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Synthesis of Enantiomerically Pure *anti*-1,2-Diaryl and *syn*-1,2-Alkylaryl *vic*-Selenoamines

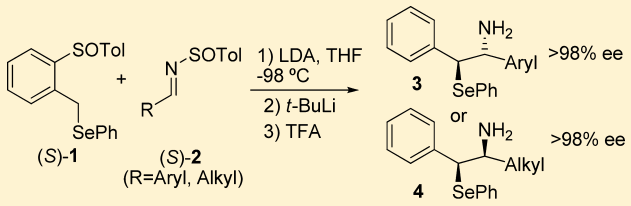
José L. García Ruano,*[,†] Esther Torrente,[†] Inés Alonso,[†] Mercedes Rodriguez,[†] Ana M. Martín-Castro,[†] Alessandro Degl'Innocenti,*[,‡] Lucrezia Frateschi,[‡] and Antonella Capperucci[‡]

[†]Departamento de Química Orgánica, Universidad Autónoma de Madrid, Cantoblanco, 28049-Madrid, Spain

[‡]Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, 50019-Sesto Fiorentino, Italy

Supporting Information

ABSTRACT: Phenylselenyl benzylcarbanion stabilized by an (*S*)-2-*p*-tolylsulfinyl group evolves in a highly stereoselective way in the reactions with (*S*)-*N*-(*p*-tolylsulfinyl)imines at −98 °C affording diastereomerically pure 1,2-selenoamino derivatives in good yields. The *syn* or *anti* relationship of the obtained compounds depends on the alkyl or aryl character of the imine. They are easily transformed into enantiomerically pure (1*R*,2*S*)-1-aryl[or (1*S*,2*S*)-1-alkyl]-2-(phenylseleno)-2-phenylethylamines by reaction with *t*-BuLi and subsequent methanolysis of the generated sulfinamide derivatives with TFA.

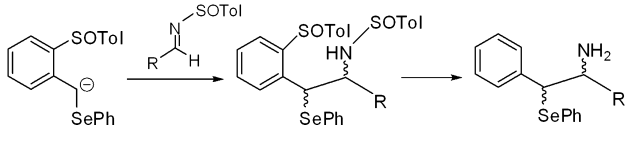


INTRODUCTION

The biological and medical properties of organoselenium compounds are increasingly appreciated mainly due to their antioxidant, antitumoral, and antimicrobial activities and their behavior as competitive inhibitors for target proteins.[1] Among these compounds, 1,2-selenoamines (or *β*-aminoselenides) are worth mentioning, although the number of synthetic methods reported for them are limited. Their syntheses have been described either by nucleophilic (hydride or organometallic) additions to *α*-phenylselenyl imines[2] or via ring-opening reactions of both *N*-acyloxazolidinones[3] and -aziridines[4] with a variety of selenium nucleophiles. Additionally, enantiomerically pure 1,2-selenoamines are interesting structural subunits that have been used as ligands in enantioselective reactions.[3,5] However, despite their interest, very few methods have been reported for synthesizing them in their enantiomerically pure form,[6,7] and they usually provide 1,2-selenoamines containing only one stereocenter bonded to the nitrogen function. Closely related optically active *β*-seleno-*α*-amino acids were obtained by selenide opening of the serine *β*-lactone[8] and *α*-seleno-*β*-amino acids by amino-phenylselenenylation of *α*,*β*-unsaturated esters, in the context of the synthesis of substituted uracils.[9] Recently, asymmetric organocatalysis has also proved effective as a method of preparing enantiomerically enriched 1,2-selenoamines via desymmetrization of *meso*-aziridines with selenium nucleophiles.[7e] Nevertheless, the synthesis of enantiomerically pure selenoamines containing two stereocenters, one of them connected to the selenium atom,[10] is still a challenging problem, and we decided to investigate it, taking advantage of our experience in the field of the organoselenium compounds.[11]

