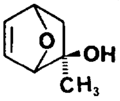

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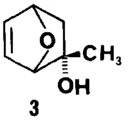

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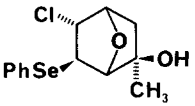

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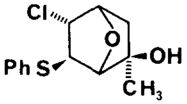

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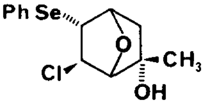

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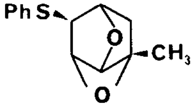

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When the <u>exo</u> isomer, 2, was treated with PhSeCl and PhSCl[4], the corresponding adducts, 4 and 5[5], were obtained in good yields. The reaction proceeded in a regio- and stereospecific manner by electrophilic <u>exo</u> attack and subsequent <u>endo</u> addition of the nucleophile on C-5, as observed for cyanoacetoxy derivative 1, (X = CN, Y = OAc)[1]. However, the reaction of <u>endo</u> carbinol 3 with PhSeCl, in identical experimental conditions, yielded exclusively phenylseleno derivative 6[6]. The reversal of the regio- and stereoselectivity of the reaction, with respect to the <u>exo</u> isomer 2, is noteworthy. Finally, treatment of 3 with PhSCl afforded a good yield of the unexpected tricyclic oxetane 7[7]. It should be pointed out that this intramolecular cyclization took place without any added base in the reaction medium[8].

The above results underline the peculiar reactivity of 7-oxanorbornenic systems[3,9]. Indeed, we have been unable to find any precedents in the literature for this differential behavior as a function of the relative stereochemistry of the molecule. Thus, it appears that the outcome of these electrophilic additions to the remote carbon-carbon double bond is controlled by the relative stereochemistry at C-2, as well as by the electronic characteristics of the substituents. Work is currently under way to clarify the reasons behind this differential reactivity and to explore its synthetic potential.

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References and Notes

1. K. A. Black and P. Vogel, J. Org. Chem., (1986), 51, 5341.
2. Utilized, for example, in a total synthesis of L-Daunosamine, A. Warm and P. Vogel, J. Org. Chem., (1986), 51, 5348.
3. O. Arjona, R. Fernández de la Pradilla, C. Manzano, S. Pérez and J. Plumet, Tetrahedron Lett., previous paper in this issue.
4. To a solution of 2-hydroxy-2-methyl-7-oxanorbornene in $CHCl_3$ was added a solution of the electrophile (PhSeCl or PhSCl) in $CHCl_3$ at room temperature. TLC analysis indicated that the reaction was practically instantaneous. The reaction mixture was then diluted with CH_2Cl_2 and washed with a 5% Na_2CO_3 solution, water and brine. The organic layer was dried over anhydrous $MgSO_4$. Removal of the drying agent and evaporation of the solvent under reduced pressure led to the crude product which was purified by column chromatography on silica gel. The yields of pure products were in the 70-80 % range.
5. Data of 4: ^1H-NMR ($CDCl_3$): δ 1.33 (s, CH_3), 1.72 (dd, 14.0, 6.0, H-3 exo), 2.38 (d, 14.0, H-3 endo), 2.67 (s, OH), 3.32 (d, 4.0, H-6), 3.91-4.15 (m, H-5), 4.11 (s, H-1), 4.53 (t, 6.0, H-4), 6.95-7.64 (5H, m, H-Ar). ^{13}C-NMR ($CDCl_3$): δ 20.6, 41.2, 46.6, 62.1, 78.2, 80.2, 92.5, 127.9, 128.6, 129.1, 134.1.
Data of 5: ^1H-NMR ($CDCl_3$): δ 1.37 (s, CH_3), 1.75 (dd, 14.0, 6.0, H-3 exo), 2.42 (d, 14.0, H-3 endo), 2.57 (s, OH), 3.35 (d, 4.0, H-6), 3.97 (dd, 6.0, 4.0, H-5), 4.03 (s, H-1), 4.57 (t, 6.0, H-4), 7.04-7.46 (5H, m, H-Ar). ^{13}C-NMR ($CDCl_3$): δ 20.7, 41.3, 53.4, 61.6, 77.9, 80.1, 91.7, 127.3, 129.0, 131.2, 134.0.
6. Data of 6: ^1H-NMR ($CDCl_3$): δ 1.37 (s, CH_3), 1.67 (ddd, 13.5, 5.8, 1.5, H-3 exo), 1.87 (s, OH)2.30 (d, 13.5, H-3 endo), 4.03 (s, H-1), 4.09 (d, 4.0, H-6), 4.22 (td, 4.0, 1.5, H-5), 4.47 (dd, 5.8, 4.0, H-4), 7.06-7.57 (5H, m, H-Ar). ^{13}C-NMR ($CDCl_3$): δ 29.1, 38.4, 45.1, 63.1, 77.5, 81.6, 90.6, 127.3, 128.9, 133.3.
7. Data of 7 (This product is arbitrarily numbered as a bicyclic derivative rather than as a dioxatricyclic derivative to facilitate comparison of the ^1H-NMR data): ^1H-NMR ($CDCl_3$): δ 1.43 (s, CH_3), 1.60 (dd, 4.5, 12.5, H-3 exo), 2.08 (d, 12.5, H-3 endo), 3.63 (s, H-5), 4.60 (dd, 3.5, 1.5, H-6), 4.90 (d, 4.5, H-4), 5.07 (d, 3.5, H-1), 7.00-7.57 (5H, m, H-Ar). ^{13}C-NMR ($CDCl_3$): δ 20.8, 43.6, 53.1, 81.1, 83.9, 92.0, 126,6, 128.9, 130.3, 133.9.
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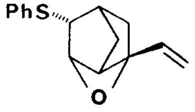

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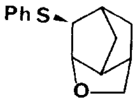

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Oxetane 9 was prepared by Fallis by sequential treatment of the corresponding alcohol with PhSCl and $^{i}Pr_2NEt$. Alternatively, oxetane 8 was obtained by sequential reaction of the corresponding alcohol with BuLi and PhSCl. See, S. M. Tuladhar and A. G. Fallis, Tetrahedron Lett., (1987), 28, 523, and references cited therein. The authors wish to thank Dr. Fallis for providing spectral data of 8 and 9.

9. See, O. Arjona, R. Fernández de la Pradilla, S. Pérez, J. Plumet. P.-A. Carrupt and P. Vogel, Tetrahedron Lett., (1986), 27, 5505.

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