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Asymmetric Syntheses with a New Nitrogen Containing Chiral Diselenide.

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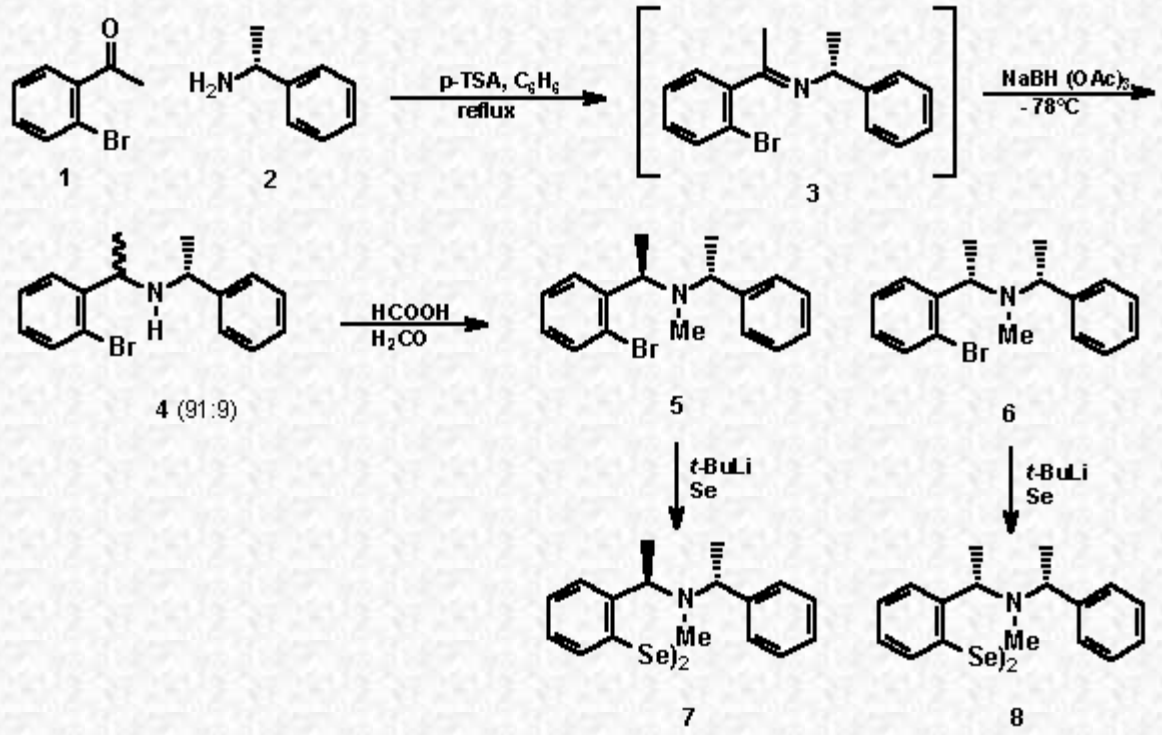
Organoselenium reagents are largely used in organic synthesis to introduce new functional groups into organic substrates under very mild experimental conditions.[1] In recent years, several research groups have described the synthesis of a number of chiral non racemic diselenides which can be transformed *in situ* into electrophilic selenenylating agents to effect efficient asymmetric syntheses.[2][3][4][5][6][7] Diselenides containing a nitrogen atom in the chiral moiety have also been employed as useful ligands in various transformations such as diethilzinc additions to aldehydes,[8] asymmetric hydrosilylation[9] and transfer hydrogenation reactions.[10] Moreover these diselenides can also be employed in the sequential catalytic stereoselective oxyselenenylation-elimination reactions using ammonium persulfate to generate the electrophilic selenenylating species and to promote the elimination process.[11]

Herein we report the synthesis of two new chiral nitrogen containing diselenides and the use of these compounds as precursors of electrophilic species in asymmetric additions of organoselenium reagents to olefins.

The condensation of the commercially available compounds **1** and **2** readily afforded the intermediate **3** which was reduced with sodium triacetoxyborohydride in acetic acid at –78°C to give a 91:9 mixture of the diastereomeric chiral secondary amines **4**. The mixture of **4** was refluxed with formic acid and formaldehyde and was thus quantitatively converted into the amines **5** and **6**. The two compounds were separated by flash chromatography and independently transformed into the corresponding diselenides **7** and **8** by treatment with t-BuLi and elemental selenium. The absolute configuration of the chiral carbon atom generated during the reduction was assigned on the basis of the observation that the debromination of **6** (t-BuLi, water) afforded the corresponding *meso* derivative.



Diselenides **7** and **8** were employed to effect asymmetric addition reactions to olefins. Preliminary experiments were carried out in the methoxyselenenylation and hydroxyselenenylation of styrene. As indicated in the following scheme the two sets of experiments gave the addition products **9a-10a** and **11a-12a**, respectively. From the data collected in Table 1 it can be seen that, using ammonium persulfate as oxidizing agent and working at room temperature, the diselenide **7** (entries 1 and 4) gave higher diastereomeric ratios than **8** (entries 2 and 5). No substantial differences were observed when the reactions were run at –78°C and using the triflate as the counter ion (entries 3 and 6).