Since the first report concerning the use of an *o*-sulfinyl group for conferring chemical and configurational stability to the benzylcarbanion derived from ethylbenzene,[12] many papers describing the highly stereoselective behavior of *o*-sulfinyl benzylcarbanions joined to different functions have been published.[13] These results would suggest that selenobenzylcarbanions could be analogously stabilized by an *o*-sulfinyl group, making possible their highly stereoselective reactions with different electrophiles, thus providing a new entry for the synthesis of a variety of enantiomerically enriched compounds bearing a selenium atom bonded to a chiral carbon atom. On the other hand, *N*-sulfinylimines, acting as electrophiles, have demonstrated a high efficiency in controlling the approach of different nucleophiles.[14] The potential interest of the enantiomerically pure substituted 2-seleno-2-phenylethylamines prompted us to investigate their preparation by reaction of phenylseleno *o*-sulfinylbenzylcarbanions with *N*-sulfinylimines, in the hope that this double asymmetric induction process would simultaneously control the configuration of the two newly formed stereogenic centers. Removal of both sulfinyl groups would provide enantiomerically pure 1,2-selenoamines (Scheme 1).

Scheme 1. Strategy for Asymmetric Synthesis of 1,2-Selenoamines



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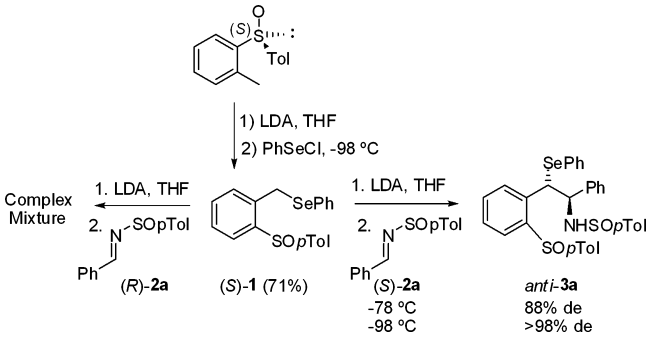
RESULTS

In order to prepare the so far unknown selenium-derived carbanion depicted in Scheme 1, the synthesis of the precursor selenide **1** was performed in high yield by reaction of (*S*)-2-*p*-tolylsulfinyltoluene[15] with LDA and further addition of PhSeCl at −98 °C (Scheme 2).

Scheme 2. Synthesis of Selenide 1 and Further Reaction with (*R*)- and (*S*)-*N*-*p*-Tolylsulfinylbenzaldimines (*R*)- and (*S*)-2a



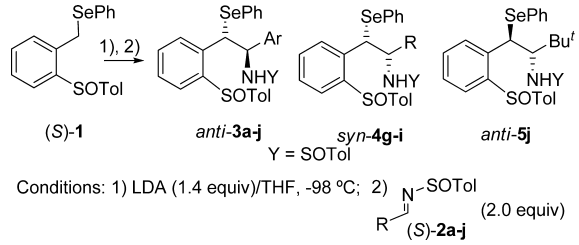
We studied the reactions of (*S*)-**1** with both enantiomers of *N*-(*p*-tolylsulfinyl)benzaldimine, (*S*)-**2a** and (*R*)-**2a** (Scheme 2). The addition of LDA to a THF solution of **1** at −78 °C produced immediately a deep red mixture, which suggested the formation of a delocalized benzylcarbanion. The addition of (*S*)-**2a** to this solution caused the immediate disappearance of the color and afforded diastereomerically enriched *anti*-**3a** (88% de). The stereoselectivity increased when the temperature lowered and only one diastereoisomer was detected at −98 °C (Scheme 2). By contrast, the reaction of (*S*)-**1** with (*R*)-**2a** was sluggish (the conversion was incomplete after long reaction times) and yielded a complex mixture at −98 °C. These results indicate that the matched pair is formed by the reactants exhibiting the same configuration at their respective sulfinyl sulfur atoms.

