Asymmetric Selenohydroxylation of Alkenes with Camphorselenenyl Sulfate

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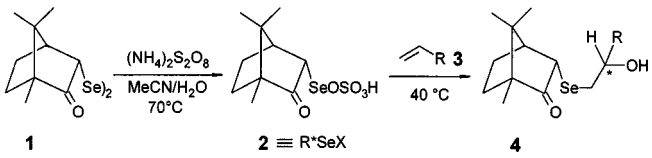
By reaction with ammonium persulfate the easily available diselenide derived from (1*R*)-(+)-camphor was converted into the camphorselenenyl sulfate. This chiral nonracemic electrophilic selenium reagent reacted with alkenes, at 40 °C in acetonitrile in the presence of water, to afford the selenohydroxylated adducts in good yields and with moderate to good facial selectivity. The two diastereomeric addition products could be separated in most cases.

Several research groups have recently employed organoselenium reagents to effect asymmetric syntheses. For this purpose a number of new chiral diselenides have been prepared and transformed in situ into electrophilic chiral non racemic selenenylating agents. These were allowed to react with alkenes in the presence of external nucleophiles or with alkenes bearing an internal nucleophilic group in an appropriate position.[1][2][3][4][5] Moderate to high asymmetric inductions were observed in the formation of the corresponding addition or cyclization products, respectively. Very recently Back and coworkers have reported that the camphor diselenide **1** can be easily prepared, in one step and on a large scale, from (1*R*)-(+)-camphor and elemental selenium.[5b] The corresponding selenenyl chloride has been employed to promote seleno-etherification and seleno-lactonization reactions with very poor diastereoselectivity. However, good results could be obtained with a modified diselenide in which the carbonyl group was converted into an oxazolidinone ring.[5a] We have recently observed that camphorselenenyl chloride, as well as the corresponding bromide and triflate, can be employed to effect the selenomethoxylation of alkenes but the facial selectivity was very poor even at very low temperatures. On the contrary, the same reactions could be effected at room temperature and occurred in high yields and with moderate to good facial selectivity when camphorselenenyl sulfate **2** was employed.[6] The reagent **2** can be easily produced in situ by the reaction of the diselenide **1** with ammonium persulfate, according to the procedure described by us for the preparation of phenylselenenyl sulfate from diphenyl diselenide.[7] We now report that camphorselenenyl sulfate **2** reacts with alkenes **3** at 40°C in acetonitrile and water to afford the selenohydroxylation products **4** in good yield and with moderate to good diastereoselectivity (Scheme 1). To our knowledge, the results here reported represent the first examples of the asymmetric selenohydroxylation of alkenes.

Scheme 1



Preliminary experiments were carried out on *trans*-3-hexene **3a** (Scheme 2 and Table 1) with camphorselenenyl bromide (generated in situ from **1** and bromine in dichloromethane) at 0°C (Method A), and camphorselenenyl sulfate at 40, 50, and 70°C (Method B) or at 40°C in the presence of trifluoromethane sulfonic acid (Method C). In every case the selenohydroxylation products **4a** were obtained as a mixture of the two possible diastereomers derived from a stereospecific *anti* addition.[8]

Scheme 2

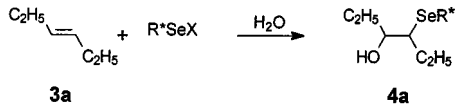


Table 1. Formation of **4a** from the selenohydroxylation reactions of *trans*-3-hexene **3a** with camphorselenenyl bromide or sulfate, R*SeX

Entry	X	Method	Reaction Temp. [°C]	Reaction Time [h]	Yield [%]	D. r.
1	Br	A	0	24	55	55:45
2	OSO_3H	B	40	36	60	91:9
3	OSO_3H	B	50	20	65	88:12
4	OSO_3H	B	70	8	70	76:24
5	OSO_3H[a]	C	40	27	75	84:16

[a] In the presence of CF_3SO_3H.