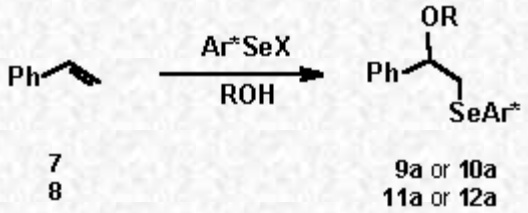
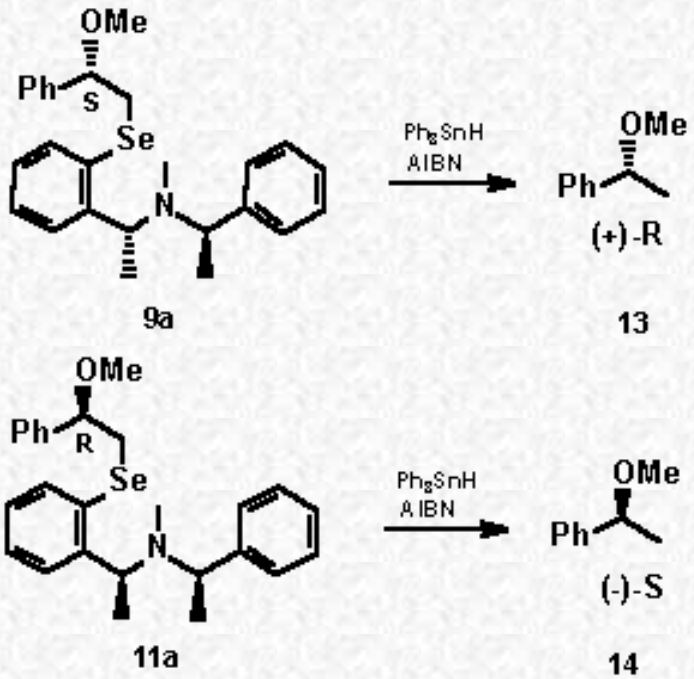


Table 1: Methoxyselenenylation and Hydroxyselenenylation of Styrene Promoted by the Diselenides **7** and **8**

Entry	Diselenide	ROH	X	T°C	Products	Yield %	d.r.	Abs. Conf.
1	**7**	CH_3OH	OSO_3H	25	**9a**	70	95:5	*R*
2	**8**	CH_3OH	OSO_3H	25	**11a**	72	81:19	*S*
3	**7**	CH_3OH	OTf	-78	**9a**	40	97:3	*R*
4	**7**	H_2O	OSO_3H	25	**10a**	70	95:5	*R*
5	**8**	H_2O	OSO_3H	25	**12a**	72	80:20	*S*
6	**7**	H_2O	OTf	-78	**10a**	40	98:2	*R*

The absolute configuration of compounds **9a** and **11a** was established by reductive deselenenylation with triphenyltin hydride and AIBN in refluxing benzene. As indicated in the following scheme compound **9a** gave the chiral ether (+)-

(R)-methoxyphenylethane **13** and compound **11a** gave the (-)-(S)-methoxyphenylethane **14**. As expected, the enantiomeric excess of **13** and **14** corresponded to diastereomeric ratio in **9a** and **11a**, respectively.



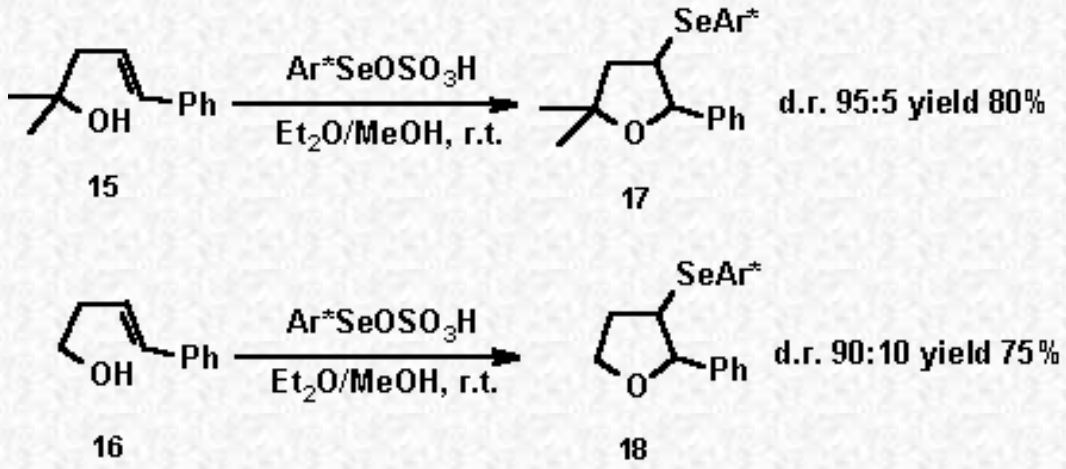
On the basis of the results of the preliminary experiments described above the selenomethoxylation and selenohydroxylation reactions of several alkenes were carried out using the diselenide **7** under the experimental conditions described in Table 1 (entries 1 and 4) .The results obtained from these experiments are collected in Table 2. In a tipical experiment ammonium persulfate and trifluoromethanesulfonic acid were added to a stirred solution of the diselenide **7** in diethyl ether. The mixture was stirred at room temperature for 15 minutes and then a solution of the alkene in methanol (entries 1,3,4,5) or in a 1:1 mixture of acetonitrile and water(entry 2) was added. Stirring was continued for 60 h. The results reported in Table 2 indicate that satisfactory to good chemical yields were obtained in every case. Good facial selectivities were observed in the case of the methoxyselenenylation reactions with the exception of the reaction carried out with cyclohexene. As observed in previous cases [12] the hydroxyselenenylation reactions gave poorer results.

