*Tetrahedron* Vol. 46, No. 24, pp. 8199-8206, 1990
Printed in Great Britain

0040-4020/90 $3.00+.00


# REGIOSELECTIVE ELECTROPHILIC ADDITIONS TO 2-ALKOXY- AND 2-ALKOXYMETHYL-7-OXABICYCLO [2.2.1] HEPT-5-ENE DERIVATIVES.

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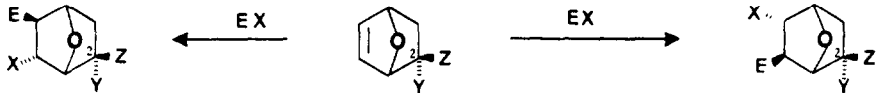
(*Received in UK* 12 *September* 1990)

Summary: The influence of the stereochemistry at C-2 on the selectivity of the reaction between PhSeBr and 2-alkoxymethyl substituted oxanorbornenes has been studied. All *endo* isomers displayed complete regio- and stereocontrol with incorporation of the electrophile on C-5.

In recent years, 7-oxabicyclo[2.2.1]heptane derivatives have become important starting materials[1]. In particular, oxanorbornenes **1** and **2**, which are readily available optically pure[2], have been employed in a number of syntheses[3]. Of special interest is the remarkable regioselective functionalization of **1** and **2** by reaction with soft electrophiles (Scheme I); thus, while **1** leads to adducts **5**, enone **2** gives rise to **6** under kinetic control[4], *via* an *exo*-episelenonium ion, which is subsequently opened by an *endo*-attack of the halide ion. Furthermore, this methodology has been utilized successfully in organic synthesis[5]. The remote control of the regioselectivity of the process by the substituents at C-2 has been attributed to homoconjugative and/or hyperconjugative effects[4,6].

**Scheme I**

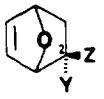



**1** Z=CN, Y=OAc
**2** Z=Y=O
**3** Z=Me, Y=OH
**4** Z=OH, Y=Me
**5** Z=CN, Y=OAc
**6** Z=Y=O
**7** Z=Me, Y=OH, EX=PhSeCl
**8** Z=OH, Y=Me, EX=PhSeCl

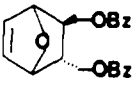
Recently, we reported several cases of related electrophilic additions[7], two of which are shown in Scheme I, namely, the **3** ⟶ **7** (along with a small amount of selenenyl oxetane produced by intramolecular

cyclization) and **4** ——>**8**. The observed regioselectivity was attributed to electrostatic and/or steric effects, but it was considered that more data were needed to clarify the relative importance of these factors and also to further define the scope of these transformations. In this paper we describe the regioselective electrophilic additions of PhSeBr to a number of alkoxy and alkoxymethyl substituted oxanorbornenes shown in Scheme II[8].

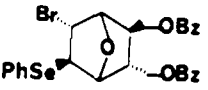
**Scheme II**



**9** Z=OBn, Y=H
**10** Z=H, Y=OBn
**11** Z=$CH_2OBn$, Y=H
**12** Z=H; Y=$CH_2OBn$
**13** Z=H, Y=$CH_2OSi^tBuMe_2$
**14** Z=$CH_2OBz$, Y=H
**15** Z=H; Y=$CH_2OBz$



**16**



**28**

**17** E= PhSe
**18** E= PhS

Oxanorbornenes **9** and **11** were considered to be sterically unbiased substrates[9] whose reactivity would give an indication of the intrinsic electronic influence of an alkoxy and alkoxymethyl substituents respectively on the endocyclic double bond. The corresponding *endo* isomers **10** and **12** were expected to allow for steric control of the reaction; while electrostatic factors could also contribute in the case of **10**, such an influence was not expected to be relevant for **12**, since the heteroatom is shifted one position away from the bicyclic moiety. It should be pointed out that most of the substrates selected for this study are readily available optically pure[10] and therefore the development of regioselective functionalizations would lead to useful synthetic intermediates. The results obtained in the course of this study are summarized in Table I.

