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STEREOSPECIFIC ANNELATIONS OF ETHYLENIC β-PHENYLSELENOETHERS BY ACID CATALYSIS

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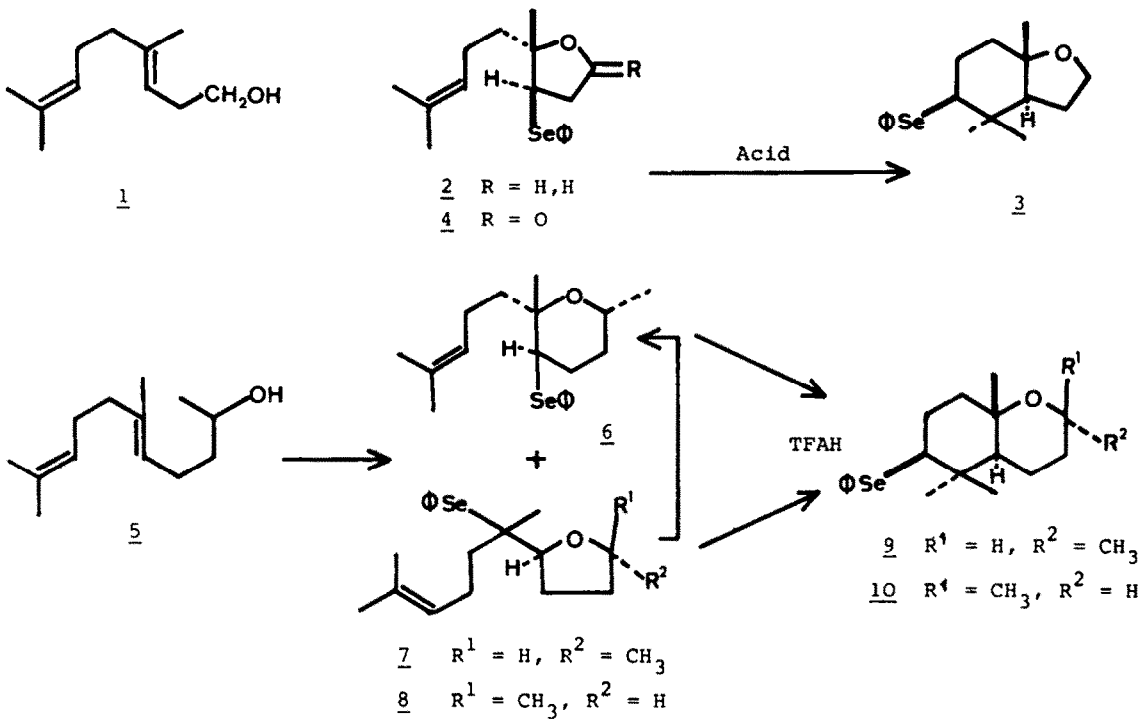
Abstract - It will be shown with several examples that it is possible to effect with exceptional ease on monounsaturated ethers, 1.5-phenylseleno group migration, quantitatively, by the action of anhydrous Lewis or Brönsted acids at 0°C. However, the presence of two C-C double bonds lowers the yield of this transformation.

This new method of ring-closure is attractive for the synthesis of polycyclic terpenes.

Recently (1) we reported the stereochemical course of an acid-catalyzed cycloisomerization which gave a bicyclic selenolactone related to the naturally occuring actinidiolides. It was suggested that this stereoselective transformation involved formation of a seleniranium cation. In this note we describe other examples chosen to explore the potential synthetic utility of this new annelation method. Homogeraniol 1 (2) was converted to selenooxolane derivative 2 which was treated with a 5 % solution of trifluoroacetic acid (TFA) in CH_2Cl_2 at 0° for 5 mn. After usual work up, the perhydrotrimethylbenzofuran 3 was isolated in 90 % yield.

When the corresponding lactone 4 was treated under the same conditions, addition of TFA to the ethylenic double-bond ($\sim$ 30 %) was also observed (1), (3). The significant difference in rates of reaction of the double bonds in 2 and 4 was also used in a more complex example (vide infra, Scheme II).

Further examples involved the compounds 6, 7 and 8, formed by reaction of 5 with PhSeCl at different temperatures (e.g. at - 78° 6:7 = 7:3, while at 20°, 8 was also present 6:7:8 = 3:1:1) (4).