Table 2: Selenoaddition Reactions Using the Diselenide **7**

Entry	Substrate	ROH	X	T°C	Products	Yield %	d.r.
1	b-Methyl-styrene	CH_3OH	OSO_3H	25	**9b**	80	95:5
2	b-Methyl-styrene	H_2O	OSO_3H	25	**10b**	80	81:19
3	2',4',6'-Trimethyl-styrene	CH_3OH	OSO_3H	25	**9c**	60	95:5
4	E-5-Decene	CH_3OH	OSO_3H	25	**9d**	79	92:8
5	Cyclohexene	CH_3OH	OSO_3H	25	**9e**	55	75:25

The efficiency of diselenide **7** was also tested in the case of ciclofunctionalization processes, For this purpose the *E*-3-alkenols **15** and **16** were treated with a stoichiometric amount of selenenylating agent prepared from **7** as described above in a 3:1 mixture of diethyl ether and methanol. The nucleophilic solvent did not compete with the

intramolecular process and only the tetrahydrofurans **17** and **18** were isolated as the reaction products. In both cases good chemical yields and facial selectivities were observed.



Finally the following scheme illustrates a further use of the diselenide **7**. Ammonium persulfate and the diselenide **7** were employed to effect the catalytic one-pot conversion of the b,g-unsatured ester **19** into the allylic ether **20** according to our recently described selenenylation-elimination procedure.[13] The results of these experiments are reported in Table 3. The reaction was first carried out in diethyl ether and methanol (2:1) in the presence of trifluoromethanesulfonic acid using stoichiometric (entry 1) and catalytic (entry 2) amounts of **7** and an excess of ammonium persulfate. Under these conditions conversion rates were very low. However, in both cases excellent facial selectivities were observed (94% ee). The reaction was repeated using a stoichiometric amount of nickel(II) nitrate as additive (entry 3). In this case the conversion rate was considerably increased but the enantioselectivity was very poor (45% ee). Further investigations are presently under way to improve the results of this one-pot selenenylation-elimination sequence.

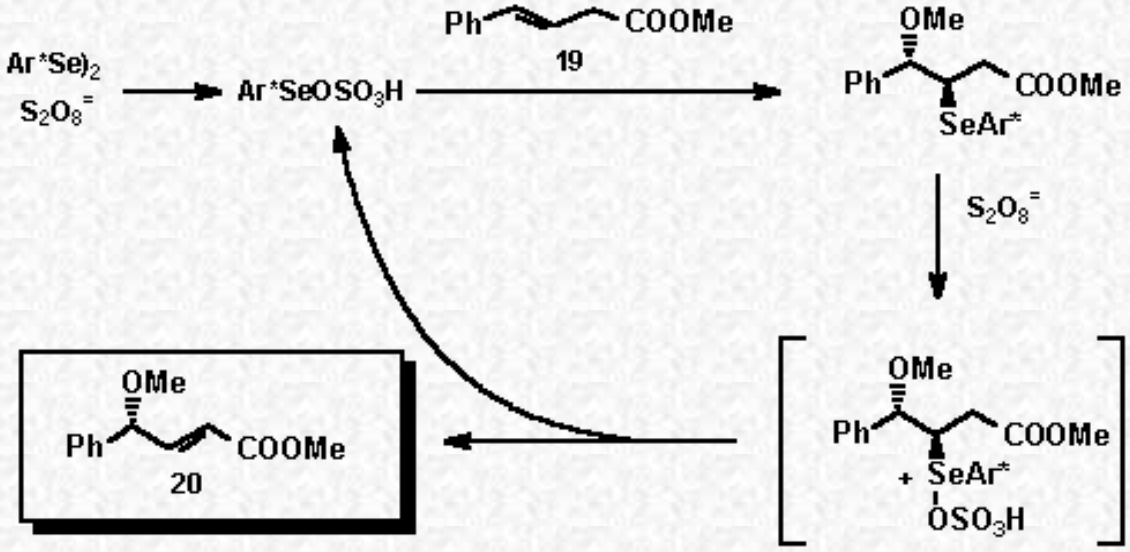


Table 3: One pot Conversion of the b,g-Unsatured Ester **19** into the Allylic Ether **20**.

Entry	% of 7	Additive	T°C	Reaction Time	Yield %	e.e. %

1	100	None	25	26 days	50	94
2	10	None	25	42 days	12	94
				110 days	50	94
3	10	$Ni(NO_3)_2$	25	4 days	50	45

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