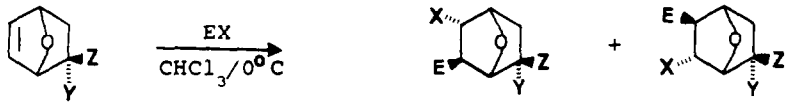
When *exo* benzyl ether **9** was treated with PhSeBr, a modest selectivity favoring adduct **20**, of general structure **B**, was encountered (entry 1). Furthermore, lowering the temperature to -78°C ($CH_2Cl_2$), provided a 1:5 ratio of adducts **19** and **20** (entry 2). In contrast, the corresponding *endo* isomer **10** gave rise to adduct **21** (**A**) exclusively under identical reaction conditions (entry 3).

The reaction of *exo* benzyloxymethyl derivative **11** (entry 4) produced a mixture slightly favoring introduction of the electrophile at C-6. The reaction between *endo* isomer **12** and PhSeBr was examined and a surprisingly facile intramolecular etherification to produce tricyclic adduct **17** was observed. Under a variety of reaction conditions always adduct **17** (or **18**

when PhSCl was employed) was isolated in excellent yields. Substrate 13 having the primary hydroxyl protected as a TBDMS ether gave similar results. Finally, protection as a benzoate prevented the intramolecular cyclization and, as shown in entry 6, an excellent yield of adduct 26 was obtained. Even the harder electrophile PhSCl afforded a good yield of 27 without any intramolecular cyclization product. For comparative purposes, *exo* benzoate 14 was also submitted to the reaction conditions and a selectivity similar to *exo* benzyl ether 11 was encountered (entry 5).

Finally, disubstituted substrate 16 which, in view of the above results, was considered to be a good test-case for the relative importance of steric control, was reacted with PhSeBr (entry 8). This process was totally regioselective affording a good yield of 28.

**Table I. Reaction between bicyclic substrates 9-16 and PhSeBr and PhSCl**




9-15 A B

| entry | substrate | EX | A | B | A/B ratio[b] | yield[a] (%) |
|---|---|---|---|---|---|---|
| 1 | 9 | PhSeBr | 19 | 20 | 1:3.6 | 76% |
| 2[c] | 9 | PhSeBr | 19 | 20 | 1:5 | 76% |
| 3 | 10 | PhSeBr | 21 | | 1:0 | 95% |
| 4 | 11 | PhSeBr | 22 | 23 | 2:1 | 75% |
| 5 | 14 | PhSeBr | 24 | 25 | 1.5:1 | 77% |
| 6 | 15 | PhSeBr | 26 | | 1:0 | 92% |
| 7 | 15 | PhSCl | 27 | | 1:0 | 80% |
| 8[d] | 16 | PhSeBr | 28 | | 1:0 | 80% |

[a]Yields of chromatographically pure products. Not optimized. [b]Measured by integration of the 300 MHz $^1$H NMR spectra of the crude reaction mixtures. [c]The reaction was performed in $CH_2Cl_2$ at -78°C. [d]See Scheme II.

The structural assignment of these products was based on their spectral data (see Experimental), especially on their $^1$H NMR spectra along with selective decoupling experiments and DNOE measurements; for instance, dibenzoate 28 presented the following NOE enhacements upon irradiation of H-6: H-3 (1.7%), H-5 (3.7%), H-2'(4.37 ppm) (6.8%), H-1 (4%), H-Ar (Se) (1.7%).

In conclusion, an *exo* benzyl ether substituent (9) displays moderate regioselectivity towards incorporation of the electrophile to C-5, however

with diminished regiocontrol[11] when compared with ketone **2**. The *exo* hydroxymethyl derivatives display low regioselectivity towards the opposite isomer **A** (entries 4,5)[12]. All substrates with *endo* substituents lead exclusively to adducts **A** in good yields. This does not preclude influence of electrostatic effects from operating in the case of **10**. The behavior of substrates **15** and **16** strongly suggest a determinant role of steric effects in these processes, particularly in the case of **16** for which, at least qualitatively, the *exo* substituent would favor somewhat isomer **B**. We are currently investigating the use of the intermediates described here in synthesis.