  1434−193X/98/1111−2275 $ 17.50+.50/0

Table 2. Selenohydroxylation of alkenes with camphorselenenyl sulfate **2** in acetonitrile and water at 40°C

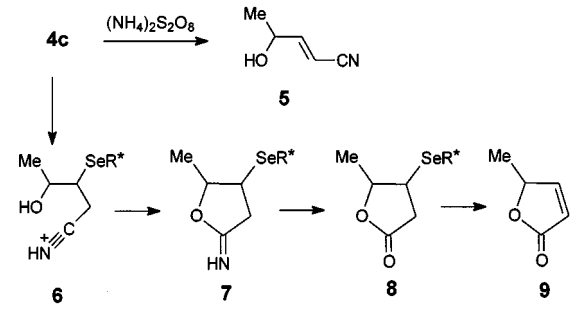
Entry	Alkenes, 3		Reaction Time [h]	Addition Products, 4	Yield [%][a]	D. r.
1	C_2H_5, C_2H_5	**3a**	36	C_2H_5, SeR*, HO, C_2H_5	**4a**[b] 60	91:9[c]
2	C_3H_7, C_3H_7	**3b**	39	C_3H_7, SeR*, HO, C_3H_7	**4b**[c] 89	94:6[c]
3	Me, CN	**3c**	60	Me, SeR*, HO, CN	**4c**[c] 60	90:10[f]
				Me, OH, R*Se, CN	**4c'**[c] 10	90:10[f]
4		**3d**	37	SeR*, OH	**4d**[b] 68	78:22[e]
5		**3e**	31	SeR*, OH	**4e**[b] 75	90:10[e]
6		**3f**	45	SeR*, OH	**4f**[d] 50	81:19[e]
7	Ph	**3g**	28	Ph, SeR*, HO	**4g**[b] 68	65:35[e]
8-	Ph	**3h**	40	Ph, SeR*, HO	**4h**[d] 62	65:35[e]

[a] Based on isolated products after column chromatography. – [b] The two diastereomers were separated and identified by ^{1}H NMR, ^{13}C NMR, and GC-MS. – [c] The minor isomer could not be obtained in a pure form. – [d] The two diastereomers were detected by GC-MS. – [e] Determined by GC-MS. – [f] Determined by ^{1}H NMR.

As already observed in the case of the asymmetric selenomethoxylation of alkenes, low yield and poor diastereoselectivity were observed when camphorselenenyl bromide was employed (Table 1, entry 1). In contrast, good results were obtained when the addition reaction was effected with the camphorselenenyl sulfate. In this case the reaction was much slower and it was therefore carried out at 40°C (entry 2). Two further experiments were carried out at 50 and 70°C (entries 3 and 4). In these cases the reaction times were obviously shorter and the reaction yields were increased. However, a progressive decrease in the diastereoselectivity was observed. Similar effects were produced by the addition of trifluoromethanesulfonic acid (entry 5). These results indicate that the nature of the counteranion has a marked effect on the course of these asymmetric selenohydroxylation reactions[9] and that the best diastereomeric ratio is obtained with camphorselenenyl sulfate at 40°C (Method B). The selenohydroxylation reactions of the alkenes **3a**–**3h** were therefore carried out under these experimental conditions. The general procedure is described in the Experimental Section. The results obtained from these experiments are indicated in Table 2. In the case of the reactions of **3c** (entry 3) small amounts of the regioisomers **4c′** were formed together with **4c**. In all the other cases the adducts were obtained as single regioisomers. Moderate diastereoselectivity was observed in the selenohydroxylation of cyclohexene, styrene, and β-methylstyrene (entries 4, 7, and 8). Good facial selectivity was instead observed in all the other cases.

From the reaction of **3c**, together with **4c** and **4c′**, two further products were also isolated in small yield. These were identified as the allylic alcohol **5** (5%) and the butenolide **9** (5%) (Scheme 3).

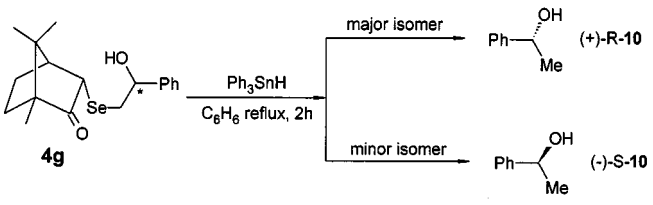
Scheme 3



The formation of these two products was not unexpected. Compound **5** clearly derives from the ammonium persulfate promoted oxidative elimination of **4c**. In fact, we have recently reported that **4c**, as well as other alkenes having similar structures, can easily give rise to a selenenylation-elimination sequence to afford **5** by treatment with catalytic amounts of phenylselenenyl sulfate and an excess of ammonium persulfate in acetonitrile and water.[10][11] As already observed in similar reactions carried out with phenylselenenyl sulfate,[12] the hydroxy selenide **4c** can easily cyclize to afford the lactone **8** from which the observed butenolide **9** is formed by elimination[13] (Scheme 3).