Then we studied the behavior of (*S*)-**1** with different *N*-sulfinylarylimines, **2b**−**f**, with the *S* configuration at the sulfur atom (matched pairs), in order to evaluate the scope of the reaction. The results are collected in Table 1. All the studied reactions are completely stereoselective, only yielding one diastereoisomerically pure selenoamine (*anti*-**3b**−**f**) regardless of the electronic character of the substituent. The yields are good in all the cases especially when an EWG is present at the iminic aromatic ring (compare entries 1−3 and 4−6, Table 1).

The behavior of the aliphatic *N*-sulfinylimines (*S*)-**2g**−**j** was studied next. In these reactions the stereoselectivity was also high. Although traces of a nonidentified minor compound were detected in the NMR spectra of the crude reactions,[16] the major components of these mixtures (**4g**−**i** and **5j**) were isolated in their diastereomerically pure form in good yields after chromatographic purification (Table 1, entries 7−10).

The synthesis of enantiomerically pure 1,2-selenoamines requires the desulfinylation of compounds **3** and **4** to proceed without affecting neither the C−Se bond nor their configurational integrity. This synthetical transformation was performed in two cases, with **3d** and **4i**, derived from aryl- and alkylimines, respectively, by a two-step sequence consisting in initial *C*-desulfinylation with *t*-BuLi, and subsequent *N*-desulfinylation with TFA[17] (Scheme 3). Under these conditions, selenoamines

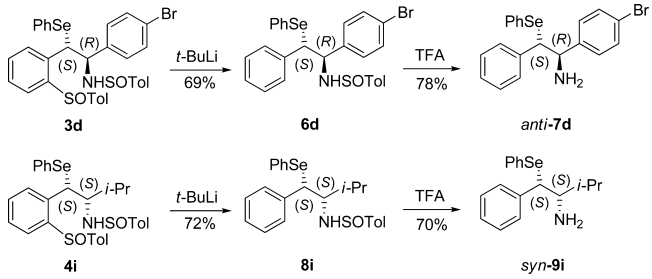
Table 1. Reactions of (*S*)-1 with Imines (*S*)-2a−j



entry	imine (R)	product (yield, %)	dr
1	**2a** (Ph)	**3a** (69)	>98:2
2	**2b** (*p*-MeC_6H_4)	**3b** (65)	>98:2
3	**2c** (*p*-$MeOC_6H_4$)	**3c** (66)	>98:2
4	**2d** (*p*-BrC_6H_4)	**3d** (70)	>98:2
5	**2e** (*p*-CNC_6H_4)	**3e** (75)	>98:2
6	**2f** (*p*-$CF_3C_6H_4$)	**3f** (73)	>98:2
7	**2g** (*n*-Pr)	**4g** (60[a])	>98:2[a]
8	**2h** (*i*-Bu)	**4h** (80[a])	>98:2[a]
9	**2i** (*i*-Pr)	**4i** (65[a])	>98:2[a]
10	**2j** (*t*-Bu)	**5j** (51[a])	>98:2[a]

[a]After chromatographic purification.

Scheme 3. *C*- and *N*-Desulfinylation: Synthesis of Enantiomerically Pure 1,2-Selenoamines



anti-**7d** and *syn*-**9i**, respectively, were obtained in >98% ee, as determined by chiral HPLC.

The impossibility of obtaining good crystals from compounds **3a**−**f**, **4g**−**i**, and **5j** prevented us from unequivocal assignment of their absolute configuration by X-ray analysis.[18] Consequently, their configurational assignment was performed by chemical correlation and NMR techniques.

Those NMR parameters of selenoamines **3a**−**f**, **4g**−**i**, and **5j** which are significant for their configurational assignment are collected in Table 2. Compounds **3a**−**f**, derived from aromatic aldimines, exhibit almost identical values for $\delta_{H(1)}$, $\delta_{H(2)}$, and $J_{1,2}$, which suggests that all of them have the same configuration. Additionally, the observed high value of $J_{1,2}$ (10.5−10.8 Hz) is indicative of the antiperiplanar arrangement of both hydrogen atoms in the preferred conformation. These compounds show a characteristic pattern of abnormally shielded aromatic signals that can only be explained by assuming an efficient π,π-stacking interaction. Detailed NOESY experiments revealed contact interactions between the *ortho* protons of the three aromatic rings bonded to the Se, C(1), and sulfinamide S atoms, respectively (see the Supporting Information for a more detailed description). Taking into account that all these compounds have the *S* configuration at their sulfinamide sulfur atoms [the reactions were performed with (*S*)-sulfinylimines], the only spatial arrangement capable of explaining the NMR parameters is that indicated in Figure 1, which is the most stable