## EXPERIMENTAL

**General** All reactions were carried out under a positive pressure of dry argon, using freshly distilled solvents. Reagents and solvents were handled by using standard syringe techniques. Hexane, ethyl acetate and chloroform were distilled from phosphorus pentoxide and dichloromethane from calcium hydride. PhSCl was prepared by the standard literature procedure[13].Analytical TLC was carried out on 0.20 mm E.Merck precoated silica gel plates (60 F-254), with detection by UV ligth, iodine or acidic vanillin solution. Column chromatography was performed using E.Merck 230-400 mesh or 70-230 mesh silica gel. Melting points were determined on a Büchi 512 apparatus and are uncorrected. Infrared spectra were recorded on either a Perkin Elmer 781 or 257 grating spectrophotometers; band positions are indicated in wavenumbers. $^1$H NMR spectra were recorded on a Brüker AM-200 or Varian VXR-300 S instrument, using $CDCl_3$ or $C_6D_6$ as solvent. $^{13}$C NMR spectra were measured on a Brüker AM-200 instrument, using $CDCl_3$ or $C_6D_6$ as solvent,and are completely decoupled. In both $^1$H NMR and $^{13}$C NMR, chemical shifts are reported in $\delta$ units downfield from tetramethylsilane. The following abbreviations are used to describe peak patterns when appropiate: br= broad, s= singlet, d= doublet, t= triplet, apt= apparent triplet q= quartet, m= multiplet. All new compounds described in this report are racemic and are numbered arbitrarily to facilitate comparison of the data.

**General Procedure for Electrophilic Additions to 7-Oxanorbornenic Systems.** To a cold (0°C) solution of 1 equivalent of the 7-oxanorbornenic derivative in chloroform (5 ml/mmol)was added anhydrous $K_2CO_3$(20%) and a precooled (0°C) solution of 1.3 equivalents of PhSeBr or PhSCl in chloroform (5 ml/mmol).The mixture was stirred at 0°C until disappearance of starting material (TLC). The reaction mixture was quenched with brine and extracted with $CHCl_3$. The organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed in vacuo.

**5-endo-Bromo-6-exo-phenylselenyl-7-oxabicyclo[2.2.1]heptan-2-exo-ol,benzyl ether (19) and 6-endo-Bromo-5-exo-phenylselenyl-7-oxabicyclo[2.2.1] heptan-2-exo-ol, benzyl ether (20).** From 96 mg (0.48 mmol) of **9** was obtained after 7 hours, 160 mg of a 1:5 mixture of **19** and **20** (76%), after chromatography (hexane : ethyl acetate, 5:1). Data of **19** : $^1$H NMR ($C_6D_6$, 300 MHz): 1.58 (1H, ddd, J=13.2, 5.9, 3.0 Hz, H-3x), 2.48 (1H, dd, J=13.8, 6.9 Hz, H-3n), 2.91 (1H, d, J=4.4 HZ, H-6n), 3.33 (1H, dd, J=6.9, 2.6 Hz, H-2n), 3.89 (1H, aptd, J=4.6-4.5, 1.8 Hz, H-5x), 4.08 (2H, q, J=12.1 Hz, $CH_2$), 4.15 (1H, apt, J=5.2-4.7 Hz, H-4), 4.55 (1H, s, H-1), 6.97-7.51 (5H, m, Ar.). $^{13}$C NMR ($C_6D_6$, 50 MHz): 34.9, 48.7, 53.0, 70.8, 79.5, 80.4, 86.3, 127.5, 138.6. Anal. Calcd. for $C_{19}H_{19}O_2BrSe$: C, 52.05; H, 4.34; Br, 18.24.

Found: C, 51.90; H, 4.23; Br, 18.12. **Data of 20** : $^{1}$H NMR ($C_6D_6$, 300 MHz): 1.41 (1H, dd, J=13.0, 6.6 Hz, H-3n), 1.58 (1H, ddd, J=13.2, 5.9, 3.0 Hz, H-3x), 3.0 (1H, d, J=4.7 Hz, H-5n), 3.86 (1H, apt, J=5.3-4.3 Hz, H-6x), 4.21 (2H, q, J=12.0 Hz, $CH_2$), 4.31 (1H, d, J=4.6 Hz, H-1), 4.32 (1H, d, J=5.9 Hz, H-4), 4.38 (1H, dd, J=6.9, 2.9 Hz, H-2n), 6.97-7.51 (5H, m, Ar). $^{13}$C NMR ($C_6D_6$, 50 MHz): 40.2, 49.8, 52.5, 71.2, 77.6, 82.7, 82.8, 127.5, 138.6. Anal. Calcd. for $C_{19}H_{19}O_2BrSe$: C, 52.05; H, 4.34; Br, 18.24. Found: C, 51.95; H, 4.30; Br, 18.20.

