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Asymmetric methoxyselenenylations with camphor-based selenium electrophiles

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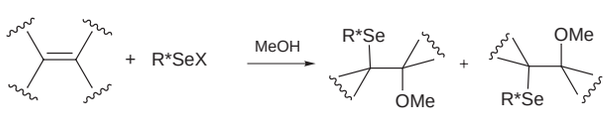
The asymmetric methoxyselenenylation of olefins was achieved with a series of camphor-based selenenyl triflates, of which the readily available 2-oxo analog 2a proved the most effective.

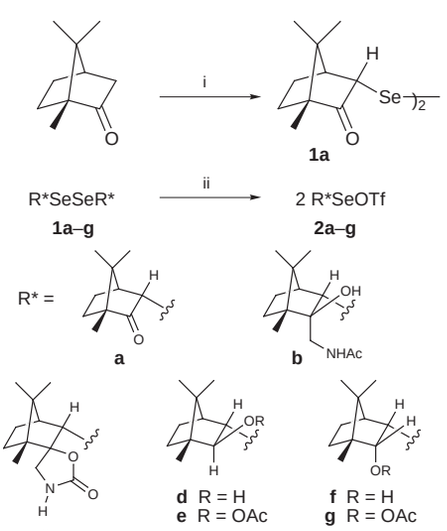
Electrophilic selenium compounds have proven of considerable utility in a variety of organic transformations.[1] Asymmetric variations of such processes are made possible by employing selenium reagents containing chiral auxiliary groups. For example, the treatment of an olefin with a chiral selenium electrophile in the presence of methanol results in an asymmetric methoxyselenenylation, leading to the formation of a β-alkylseleno methyl ether containing up to two new chiral centers (Scheme 1). Such processes are known to proceed *via*



Scheme 1 R* = chiral auxiliary group; X = leaving group.

anti-addition,[2] resulting in the formation of two diastereomeric products, whose ratio is controlled by the chiral auxiliary group. Enantioselective access to deselenized products is then made possible by oxidative or reductive removal of the selenium residue. Thus, several groups have devised chiral selenium electrophiles for use in asymmetric methoxyselenenylations.[3]

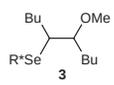
Over the past few years, we have prepared a series of novel diselenides **1a**–**g** derived from camphor for use in our ongoing studies of asymmetric selenium reactions.[4,5] Diselenide **1a** was obtained in one step from the lithium enolate of camphor and elemental selenium,[4b] and was in turn easily converted into diselenides **1b**–**g** (Scheme 2).[4c,5] We recently reported that the



Scheme 2 *Reagents and conditions*: i, LDA, Se, then O_2; ii, Br_2, AgOTf.

selenenyl chlorides derived from **1a–c** can be employed in asymmetric selenium-mediated cyclizations of unsaturated alcohols and carboxylic acids, with **1c** affording the highest diastereoselectivity.[5] Subsequently to our disclosure of the preparation of the novel diselenides **1a**–**c** and of their application to asymmetric cyclizations,[4,5] Tiecco and coworkers[6] reported the use of **1a** in methoxyselenenylations, *via* the corresponding selenenyl sulfate. We now report the results of our investigation of asymmetric methoxyselenenylations with electrophiles derived from **1a**–**g**.[7]

Table 1[a] Methoxyselenenylation of *trans*-dec-5-ene



Entry	R*SeOTf	Isolated yield of **3** (%)	dr[b,c]
1	**2a**	88	94:6
2	**2b**	[d]	
3	**2c**	65	66:34
4	**2d**	63	82:18
5	**2e**	51	85:15
6	**2f**	[e]	
7	**2g**	[e]	

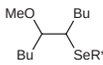
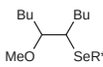
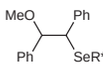
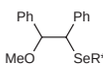
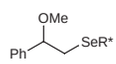
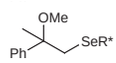
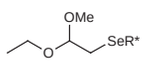
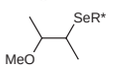
[a] All reactions were performed in dichloromethane at −78 °C. [b] dr = diastereomeric ratio. [c] Measured by NMR integration. [d] Triflate **2b** cyclized to the corresponding selenenamide. [e] No methoxyselenenylation occurred under these conditions.

An evaluation of the camphorselenenyl triflates **2a**–**g**, derived from **1a**–**g** (Scheme 2), in the methoxyselenenylation of *trans*-dec-5-ene at −78 °C in dichloromethane was first performed. Triflates **2a**, **2c**, **2d** and **2e** behaved in the expected manner, affording the corresponding adducts **3a**, **3c**, **3d** and **3e**, respectively (Table 1). Under these conditions, triflate **2b** underwent cyclization to the corresponding selenenamide,[8] while **2f** and **2g** also failed to afford the corresponding adducts **3**, presumably because of strong coordination of the *endo*-oxygen functions with the selenium moiety. Interestingly, triflate **2a**, which was derived from **1a**, the most readily available of the above diselenides, afforded the highest diastereoselectivity of the corresponding adduct **3**, compared to **2c**, **2d** and **2e**. The selenenyl chloride and bromide derived from **1a** gave lower chemical yields and diastereomeric ratios (dr's), while the corresponding selenenyl tetrafluoroborate and hexafluorophosphate gave comparable dr's to the triflate, but in some cases lower yields. Substantially lower dr's resulted when the reaction was performed at higher temperatures.