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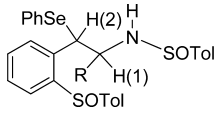
Table 2. Significant Chemical Shifts and Vicinal Coupling Constants for Compounds 3a–f, 4g–i, and 5j



compd (R)	δ H(1) (ppm)	δ H(2) (ppm)	$J_{1,2}$ (Hz)	δ NH (ppm)	$J_{1,NH}$ (Hz)
3a (Ph)	4.77	4.77	10.8	4.28	8.1
3b (*p*-Tol)	4.77	4.77	10.6	3.98	8.0
3c (*p*-CN-C_6H_4)	4.74	4.74	10.5	5.99	7.2
3d (*p*-MeO-C_6H_4)	4.75	4.75	10.5	4.08	8.1
3e (*p*-Br-C_6H_4)	4.75	4.75	10.6	5.03	7.4
3f (*p*-CF_3-C_6H_4)	4.75	4.75	10.8	5.51	6.9
4g (*n*-Pr)	3.85	4.53	9.8	2.66	9.8
4h (*i*-Bu)	3.86	4.55	9.0	2.58	9.8
4i (*i*-Pr)	3.86	4.56	11.4	2.74	9.8
5j (*t*-Bu)	3.66	4.17	11.0	5.24	1.8

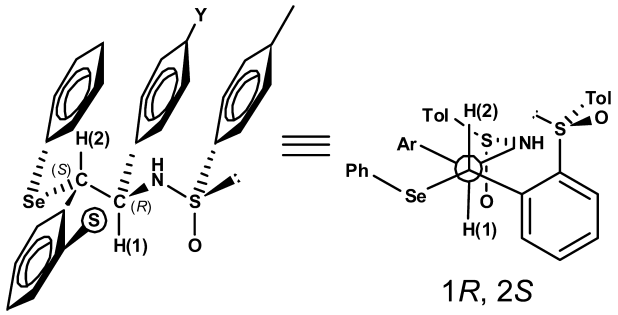
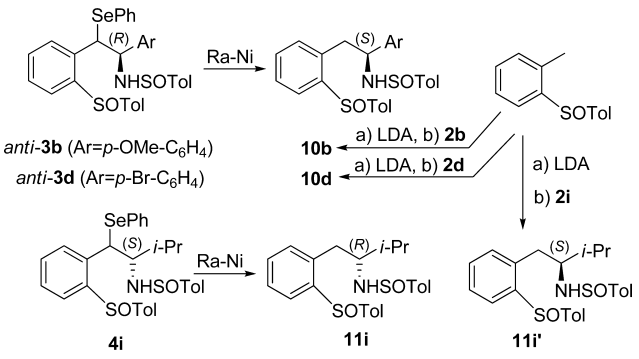


Figure 1. Spatial arrangement accounting for the NMR data of compounds **3a–3f**.

conformation of the diastereoisomer 1*R*,2*S*, since it avoids the strong stereoelectronic repulsion of the aromatic rings bonded to C(1) and C(2). In this conformation, H(1) and H(2) display an antiperiplanar arrangement.

In order to confirm this assignment, we performed the deselenation reaction of compounds **3b** and **3d** with Ra-Ni in THF at rt, which provided sulfinamides **10b** and **10d**, respectively (Scheme 4). The synthesis of these compounds

Scheme 4. Chemical Correlation for the Assignment of C(1) Configuration for Aromatic and Aliphatic Selenoamines



had been previously reported by reactions of (*S*)-2-(*p*-tolylsulfinyl)toluene with (*S*)-**2b** and (*S*)-**2d**[15] (see the Supporting Information for details). This chemical correlation allowed us to unequivocally assign the *S* configuration to C(1) of **10b** and **10d** and therefore the *R* one for their precursors **3b** and **3d**, thus confirming the assignment based on their NMR parameters (see above).