**5-endo-Bromo-6-exo-phenylselenyl-7-oxabicyclo[2.2.1]heptan-2-endo-ol, benzyl ether (21).** From 90 mg (0.44 mmol) of **10** was obtained after 5 hours, 85.4 mg of **21** (95%), after chromatography (hexane : ethyl acetate, 10:1, Rf= 0.25). $^{1}$H NMR ($CDCl_3$, 300 MHz): 2.05 (1H, dddd, J=13.4, 9.8, 5.6, 1.7 HZ, H-3x), 2.22 (1H, dd, J=13.4, 3.7 Hz, H-3n), 3.97-4.07 (1H, m, H-2), 4.03 (1H, d, J=4.9 Hz, H-6), 4.13 (1H, aptd, J=4.9, 1.7 Hz, H-5), 4.26 (1H, d, J=11.7 Hz, $CH_2$), 4.39 (1H, d, J=11.7 Hz, $CH_2$), 4.46 (1H, d, J=4.9 Hz, H-1), 4.50 (1H, apt, J=5.2 Hz, H-4), 7.19-7.32 (8H, m, Ar.), 7.59-7.63 (2H, m, Ar.). $^{13}$C NMR ($CDCl_3$, 50 MHz): 31.0, 45.3, 53.1, 72.2, 78.6, 81.8, 84.9, 127.5, 127.7, 127.8, 128.4, 129.0, 129.2). IR ($CHCl_3$): 3700, 3600, 1730, 1600, 1490, 1450, 1360, 1120, 1060, 1040, 1020. Anal. Calcd. for $C_{19}H_{19}O_2BrSe$: C, 52.05; H, 4.34; Br, 18.24. Found: C, 52.10; H, 4.50; Br, 18.30.

**2-*exo*-Benzyloxymethyl-5-*endo*-Bromo-6-*exo*-phenylselenyl-7-oxabicyclo[2.2.1] heptane (22), and 2-*exo*-Benzyloxymethyl- 6-*endo*-Bromo-5-*exo*-phenylselenyl -7-oxabicyclo [2.2.1]heptane (23).** From 90 mg (0.41 mmol) of **11** after 5 min., was obtained 139 mg of a 2:1 mixture of **22** and **23** (75%). Careful chromatography ( hexane :ethyl acetate, 5:1) afforded pure samples of both isomers. Data of **22** : $^{1}$H NMR ($CDCl_3$, 300 MHz): 1.26 (1H, dtd, J=12.9, 5.0, 1.7 Hz, H-3x), 2.23 (1H, m, H-2), 2.52 (1H, dd, J=12.9, 8.7 Hz, H-3n), 3.23 (1H, dd, J=9.2, 5.9 Hz, H-2'), 3.30 (1H, t, J=9.3 Hz, H-2'), 3.30 (1H, d, J=4.0 Hz, H-6), 4,12 (1H, aptd, J=4.3, 1.7 Hz, H-5), 4.45-4.53 (2H, m, $CH_2$),4.49 (1H, s, H-1), 4.57 (1H, t, J=5.0 Hz, H-4), 7.28-7.36 (8H, m, Ar.), 7.59-7.63 (2H, m, Ar.). $^{13}$C NMR ($CDCl_3$, 50 MHz): 28.8, 43.3, 52.4, 53.3, 72.2, 73.1, 80.4, 85.1, 127.6, 127.7, 127.9, 128.4, 129.2, 134.4, 138.1. Anal. Calcd. for $C_{20}H_{21}O_2BrSe$: C, 53.09; H, 4.64; Br, 17.67. Found: C, 52.95; H, 4.58; Br, 17.59. **Data of 23** : $^{1}$H NMR ($C_6D_6$, 300 MHz): 1.36 (1H, dt, J=12.6, 4.9 Hz, H-3x), 1.74 (1H, dd, J=12.6, 8.5 Hz, H-3n), 3.01 (1H, m, H-2), 3.25 (1H, dd, J=9.2, 6.2 Hz, H-2'), 3.28 (1H, d, J=4.0 Hz, H-5), 3.36 (1H, t, J=9.3 Hz, H-2'), 4.12 (1H, aptt, J=4.6 Hz, H-6), 4.49 (1H, d, J=5.3 Hz, H-4), 4.51 (1H, d, J=4.7 HZ, H-1), 4.47-4.57 (2H, m, $CH_2$), 7.31-7.36 (8H, m, Ar.), 7.60-7.63 (2H, m, Ar.). NOE: between H-3n / H-2: 9.2% , H-3n / H-5: 8.6% . $^{13}$C NMR ($CDCl_3$, 50 MHz): 34.2, 37.4, 52.7, 53.1, 72.0, 73.0, 82.0, 83.5, 127.7, 128.0, 128.4, 129.3, 134.6, 137.3. Anal. Calcd. for $C_{20}H_{21}O_2BrSe$: C, 53.09; H, 4.64; Br, 17.67. Found: C, 53.01; H, 4.70; Br, 17.75.