Absolute configuration was established only in the case of the addition products **4g** deriving from styrene. Reductive deselenenylation with triphenyltin hydride and AIBN in refluxing benzene was carried out on the two separated diastereomers (Scheme 4). The major isomer afforded pure (+)-(*R*)-1-phenylethan-1-ol **10** (92% yield) and the minor isomer gave pure (−)-(*S*)-1-phenylethan-1-ol **11** (90% yield).

Scheme 4



The results here presented indicate that camphorselenenyl sulfate, generated in situ from the easily available camphor diselenide **1**, can be conveniently employed to effect the asymmetric selenohydroxylation of alkenes. The diastereomeric hydroxy selenides are generally formed with good facial selectivity and can be easily separated in most cases. These addition products can be subjected to classical

reductive or oxidative deselenenylation reactions to afford enantiomerically pure saturated or allylic alcohols, respectively.

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Experimental Section

General Procedure for the Selenohydroxylation of Alkenes: A mixture of the diselenide **1** (0.55 mmol) and ammonium persulfate (0.55 mmol) in acetonitrile (3 ml) was refluxed for 15 min and then cooled at 40°C. A solution of the alkene, **3a−3h**, (1 mmol) in acetonitrile (2.5 ml) and water (5 ml) was added and the mixture was stirred for the time indicated in Table 2. The progress of the reaction was monitored by TLC and GC-MS. The reaction mixture was poured into water and worked up in the usual way. GC-MS and ^{1}H-NMR analyses of the reaction mixture indicated that the addition products **4a−4h** were formed as a mixture of two diastereomers in the ratios indicated in Table 2. The reaction products were isolated by medium pressure column chromatography on silica gel. In most cases the two diastereomers were separated and were fully characterized by GC-MS, ^{1}H NMR, and ^{13}C NMR. Reaction yields and diastereomeric ratios are indicated in Table 2. Spectral data of some representative reaction products are reported below.

(1R,3S,4S)-3-[(1-Ethyl-2-hydroxybutyl)selanyl]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (**4a**, minor isomer): Oil. − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.85 (ddd, 1 H, *J* = 3.0, 4.2, and 7.6 Hz), 3.76 (dd, 1 H, *J* = 2.2 and 4.7 Hz), 3.62 (br s, 1 H), 3.19 (ddd, 1 H, *J* = 3.0, 3.9, and 10.0 Hz), 2.2 (dd, 1 H, *J* = 4.1 and 4.7 Hz), 1.8−1.4 (m, 8 H), 1.1 (t, 3 H, *J* = 7.3 Hz), 1.02 (s, 3 H), 1.0 (t, 3 H, *J* = 6.6 Hz), 0.94 (s, 3 H), 0.91 (s, 3 H). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 220.5, 76.7, 58.2, 52.6, 49.0, 46.9, 43.6, 30.3, 27.0, 23.5, 21.3, 19.5, 19.3, 13.4, 10.8, 9.6. − MS *m/z* (relative intensity): 332 (2), 274 (6), 232 (12), 152 (100), 137 (20), 124 (49), 109 (49), 95 (10), 83 (28), 59 (11), 55 (24). − $C_{16}H_{28}O_2Se$ (331.29): calcd. C 58.01, H 8.52; found C 58.45, H 8.05.