Scheme I

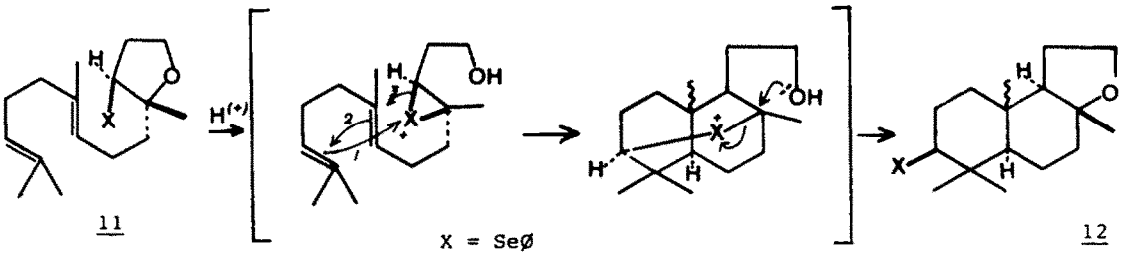
The action of a 5 % solution (ether/CH_2Cl_2) of commercial sulfuric acid (95 %) résulted in the exclusive transformation of 7 or 8 into 6, and established in this way the thermodynamically more stable nature of this isomer (5). TFA 5 % (CH_2Cl_2) gave rise to both stereoisomeric perhydrobenzopyrans 9 and 10 (ratio ~ 1 : 1), which starting isomer was used.

These cyclizations were as rapid as that of 2. Competing addition by TFA was not observed. The epimers (9 and 10) differed in the stereochemistry only about the 2-C methyl-group and each remained unchanged under comparable acidic conditions (10 % H_2SO_4, 2 hrs at 20°).

The structures of the products were readily established on the basis of ^1H NMR spectra (6). Formation of the same mixture of 9 and 10 whichever starting isomer was suggests that the products arose via a common transition state probably of seleniranium type.

Finally, we turned our attention to the closely related ether 11 which has two ethylenic double bonds. It was synthesized from trans-homofarnesol (7) and PhSeCl in the manner already described. When 11 was treated as previously described (TFA 5 %, 10 mn), a complex mixture of products was formed (8).

Besides some unreacted starting material, major components corresponded to addition of the acid, but it is of note that 12 was also produced in a moderate yield (~10 %). The relative stereochemistry of 12 was assigned after separation, by correlation of its NMR chemical shifts with those of the simpler compound 3 and parallel with the literature data in the field of the drimanic skeleton (9).



Scheme II

Such a participation of both C-C double bonds of 11 is not surprising on a theorical viewpoint, however the most interesting parameter is the distance between the migrating group and the migration terminus. Although it is possible to rationalize this behaviour with a mechanism involving similar transition states (or intermediates) as invoked for lactones (1) (Scheme II), intermolecular reaction path cannot be rejected. Therefore, working presently on new examples to get other experimental details upon stereochemistry of such polycyclizations, we prefer to delay the mechanistic discussion of the reaction 11 → 12. We reserve to our next paper a more sophisticated interpretation of these acidic transformations.

We are also currently applying this new ring closure to the syntheses of some interesting terpenoids.

EXPERIMENTAL

The NMR spectra were recorded at 90 MHz in $CDCl_3$ with TMS as internal standard. Chemical shifts are in ppm.

Infrared spectra were run on Perkin-Elmer model 297 spectrophotometer.

R_f values are quoted for Merck silical gel 60 GF_{254} ref 5735.

All new compounds had satisfactory microanalytical data (C,H ; ± 0.3 %).

(2S, 3R ; 3S, 2R) 2-methyl-2-(4-methyl-pent-3-enyl)-3-phenylselenooxolane (2)

To a mixture of homogeraniol 1 (505 mg, 3 mmol) obtained by $LiAlH_4$ reduction of homogeranic acid (2) and triethylamine (305 mg, 3 mmol) in CH_2Cl_2 (5 mL), was added glacial acetic acid (210 mg, 3.5 mmol) in CH_2Cl_2 (5mL). After 10 mn at room temp, the mixture was cooled to 0° and a solution of phenylselenenyl chloride (595 mg, 3.1 mmol) in CH_2Cl_2 (5 mL) was added dropwise under dry N_2. The mixture was allowed to warm to room temp, and stirred for 6 hours before being diluted with saturated $NaHCO_3$ aq (20 mL) and ether (60 mL). Concentration in vacuo of the organic layer, dried ($MgSO_4$) gave an oil which was chromatographed on silica (20 g, C_6H_6) to give the ether (2) (420 mg, 65 %) homogeneous by tlc.