**2-*exo*-phenylselenyl-4,8-dioxatricyclo [4.2.1.0.$^{3,7}$]nonane (17).** From 100 mg (0.46 mmol) of **12** after 45 min., was obtained 120 mg of **17** (93%), after chromatography ( hexane :ethyl acetate, 5:1, Rf=0.17). $^{1}$H NMR ($CDCl_3$, 300 MHz): 1.53 (1H, dd, J=12.6, 2.1 Hz, H-3n), 2.23 (1H, ddd, J=12.6, 10.6, 5.2 Hz, H-3x), 2.58 (1H, m, H-2), 3.25 (1H, s, H-5), 3.84 (1H, d, J=8.8 Hz, H-2'), 3.90 (1H, dd, J=8.8, 4.0 Hz, H-2'), 4.41 (1H, d, J=4.8 Hz, H-6), 4.48 (1H, d, J=5.2 Hz, H-4), 5.07 (1H, apt, J=4.9 Hz, H-1), 7.26-7.41 (3H, m, Ar.), 7.54-7.57 (2H, m, Ar.). $^{13}$C NMR ($CDCl_3$, 50 MHz): 38.1, 38.4, 52.7, 72.1, 79.4, 83.1, 84.3, 127.2, 129.2, 129.6, 133.0. IR ($CHCl_3$): 3700, 3500, 2940, 2900, 1600, 1500, 1450, 1380, 1330, 1320, 1310, 1280, 1230, 1190, 1170, 1100, 1080, 1060, 1040. Anal. Calcd. for $C_{13}H_{14}SeO_2$: C, 55.50; H, 5.02. Found: C, 55.40; H, 4.95.

**2-*exo*-phenylsulfenyl-4,8-dioxatricyclo [4.2.1.0.$^{3,7}$]nonane (18).** From 120 mg (0.54 mmol)of **12** after 5 min., was obtained 89.7 mg of **18** as a white

solid (71%)., after chromatography ( hexane : ethyl acetate, 4:1). mp:60-61°C. $^1$H NMR ($CDCl_3$, 300 MHz): 1.50 (1H, dd, J=12.6, 2.1 Hz, H-3n), 2.19 (1H, ddd, J=12.6, 10.5, 5.1 Hz, H-3x), 2.53 (1H, m, H-2), 3.20 (1H, s, H-5), 3.83 (1H, d, J=8.7 Hz, H-2'), 3.89 (1H, dd, J=8.7, 4.2 Hz, H-2'), 4.19 (1H, d, J=4.5 Hz, H-6), 4.38 (1H, d, J=5.4 Hz, H-4), 5.03 (1H, apt, J=4.8 Hz, H-1), 7.16-7.36 (5H, m, Ar.). $^{13}$C NMR ($CDCl_3$, 75 MHz): 37.9, 38.0, 56.9, 72.2, 78.5, 82.8, 83.5, 125.9, 128.9, 129.1, 135.0. Anal. Calcd. for $C_{13}H_{14}SO_2$: C, 66.51; H, 6.01; S, 13.63. Found: C, 66.65; H, 5.93; S, 13.52.