The NMR parameters for compound **5j** also allowed us its unequivocal configurational assignment from the assumption of the *S* configuration of its two sulfur atoms. The $J_{1,2}$ value (11 Hz, Table 2) indicates that H(1) and H(2) adopt an antiperiplanar arrangement in the clearly favored conformation. Additionally, the NMR parameters associated to the aminic proton (δ 5.24 ppm and $J_{1,NH}$ 1.8 Hz) are clearly indicative of the existence of an intramolecular hydrogen bond fixing its spatial arrangement, which should be *gauche* with respect to H(1). In Figure 2 are depicted the two feasible structures

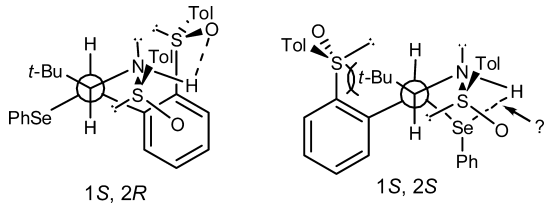


Figure 2. Spatial arrangements compatible with the NMR data observed for **5j**.

compatible with these NMR data. The sulfinyl oxygen is associated to NH in diastereoisomer 1*S*,2*R*, whereas the selenium atom is acting as a hydrogen bond acceptor in the isomer 1*S*,2*S*.[19] However, the conformation depicted in Figure 2 for the isomer 1*S*,2*S* will be strongly destabilized by the steric repulsion (*t*-Bu/Ar) and, therefore, should not be considered as the most stable one. Moreover, the ability of the selenium atom as a hydrogen bond acceptor is rather limited. By contrast, the conformation shown for the 1*S*,2*R* isomer will be clearly predominant by steric reasons. All these considerations strongly support the configuration 1*S*,2*R* for compound **5j**.

Finally, compounds **4g–i** exhibit almost identical chemical shifts for H(1), H(2), and NH, respectively (Table 2), which suggests the same configuration for all of them. Deselenation of **4i** with Ra-Ni (Scheme 4) yielded **11i**, which is diastereoisomer of the compound [2*S*,(*S*)*S*]-**11i**′ obtained by reaction of (*S*)-2-(*p*-methylsulfinyl)toluene with LDA and (*S*)-**2i**[15] (Scheme 4). This proves that both compounds differ in the configuration of the aminic carbon atom. This correlation allowed us to unequivocally assign the *R* configuration to the carbon of **11i** and, therefore, the *S* one to its precursor **4i** (Scheme 4). Taking into account the values of the vicinal coupling constants for

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4g−i ($J_{1,NH}$ 9.8 Hz and $J_{1,2}$ 9−11.4 Hz, Table 2), which evidence the *anti* relationship of the involved protons and the low value of δ NH (ca. 2.5 ppm), which suggests that it is not involved in any hydrogen bond, the spatial arrangements which are compatible with these NMR data for compounds having the *S* configuration at C(1) are depicted in Figure 3.

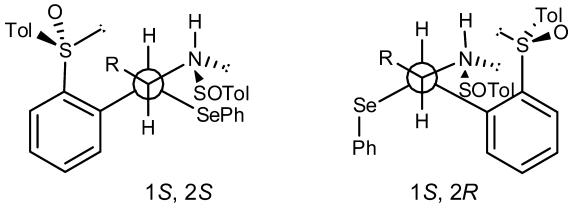

Figure 3. Spatial arrangements with *S* configuration at C(1) compatible with the NMR data observed for **4g−4i**.