The results of the asymmetric methoxyselenenylations of a series of other olefins under the above optimized conditions are shown in Table 2. The products were isolated by chromatography (generally the diastereomers were obtained unseparated) and characterized by IR, ^{1}H- and ^{13}C-NMR, and low and high resolution mass spectroscopy. The dr's were determined by ^{1}H- or ^{77}Se-NMR integration.

A typical procedure follows (Entry 1 in Table 2): Diselenide **1a** (50 mg, 0.11 mmol) and 100 mg of 4 Å molecular sieves were stirred in 3 mL of dry dichloromethane. A 1.0 M solution of bromine (0.11 mL, 0.11 mmol) in tetrachloromethane was added dropwise at −78 °C under nitrogen, with stirring. After 15 min, a 0.70 M methanol solution of silver triflate (0.45 mL, 0.30 mmol) was added, followed after another 15 min by *trans*-

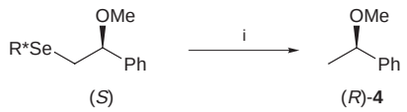
Table 2[a] Methoxyselenenylations of olefins with **2a**

Entry	Substrate	Product	Isolated yield (%)	dr[b,c]
1			88	94:6
2			88	75:25
3			65[d]	84:16
4			66	69:31
5			77	74:26
6			88	83:17
7			71	81:19
8			69	87:13
9			71	75:25
10			90	84:16
11			73	86:14

[a] All reactions were performed in dichloromethane at −78 °C. [b] dr = diastereomeric ratio. [c] Measured by ^{1}H- or ^{77}Se-NMR integration. [d] The product contained a small amount of diselenide **1a** after chromatography. The yield is based on NMR integration of the isolated product mixture.

dec-5-ene (0.10 mL, 0.53 mmol). Stirring was continued for 1 h at −78 °C. The reaction was quenched with aqueous $NaHCO_3$, diluted with 10 mL of dichloromethane, washed with water and brine, dried, filtered, and concentrated *in vacuo*. The residue was chromatographed (elution with 5% ethyl acetate–hexanes) to afford 78 mg (88%) of the addition product as a pale yellow oil: IR (film) 1738 (C=O) cm^{-1}; ^{1}H NMR (major diastereomer): δ 3.78 (d, J 4.7 Hz, 1 H), 3.42 (s, 3 H), 3.49–3.32 (m, 2 H), 2.21–2.19 (m, 1 H), 1.86–1.25 (m, 16 H), 1.02 (s, 3 H), 0.93 (s, 3 H), 0.92 (s, 3 H), 0.92–0.89 (m, 6 H); (minor diastereomer): δ 3.99 (d, J 4.8 Hz, 1 H), 3.39 (s, 3 H); ^{13}C NMR (major diastereomer): δ 218.5, 85.4, 58.4, 58.2, 48.9, 47.0, 46.6, 46.0, 31.7, 31.4, 30.9, 30.6, 28.5, 23.7, 23.1, 22.8, 19.8, 14.3 (two signals), 14.2, 10.0; (minor diastereomer): δ 85.8, 57.9, 30.7 (two signals), 23.5, 19.8; m/z (rel. int.) 402 (21%, M$^+$), 370 (19), 230 (50), 151 (65), 101 (100), 69 (99) (Calc. for $C_{21}H_{38}O_2Se$: 402.2040. Found: 402.2059).

The absolute configuration of the major product in entry 5 was determined to be (*S*) by reductive deselenization[9] to the (*R*)-methyl ether **4** (Scheme 3), the major enantiomer of which was identical to the product of *O*-methylation of authentic (*R*)-1-phenylethanol, as determined by GC analysis with a Cyclodex B column. The enantiomeric ratio of the deselenized product was 72:28, in excellent accord with the dr of its precursor (74:26).



(*S*) (*R*)-**4**

Scheme 3 *Reagents and conditions*: i, Ph_3SnH, AIBN, toluene, Δ.

The above results indicate that this protocol provides moderate to high diastereoselectivity with a diverse range of olefins, including aryl, alkyl, mono-, di- and trisubstituted substrates. In contrast to the asymmetric cyclizations reported earlier,[5] *trans*-olefins afford substantially higher dr's than their *cis* isomers (*cf*. entry 1 *vs.* 2 and entry 3 *vs.* 4 in Table 2). The choice of C-2 substituent in the camphor moiety is crucial and its requirements are, surprisingly, different from those of the related asymmetric cyclizations. The stereoselectivity is enhanced by low temperatures and non-nucleophilic counterions, and dr's obtained with the above protocol are comparable to or higher than those obtained with the corresponding selenenyl sulfate.[6]

Acknowledgements

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