**2-*exo*-Benzoyloxymethyl-5-*endo*-Bromo-6-*exo*-phenylselenyl-7-oxabicyclo[2.2.1] heptane (24) and 2-*exo*-Benzoyloxymethyl-6-*endo*-Bromo-5-*exo*-phenylselenyl -7-oxabicyclo [2.2.1]heptane (25).** From 160 mg (0.7 mmol) of **14** after 5 min. was obtained 251.2 mg of a 1.5:1 mixture of **24** and **25** (77%). Careful chromatography ( hexane :ethyl acetate, 1:1) afforded pure samples of both isomers. Data of **24** : $^1$H NMR ($C_6D_6$, 300 MHz): 0.85 (1H, m, H-3x), 1.79 (1H, m, H-2), 2.19 (1H, dd, J=13.1, 8.7 Hz, H-3n), 3.14 (1H, d, J=4.1 Hz, H-6), 3.74 (1H, dd, J=10.9, 9.6 Hz, H-2'), 3.86 (1H, aptd, J=4.5, 1.7 Hz, H-5), 3.93 (1H, dd, J=10.9, 5.9 Hz, H-2'), 4.05 (1H, apt, J=4.9 Hz, H-4), 4.37 (1H, s, H-1), 6.9-7.13 (2H, m, Ar.). NOE: between H-6 / H-1:2.9 % , H-6 / H-2:8.8 % , H-6 / H-Ar:1.2 % , H-6 / H-5:2.1 % . $^{13}$C NMR ($CDCl_3$, 50 MHz): 28.7, 42.4, 52.0, 52.3, 65.8, 80.5, 84.7, 127.9, 128.4, 128.7, 128.9, 129.6, 133.0, 134.2, 134.6, 166.2. Anal. Calcd. for $C_{20}H_{19}O_3BrSe$: C, 51.50; H, 4.08; Br, 17.14. Found: C, 51.39; H, 4.10; Br17.22. Data of **25** : $^1$H NMR ($C_6D_6$, 300 MHz): 0.88 (1H, m, H-3x), 1.08 (1H, dd, J=12.7, 8.6 Hz, H-3n), 2.92 (1H, m, H-2), 3.08 (1H, d, J=4.2 Hz, H-5), 3.91-3.99 (2H, m, H-2'), 3.97 (1H, apt, J=4.5 Hz, H-6), 4.12 (1H, d, J=4.9 Hz, H-1), 4.23 (1H, d, J=5.5 Hz, H-4), 6.91-7.13 (6H, m, Ar.), 7.48-7.52 (2H, m, Ar.), 8.12-8.15 (2H, m, Ar.). $^{13}$C NMR ($CDCl_3$, 50 MHz): 34.1, 36.9, 52.3, 52.7, 65.9, 81.9, 83.6, 128.1, 128.4, 128.7, 128.9, 129.3, 133.0, 134.2, 134.6, 166.2. Anal. Calcd. for $C_{20}H_{19}O_3BrSe$: C, 51.50; H, 4.08, Br, 17.14. Found: C, 51.58; H, 4.0; Br, 17.05.

