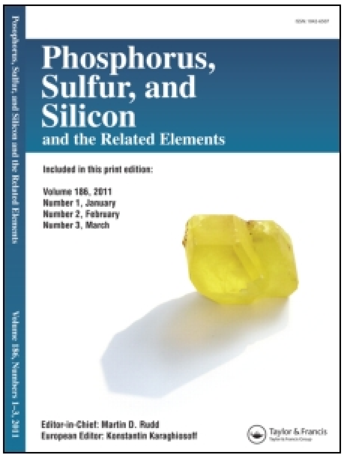

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PREVENTION OF RACEMIZATION OF THE CHIRAL CARBON IN THE EPISELENONIUM ION INTERMEDIATE: STERIC PROTECTION AND ELECTRON-WITHDRAWING EFFECT

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To prevent the racemization of the chiral carbon in the episelenonium ion intermediate bearing an aryl group on the selenium atom, both the bulky substituent(s) on the ortho position(s) of the aryl group and electron-withdrawing substituent(s) in the aryl group are found to play an important role.

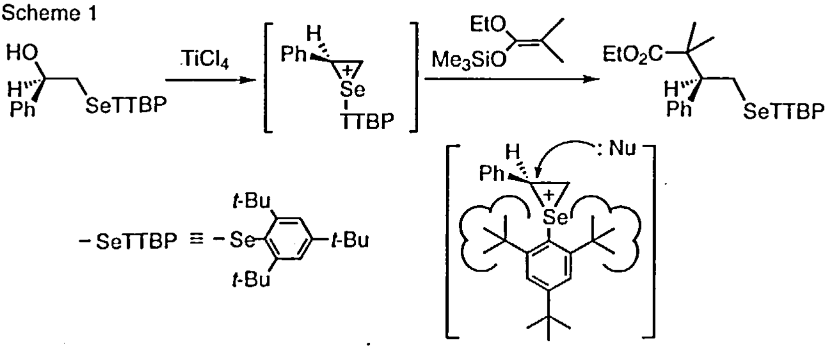
KEY WORDS: chiral episelenonium ion; steric protection; selenurane; 2,4,6-tri-*tert*-butylphenylseleno group; 2,6-bis(trifluoromethyl)phenylseleno group

We have already reported that steric protection of the selenium atom in the episelenonium ion intermediate by the bulky 2,4,6-tri-*tert*-butylphenyl (TTBP) group prevents both racemization of the chiral carbon in the three-membered ring and the attack by carbon nucleophiles on the selenium atom; the latter would afford carbon-selenium bond formation products.[1] Thus, the reaction of chiral alcohols bearing TTBPSe group on the adjacent carbon atom with carbon nucleophiles in the presence of a Lewis acid proceeds through the episelenonium ion intermediate to selectively afford carbon-carbon bond formation products without the loss of any optical purities (Scheme 1).

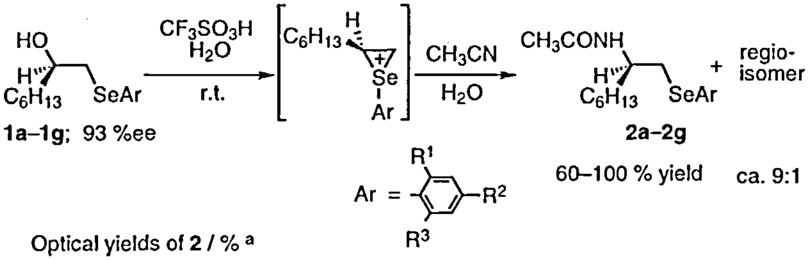
We report herein that an electron-withdrawing group on the arylseleno group also contributes to prevent racemization of the chiral carbon in the episelenonium ion intermediate. Aryl groups in **1a** and **1e**

(Scheme 2) would show a similar effect concerning steric protection, since there are no substituents at the ortho positions. However, in Ritter-type reactions, the optical yield of the amide **2e** bearing the electron-withdrawing trifluoromethyl group at the para position of the arylseleno group was found to be much better than that of **2a** bearing no substitutent (Scheme 2).

Scheme 1



Scheme 2



1a–1g; 93 %ee

2a–2g

60–100 % yield ca. 9:1

Optical yields of **2** / % [a]

	R^1	R^2	R^3			R^1	R^2	R^3	
a	H	H	H	13	**e**	H	CF_3	H	70
b	Me	H	Me	30	**f**	CF_3	H	H	98
c	*i*-Pr	*i*-Pr	*i*-Pr	35	**g**	CF_3	H	CF_3	99[c]
d	*t*-Bu	*t*-Bu	*t*-Bu	100[b]					

[a] Carried out using the alcohol (0.1 mmol) and a mixture of CF_3SO_3H and H_2O (1 mmol; 1:1 by molar ratio) in CH_3CN (100 mL). A solution of the alcohol was added to a solution of the acid.