The configuration 1*S*,2*R* had been assigned to **5j** (Figure 2), where the NH was associated by a hydrogen bond to the sulfinyl oxygen exhibiting a different orientation to that shown in Figure 3. As the change of the alkyl group cannot alter this situation, we must conclude that **4g−i** have a different configuration to that of **5j**. This conclusion can also be deduced from the significant differences observed in the NMR parameters of these compounds (Table 2). It suggests that 1*S*,2*S* must be the configuration of the asymmetric carbon atoms of compounds **4g−i**.

DISCUSSION

In order to understand the stereochemical results of these reactions, the plausible structures, in the solvent phase, of the species resulting from the reaction of (*S*)-**1** with LDA as well as the stability of different conformers of sulfinylimines were studied theoretically at the DFT (mPW1PW91)[20] level, with the CPCM model,[21] by using the Gaussian09 program.[22,23] The most stable structures found for model carbanion-Li^+ complexes and free carbanion are shown in Figure 4. Dimethyl ether and dimethylamine were used as simplified models for solvent and base, respectively, and have been included as ligands for the lithium atom. The tolyl group has also been simplified as a phenyl one. The most stable is carbanion-Li^+ complex **I**, stabilized by a hydrogen bond with the dimethylamine ligand, that would be probably the first to be formed after the deprotonation step. Conformation **II**, somehow higher in energy, would allow the approach of the imine to the almost completely unhindered lower *re*-face affording products with 2*S* configuration, such as *anti*-**3** and *syn*-**4**. Participation of the free carbanion **III**, much more unstable, can be considered negligible. On the other hand, with respect to the favored conformation of the imine partner, that one displaying the sulfinyl oxygen in the *s-cis* arrangement with respect to the C═N (Figure 4) resulted to be more stable regardless of the alkyl or aryl character of R, the hydrogen bond O---HC being one of the most important factors in its stabilization.

According to these calculations, the approach of the unhindered face of the carbanion **II** to the less hindered *si*-face of aromatic imines in their more stable conformation (**A** approach, Scheme 5) could easily account for the 1*R*,2*S* configuration assigned for *anti*-**3** compounds. This is the stereochemistry of the major isomers obtained in the reactions of 2-(*p*-tolylsulfinyl)ethylbenzene with *N*-sulfinylimines.[12] The fact that the opposite configuration at both asymmetric carbon atoms (1*S*,2*R*) has been assigned to *anti*-**5j** indicates that the approach **B** (Scheme 5) involving the most hindered face of the carbanion and the *re*-face of the imine must be now the favored one. In order to explain this proposal, we assume a strong destabilization of the approach **A** due to the steric interactions of the bulky *t*-Bu group. The association of the sulfinyl oxygen to the NH of the lithium-associated amine (breaking the hydrogen bond with the benzylic carbanion) locates the electrophile on the upper face of the carbanion (this situation has also been observed in reactions of iodobenzylcarbanions[13a]). The favored approach takes place minimizing the steric interactions of the *t*-Bu group, as well as the electronic repulsion of the lone electron pair at iminic nitrogen with the selenium atom and the benzylic ring. Consequently, the *s-trans* conformation (Figure 4) of the *N*-sulfinylimine is the reactive one in this case.

However, we have not any precedent able to explain the formation of the *syn*-**4** products obtained in the reaction with alkylimines. In this case, the approach **A** at Scheme 5 seems to be unfavored. Therefore, another approach involving that the less hindered *re*-face of the carbanion attacks the less stable *s-trans* conformation of the imine (Figure 4) should be assumed. To shed some light about this question, the possible transition states for the reaction of the simplest alkylimine (R = Me) with