**2-*endo*-Benzoyloxymethyl-5-*endo*-Bromo-6-*exo*-phenylselenyl-7-oxabicyclo [2.2.1]heptane (26).** From 120 mg (0.52 mmol) of **15** after 2 days was obtained 223 mg of **26** as a white solid (92%) after chromatography ( hexane :ethyl acetate, 5:1). mp:77-79°C. $^1$H NMR ($C_6D_6$, 300 MHz): 1.44 (1H, dddd, J=13.1, 11.6, 5.5, 1.7 Hz, H-3x), 1.74 (1H, dd, J)12.9, 5.7 Hz, H-3n), 2.30 (1H, m, H-2), 3.71 (1H, d. J=4.2 Hz, H-6), 3.96 (1H, aptd, J=4.4, 1.7 Hz, H-5), 4.05 (1H, dd, J=11 5, 10.7 Hz, H-2'), 4.08 (1H, t, J=5.1 Hz, H-4), 4.33 (1H, dd, J=11.6, 6.2 Hz, H-2'), 4.51 (1H, d, J=5.0 Hz, H-1), 6.79-6.83 (2H, m, Ar.)7.03-7.18 (4H, m, Ar.), 7.45-7.48 (2H, m, Ar.). $^1$H NMR ($CDCl_3$, 300 MHz): 1.97-2.12 (2H, m, H-3n, H-3x), 2.71 (1H, m, H-2), 3.36 (1H, d, J=4.0 Hz, H-6), 4.13 (1H, apt, J=4.4 Hz, H-5), 4.25 (1H, t, J=11.1 Hz, H-2'), 4.57-4.66 (3H, m, H-1, H-2', H-4), 7.07-7.60 (8h, m, Ar.), 7.85-7 88 (2H, m, Ar.). NOE: between H-6 / H-1:3.3 %, H-6 / H-Ar.:1.4 % , H-6 / H-2':6.1 % , H-6 / H-2':1.4 % . $^{13}$C NMR ($C_6D_6$, 50 MHz): 27.6, 41.7, 48.0, 54.1, 64.2, 81.0, 85.9, 129.3, 129.5, 129.6, 129.9, 130.34, 134.5, 137.9, 165.6. IR (KBr): 3700; 3540, 3420, 3080, 2980, 294 , 2880, 1790, 1740, 1620, 1600, 1490, 1470, 1450, 1400, 1360, 1330, 1280, 1230, 1200, 1160, 1130. Anal. Calcd. for $C_{20}H_{19}O_3BrSe$: C, 51.50; H, 4.08; Br, 17.14. Found: C, 51.48; H, 4.12; Br, 16.80.

**2-*endo*-Benzoyloxymethyl-5-*endo*-Chloro-6-*exo*-phenylsulfenyl-7-oxabicyclo [2.2.1]heptane (27).** From 90 mg (0.4 mmol) of **15** after 2 days was obtained 98.4 mg of **27** as a white solid (80%) after chromatography ( hexane :ethyl acetate, 3:1). mp:66-67°C. $^1$H NMR ($CDCl_3$, 300 MHz): 2.01-2.07 (2H, m, H-3x, H-3n), 2.79 (1H, m, H-2), 3.63 (1H, d, J=4.0 Hz, H-6), 4.09 (1H, apt, J=4.0 Hz, H-5), 4.31 (1H, t, J=11.1 Hz, H-2'), 4.55-4.70 (3H, m, H-1, H-4, H-2'), 7.11 (3H, m, Ar.), 7.41 (4H, m, Ar.), 7.61 (1H, m, Ar.), 7.91 (2H, m, Ar.). $^{13}$C NMR ($CDCl_3$, 50 MHz): 26.1, 40.5, 53.6, 62.9, 64.1, 80.7, 84.8, 127.34, 128.4, 129.1, 129.6, 131.7, 133.1, 134.2, 166.1. IR (KBr): 3690,

3610, 3110, 1730, 1620, 1600, 1530, 1490, 1460, 1400, 1280. Anal. Calcd. for $C_{20}H_{19}O_3ClS$: C, 64.17; H, 5.08; Cl, 9.49. Found: C, 64.09; H, 5.01; Br, 9.42.