R_f = 0.2 (C_6H_6) ν_{max} 1040 (C=O), 1580, 740, 695 (C_6H_5) cm^{-1} ; δ_H ($CDCl_3$) 1.25 (s, CH_3), 1.59 (br s, CH_3), 1.67 (br s, CH_3), 1.80-2.60 (m, 3 x CH_2), 3.48 (dd, J 11 and 8 Hz), 3.70-4.00 (m, 1 x CH_2), 5.2 (m,1H), 7.3-7.8 (m, 5H).

4.4.7aβ-trimethyl-5β-phenylseleno-2.3.3aα.4.5.6.7.7aβ-octahydrobenzofuran (3)

2 (323 mg, 1 mmol) was added to 5 mL of a 5 % solution of trifluoroacetic acid in CH_2Cl_2 at 0°.

The mixture was stirred 5 mn before being diluted with water (50 mL) and ether (50 mL) then neutralized with sodium carbonate. Isolated in the normal manner, crude 3 was chromatographed (10 g SiO_2, C_6H_6) to eliminate traces of $(C_6H_5Se)_2$ from compound 3 (294 mg, 91 %). ν_{max} 1580, 1470, 1370, 1215, 1160, 740, 690 cm^{-1}. δ_H ($CDCl_3$) 0.94 (s, CH_3), 1.13 (s, CH_3), 1.27 (s, CH_3), 1.5-2.3 (m, 7H), 3.02 (dd, J=12 and 6 Hz, 1H), 3.7-4.1 (m, CH_2), 7.3-7.8 (m, 5H).

(E)-6.10-dimethylundeca-5.9-dien-2-ol (5)

Prepared in a quantitative yield at 10°, by reduction of trans-geranylacetone (1.94 g, 10 mmol) with $NaBH_4$ (380 mg, 10 mmol) in hydromethanolic solution.

(2S, 3R, 6R ; 2R, 3S, 6S) 2.6-dimethyl-2-(4-methylpent-3-enyl)-3-phenylseleno-oxane (6) and (2S, 5R ; 2R, 5S) 2-(1.5-dimethyl-1-selenophenyl-hex-5-enyl)-5-methyl-oxolane (7)

To a magnetically stirred mixture of 5 (980 mg, 5 mmol), acetic acid (360 mg, 6 mmol), triethylamine (505 mg, 5 mmol) in dry CH_2Cl_2 (30 mL) under N_2 and cooled at - 78° was added dropwise PhSeCl (977 mg, 5.1 mmol) in dry CH_2Cl_2 (15 mL). The mixture was stirred for 1 h at - 78° and then allowed slowly to warm to - 20° (over 2h). The mixture was poured into water and extracted with ether. The extracts were washed, dried ($MgSO_4$) and concentrated in vacuo to give 1.66 g (94 %) of a yellowish oil. Medium pressure liquid chromatography (SiO_2-C_6H_6) afforded 890 mg of 6 and 360 mg of 7.

6 R_f = 0.5 (C_6H_6) ν_{max} 1580, 1470, 1435, 1370, 1085, 735, 690 cm^{-1}. δ_H ($CDCl_3$) 1.07 (d, J=6 Hz, CH_3), 1.19 (s, CH_3), 1.62 (br s, CH_3), 1.70 (br s, CH_3), 1.70-2.25 (m, 4 x CH_2), 3.25 (dd, J=10 and 8 Hz, 1H), 3.60-4.00 (m, 1H), 5.20 (br s, 1H), 7.3-7.8 (m, 5H).

7 R_f = 0.36 (C_6H_6) ν_{max} 1585, 1470, 1435, 1375, 1085, 1060, 740, 690 cm^{-1}. δ_H ($CDCl_3$) 1.14 (d, J=7 Hz, CH_3), 1.27 (s, CH_3), 1.64 (br s, CH_3), 1.69 (br s, CH_3), 1.75-2.50 (m, 4 x CH_2), 3.90-4.30 (m, 1H), 5.2 (br t, 1H), 7.3-7.8 (m, 5H).

Note : When the reaction was carried out at room temperature instead of - 78°, 8 was also formed.

8 R_f = 0.43 (C_6H_6), IR very similar to 7.

δ_H ($CDCl_3$) 1.17 (d, J=7 Hz, CH_3), 1.27 (s, CH_3), 1.65 (br s, CH_3), 1.70 (br s, CH_3), 1.75-2,50 (m, 4 x CH_2), 3.8-4.2 (m, 1H), 5.2 (br t, 1H), 7.3-7.8 (m, 5H).