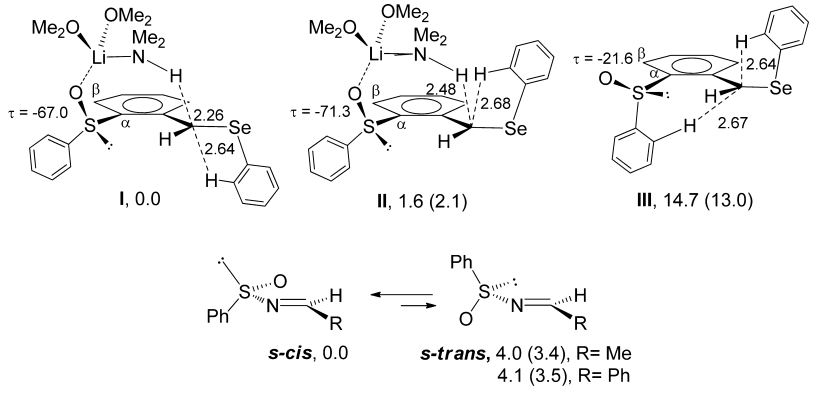

Figure 4. Molecular structures, representative distances (Å), torsion angles (τ in deg), and energies ($CPCM_{(THF)}$/mPW1PW91/6-311G(d,p) and SDB-cc-pVTZ //6-31G(d) and LANL2DZ*; kcal·mol^{-1}) of possible carbanionic species and conformations of sulfinylimines. The first value indicates the relative energy with ZPE correction included, of **II** and **III** (+Li($NHMe_2$)(OMe_2)$_3$-OMe_2) with respect to **I**, considered as the most stable one. Free energy correction is indicated in parentheses.

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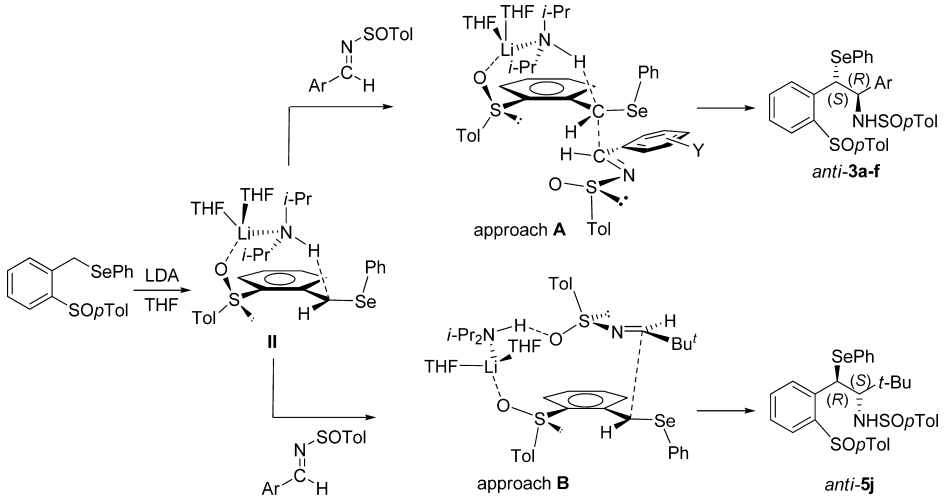
Scheme 5. Stereochemical Pathway Accounting for the Selectivity of the Synthesis of 1,2-Selenoamines 3a−f and 5j



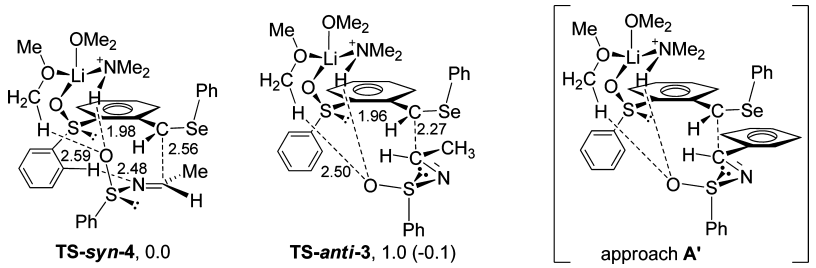


Figure 5. Molecular structures, representative distances (Å), and energies ($CPCM_{(THF)}$/mPW1PW91/6-311G(d,p) and SDB-cc-pVTZ //6-31G(d) and LANL2DZ*; kcal·mol^{-1}) of the possible transition states involved the reaction with alkyl imines. The first value indicates the relative energy with ZPE correction included and free energy correction is indicated in parentheses.

the carbanion **II** (Scheme 4) derived from (*S*)-**1** were theoretically studied (Figure 5).