**5-*endo*-Bromo-2-*endo*-3-*exo*-dibenzoyloxymethyl-6-*exo*-phenylselenyl-7-oxabicyclo [2.2.1]heptane (28).** From 100 mg (0.27 mmol) of **16** after 24 hours was obtained 130 mg of **28** (80%) as a white solid after chromatography (hexane: ethyl acetate, 5:1, Rf=0.23). mp=116-118°C. $^1$H NMR ($CDCl_3$, 300 MHz): 2.42 (1H, apsext, J=5.3 Hz, H-2x), 2.88 (1H, m, H-3n), 3.67 (1H, d, J=4.1 Hz, H-6), 4.17 (1H, apt, J=4.6 Hz, H-5), 4.24-4.39 (3H, m, 2H-3', H-2'), 4.53 (1H, d, J=5.1 Hz, H-4), 4.61 (1H, dd, J=11.5, 5.2 Hz, H-2'), 4.66 (1H, d, J=5.3 Hz, H-1), 7.06-7.16 (3H, m, Ar.), 7.38-7.45 (4H, m, Ar.), 7.52-7.59 (4H, m, Ar.), 7.86-7.89 (2H, m, Ar.), 8.02-8.05 (2H, m, Ar.). NOE: between H-6 / H-1:4 % , H-6 / H-Ar:1.7 % , H-6 / H-5:3.7 % , H-6 / H-2':6.8 % , H-6 / H-3:1.7 % . $^{13}$C NMR ($CDCl_3$, 50 MHz): 40.3, 45.7, 47.2, 52.3, 63.6, 65.7, 82.8, 86.0, 128.1, 128.4, 129.2, 129.4, 129.6, 129.7, 133.2, 134.4, 165.9, 166.2. IR (KBr): 3080, 2970, 2940, 2870, 1740, 1470, 1330, 1270, 1120, 1040. Anal. Calcd. for $C_{28}H_{25}O_5BrSe$: C, 56.0; H, 5.83; Br, 13.31. Found: C, 55.89; H, 5.60; Br, 13.13.

**Acknowledgment.** This research was supported by D.G.I.C.Y.T. (Grant No. PB87-0064) and by the C.S.I.C. We thank the Universidad Complutense for a fellowship to A.V.

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(8) Benzyl ether **9** was prepared by a modification of the procedure described by Rickborn for the analogous methyl ether. See: Misaderghi, S.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 4340-4345. Hydroxymethyl derivatives **11-15** were prepared from the *endo, exo* mixture of 7-oxabicyclo[2.2.1] hept-5-en-2-carboxylic acids (See:Moore, J.A.; Partain, E. *J. Org. Chem.* **1983**, *48*, 1105-1106 by: 1) Chromatography on silica gel (ether, hexane,2:1) 2) LAH/THF 3) NaH, BnBr, DMF or BzCl, pyridine respectivily. Dibenzoate **16** was prepared from the corresponding diol (See: Paquette, L.A.; Kavetz, T.M.; Charamilind P. *Tetrahedron* **1986**, *42*, 1789-1795) and BzCl, pyridine.

All other substrates were prepared by standars methods from readily avaible starting materials.

(9) However, small distortions of the bicyclic system due to *exo* substitution cannot be ruled out.

(10) 7-Oxabicyclo [2.2.1] hept-5-en-2-*endo*-ol can be obtained from optically pure ketone **2** ($NaBH_4$/MeOH), or by enzymatic resolution of the corresponding butyrate. See ref 2. For the resolution of *endo*-7-oxabicyclo [2.2.1] hept-5-ene-2-carboxylic acid, see: Ogawa, S.; Iwasawa, Y.; Nose, T.; Suami, T.; Ohba, S.; Ito, M.; Saito, Y. *J.Chem. Soc. PerKin Trans. I* 1985, 903-906. For The synthesis of both enantiomers of 2-*endo*-3-*exo*-bis(hydroxymethyl)bicyclo [2.2.1] hept-5-ene, see: Horton,D.; Machimani, T.; Takagi, Y. *Carbohydr. Res.* 1983,121, 135-161.

(11) It should be pointed out that in ketone **2** electronic and steric effects favor the observed regioisomer. On the other hand, it appears that a benzyl ether substituent behaves as a remote electron donating substituent, which, to the best of our knowledge is not a well known phenomenon. At any rate, the introduction of an *endo* methyl group, as in **4**, completely overrides the electronic influence of the hydroxy functionality, presumably similar to that of a benzyloxy substituent.

(12) The observed selectivity may arise from a small, but nevertheless significant, distortion of the bicyclic moiety although an electronic contribution cannot be discarded.

(13) Fieser and Fieser, *Reagents for Organic Synthesis,* Vol.5, p.523, John Wiley and Sons Inc., USA.