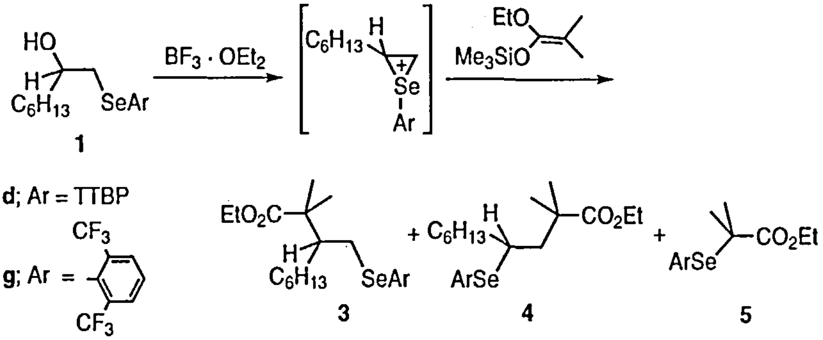
[b] CH_3CN (1 mL) was used.

[c] Carried out using CF_3SO_3H and H_2O (0.1 mmol) in CH_3CN (1 mL). A solution of the acid was added to a solution of the alcohol.

Steric and electron-withdrawing effects seem to work additively, since the optical yield of the amide **2f** bearing the trifluoromethyl group at the ortho position of the arylseleno group was found to be better than that of the para-substituted **2e**. When two trifluoromethyl groups were introduced at the ortho positions of the arylseleno group, the optical yield of **2g** was almost quantitative even with a higher concentration (0.1 mol/L) of the substrates which is favorable for racemization.[1] This result is very similar to the result of TTBP substituted **2d** (Scheme 2).

It is interesting to compare the trifluoromethyl and *tert*-butyl groups in terms of steric protection of the selenium atom in the episelenonium ion intermediate. Thus, we carried out the reaction of (racemic) **1d** and **1g** with a carbon nucleophile (Scheme 3). During the reaction of **1d** with ketene silyl acetal in the presence of boron trifluoride, carbon–carbon bond formation products **3d** and **4d** were selectively produced (87% total yield, 86:14), indicating that steric protection by the TTBP group is the same as we previously reported. In a similar reaction using **1g**, on the other hand, carbon–carbon bond formation products **3g** and **4g** were obtained in 27% total yield accompanied by the carbon–selenium bond formation product **5** (20% yield), clearly indicating that the selenium atom of the episelenonium ion intermediate is not sufficiently protected by the 2,6-bis(trifluoromethyl)phenyl group.

Scheme 3

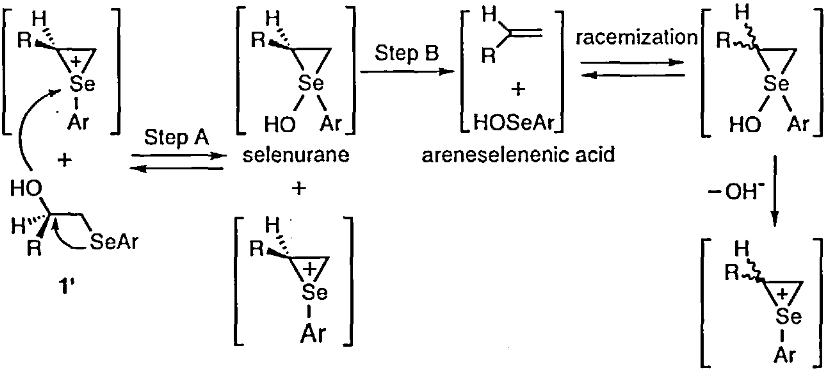


The almost quantitative optical yield of **2g** (Scheme 2) under a limited steric protection clearly showed again that the electron-withdrawing effect contributes, in addition to the steric effect, to preventing the racemization of the chiral carbon in the episelenonium ion intermediate.

The mechanism of the racemization of the chiral carbon atom in the episelenonium ion intermediate should include two steps; one is inhibited by steric protection of the selenium atom and the other is inhibited by electron-withdrawing group(s) in the arylseleno group. The most probable mechanism is visualized in Scheme 4. Based on the fact that the rate of the racemization is dependent on the concentration of the substrate and the fact that the addition of an acid solution to a solution of the substrate is favorable for racemization,[1] the first step seems to be the attack of the hydroxy group of the substrate on the selenium atom of the episelenonium ion intermediate to afford another episelenonium ion and the selenurane intermediates. The fission of the selenurane to an olefin and areneselenenic acid followed by recombination would produce the racemized selenurane intermediate which can produce the racemized episelenonium ion intermediate.

It should be noted here that the selenium atom in the areneselenenic acid is positively charged and works like an electrophile. It is reasonable that the first step (Step A in Scheme 4) is inhibited by steric protection of the selenium atom and Step B is inhibited by the electron-withdrawing group on the arylseleno group. As one of the proofs that Step B is responsible for the racemization of the chiral carbon, we succeeded in the detection of the olefin (dodecene) in the Ritter-type reaction using **1'a** (R = $C_{10}H_{21}$) to afford a completely racemized amide.

Scheme 4



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