(1R,3S,4S)-3-[(1-Ethyl-2-hydroxybutyl)selanyl]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (**4a**, major isomer): Oil. − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.85 (br s, 1 H), 3.59 (dd, 1 H, *J* = 2.2 and 4.7 Hz), 3.5−3.4 (m, 1 H), 3.13 (ddd, 1 H, *J* = 2.9, 5.1, and 9.3 Hz), 2.2 (dd, 1 H, *J* = 4.0 and 4.7 Hz), 1.8−1.3 (m, 8 H), 1.0 (t, 3 H, *J* = 7.2 Hz), 0.98 (t, 3 H, *J* = 7.4 Hz), 0.94 (s, 3 H), 0.86 (s, 3 H) 0.82 (s, 3 H). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 219.3, 75.4, 58.5, 56.8, 49.4, 48.5, 46.9, 30.6, 26.3, 25.2, 23.4, 19.7, 19.3, 13.4, 10.7, 9.7. − MS *m/z* (relative intensity): 332 (2), 274 (8), 232 (12), 163 (7), 152 (100), 137 (20), 124 (48), 109 (49), 95 (8), 83 (25), 81 (13), 59 (12), 55 (24), 43 (12), 41 (22). − $C_{16}H_{28}O_2Se$ (331.29): calcd. C 57.90, H 8.15; found C 58.45, H 8.05.

(1R,3S,4S)-3-{[(2R)-2-Hydroxy-2-phenylethyl]selanyl}-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (**4g**, minor isomer): Oil. − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.4−7.2 (m, 5 H), 5.0 (1 H, dd, *J* = 3.0 and 9.5 Hz), 4.55 (br s, 1 H), 3.74 (dd, 1 H, *J* = 2.0 and 4.7 Hz), 3.22 (dd, 1 H, *J* = 3.0 and 13.5 Hz), 3.01(dd, 1 H, *J* = 9.5 and 13.5 Hz), 2.28 (dd, 1 H, *J* = 4.2 and 4.7 Hz), 2.0−1.5 (m, 4 H), 0.94 (s, 3 H), 0.88 (s, 3 H), 0.82 (s, 3 H). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 219.5, 143.4, 128.4, 127.6, 125.7, 74.5, 58.3, 49.1, 47.7, 46.9, 36.3, 30.5, 23.4, 19.7, 19.3, 9.7. − MS *m/z* (relative intensity) 352 (2), 246 (100), 244 (50), 184 (11) 152 (73), 137 (32), 124 (68), 123 (84), 109 (54), 105 (21), 104 (18), 95 (16), 91 (22), 83 (29), 77 (35), 55 (30), 41 (27). − $C_{18}H_{24}O_2Se$ (351.28): calcd. C 61.54, H 6.89; found C 61.40, H 6.95.

(1R,3S,4S)-3-{[(2S)-2-Hydroxy-2-phenylethyl]selanyl}-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (**4g**, major isomer): Oil. − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.4−7.2 (m, 5 H), 4.9 (dd, 1 H, *J* = 4.1 and 6.9 Hz), 3.5 (dd, 1 H, *J* = 1.9 and 4.7 Hz), 3.15 (dd, 1 H, *J* = 4.1 and 13.0 Hz), 3.05 (dd, 1 H, *J* = 6.9 and 13.0 Hz), 2.1 (dd, 1 H, *J* = 4.2 and 4.7 Hz), 1.8−1.3 (m, 5 H), 0.93 (s, 3 H), 0.87 (s, 3 H), 0.80 (s, 3 H). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 219.5, 143.2, 128.4, 127.5, 125.8, 72.5, 58.2, 48.9, 47.6, 46.9, 35.9, 30.6, 23.4, 19.7, 19.4, 9.7. − MS *m/z* (relative intensity): 352 (3), 246 (100), 244 (50), 184 (14), 152 (93), 137 (40), 124 (83), 123 (97), 109 (60), 105 (24), 104 (33), 95 (21), 91 (24), 83 (30), 77 (40), 55 (26), 41 (23). − $C_{18}H_{24}O_2Se$ (351.28): calcd. C 61.54, H 6.89; found C 61.45, H 6.70.

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[8] In all the examples reported in this paper *anti* addition is assumed on the basis of literature precedents.[7][2a]

[9] Similar changes in facial selectivity on passing from the camphorselenenyl bromide to the sulfate were also observed in the case of the asymmetric selenomethoxylation of alkenes.[6] Similar variations were also observed in other cases.[1a][3b] This effect of the counteranion on the facial selectivity of the addition reaction is presently under further investigation.

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