6β-phenylseleno-2α.5.5.8aβ-tetramethyl-3.4.4aα.5.6.7.8aβ-octahydro-2-H-1-benzopyran (9) and 6β-phenylseleno-2β.5.5-8aβ-tetramethyl-3.4.4aα.5.6.7.8.8aβ-octahydro-2H-1-benzopyran (10)

The annelation procedure of pure 6, 7 or 8 or mixtures of them using TFA was repeated as described above. Normal work-up was used and the crude product was chromatographed (SiO_2, C_6H_6). 9 and 10 were formed in equal amounts.

9 R_f = 0.2 (C_6H_6) ν_{max} : 1580, 1470, 1435, 1375, 1130, 1095, 1075, 1020, 740, 695 cm^{-1}.

δ_H ($CDCl_3$) 0.85 (s, CH_3), 1.08 (d, J = 7 Hz, CH_3), 1.22 (s, CH_3), 1.26 (s, CH_3), 1.5-2.2 (m, 9H), 3.10 (d, J = 10.5 and 6 Hz, 1H), 3.80 (m, 1H), 5.3-5.8 (m, 5H).

10 R_f = 0.15 (C_6H_6) ν_{max} identical to 9 except 1085 instead of 1095 cm^{-1}. δ_H ($CDCl_3$) 0.92 (s, CH_3), 1.15 (d, J = 7 Hz, CH_3), 1.23 (s, CH_3), 1.26 (s, CH_3), 1.5-2.2 (m, 9H), 3.08 (dd, J = 10,5 and 6 Hz, H(a)), 4.02 (m, 1H), 5.3-5.8 (m, 5H).

(2S, 3R ; 2R, 3S) 2-methyl-2-(4.8-dimethylocta-3.7-dienyl)-3-phenylselenooxolane (11)

According to the procedure described for the synthesis of 2 from 1, 11 (352 mg, 60 %) was obtained from trans-homofarnesol (7) (354 mg, 1.5 mmol).

R_f = 0.2 (C_6H_6) ν_{max} 1580, 1475, 1435, 1370, 1040, 1020, 800, 740, 690, 675 cm^{-1}.
δ_H ($CDCl_3$) 1.26 (s, CH_3), 1.63 (s, CH_3), 1.71 (s, CH_3), 1.85-2.50 (m, 5 x CH_2), 3.35-3.65 (m, 1H), 3.7-4.1 (m, 2H), 5.20 (m, 2H), 7.3-7.8 (m, 5H).

Compound 12

According to the procedure described for the synthesis of 3 from 2, 12 (12 mg, 10 %) was isolated by liquid chromatography from 11 (120 mg, 0.34 mmol).

R_f = 0.7 (ether/hexane 6 : 4).

δ_H ($CDCl_3$) 0.90 (s, CH_3), 0.98 (s, CH_3), 1.09 (s, CH_3), 1.24 (s, CH_3), 1.50-2.20 (m, 12 H), 3.05 (dd, J 11 and 8Hz,1H), 3.75-4.0 (m, CH_2), 7.3-7.8 (m, 5H).

REFERENCES AND FOOT NOTES

All compounds are racemic mixtures, but only one enantiomer is depicted for convenience.

1) F. Rouessac and H. Zamarlik, Tetrahedron Lett., 1981, 2643.

2) Authors thank M. Taafrout for a gift of homogeraniol. Characteristics in agreement with M. Kobayashi, L.F. Valente and E. Negishi, Synthesis, 1980, 1034.

3) When Brönsted acids are used good yields are obtained when two conditions are observed : absence of water and use of anions of low nucleophilicity for the intermediates of the reaction. Lewis acids may be also used to isomerize 2 (e.g. $SnCl_4$ 0.5 M at - 30°) but these reagents did not allow comparaison with earlier published work (ref.1).

4) The lack of regiospecificity of PhSeCl is in accordance with the literature, see inter alia D. Goldsmith, D. Liotta, C. Lee and G. Zuira, Tetrahedron Lett., 1979, 4801.

5) It appears that dilute H_2SO_4 may open the oxolane derivative but not the oxane ring of 6, 9 or 10.

6) See experimental - Otherwise ^1H NMR spectra of bromoanalogs of 9 and 10 have been described (T.R. Hoye and M.J. Kurth, J. Org. Chem., 44, 3461 (1979)) and reductive removal of the C_6H_5Se group by Raney nickel upon 10 gave the corresponding benzopyran whose ^1H NMR spectrum was known (F.B. Whitfield and G. Stanley, Austr. J. Chem., 30, 1073 (1977)).

7) Homologation of trans-farnesol via homofarnesic acid will be published later.

8) At least six products as indicated by TLC analysis.

9) The ^1H NMR spectrum of 12 exhibited one sharp signal at 0.90 ppm which suggested that the angular methyl group was probably axial.