We have found two TS's, **TS**-*syn*-**4** and **TS**-*anti*-**3**, yielding compounds *syn*-**4** and *anti*-**3**, respectively. Both structures are stabilized by a hydrogen bond between the sulfinyl oxygen of the sulfinylimine and the N−H of the amine acting as a ligand of the lithium. It suggests that the reaction starts by the initial formation of this bond and the consequent cleavage of the N−H---C present in **II**. As the upper face of this structure is densely hindered, the approach of the electrophile will take place from the lower face. The two obtained TS's differ in the face of the *N*-sulfinylimine (*si* or *re*) approaching the carbanion. To reach **TS**-*syn*-**4** the imine partner adopts the less stable *s-trans* conformation (Figure 4), but this relative destabilization must be compensated by the additional hydrogen bond between the iminic nitrogen and the *ortho* hydrogen of the sulfinyl group in the carbanion moiety (it does not exist in **TS**-*anti*-**3**). As a consequence, **TS**-*syn*-**4** is slightly more stable than **TS**-*anti*-**3**. On the other hand, **TS**-*syn*-**4** must be earlier than **TS**-*anti*-**3** because the forming bond is clearly longer in the first one (2.56 instead of 2.27 Å, see Figure 5). When the size of R^1 increases, both TS's will be sterically destabilized, but this effect will be much more important in **TS**-*anti*-**3** because of the smaller distance of the forming bond. It means that the small energetic differences observed in the calculation must be larger when other alkyl groups different to methyl are present, which would explain the preferred formation of the diastereoisomers *syn*-**4** observed in Table 1. In the case of aromatic imines, a transition state similar to **TS**-*anti*-**3** (approach **A**′ in Figure 5, only differing from the approach **A** at Scheme 5 in the position of the hydrogen bonds) could be postulated as the most stable one by assuming stabilizing π,π-stacking interactions between the electron-poor aromatic ring joined to C═N and the electron-rich ring joined to the carbanion.

In summary, we have demonstrated that the synthesis of enantiomerically pure 1,2-selenoamines containing two stereocenters, one of them bonded to the selenium atom, can be performed by reaction of (*S*)-α-(phenylselenyl)-2-(*p*-tolylsulfinyl) toluene, with *N*-(*p*-tolylsulfinyl)imines and LDA and further desulfinylation with *t*-BuLi and TFA. The *syn* or *anti* stereochemistry of the resulting compounds is closely dependent on the aliphatic or aromatic character of the starting imines.

■ EXPERIMENTAL SECTION

General Procedures. NMR spectra were registered (200 or 300, 50, and 38 MHz for ^{1}H, ^{13}C, and ^{77}Se NMR, respectively) in $CDCl_3$ and CD_3OD solutions. Mass spectra (MS) were determined by ESI. All reactions were carried out in anhydrous solvents under argon atmosphere. Commercially available anhydrous tetrahydrofuran (THF) was dried over 4 Å molecular sieves. Flash column chromatography was performed using silica gel (230−400 mesh).

2-[(S)-2-(p-Tolylsulfinyl)benzyl]phenylselenide (1). To a solution of *i*-Pr_2NH (3.92 mmol, 395.9 mg, 1.8 equiv) in anhydrous THF (8 mL) at 0 °C under argon atmosphere was added a solution of *n*-BuLi (2.3 M in hexane, 3.05 mmol, 1.4 equiv). After 10 min of stirring, the mixture was cooled at −98 °C, and then a solution of (2.18 mmol, 500 mg, 1.0 equiv) in anhydrous THF (8 mL) was added. After 10 min of stirring at −98 °C, a solution of phenylselenyl chloride (6.54 mmol, 1.25 g, 3.0 equiv) in anhydrous THF (4 mL) was added quickly. The reaction was monitored by TLC. Upon transformation of the starting material (10 min), the reaction was hydrolyzed with saturated aqueous NH_4Cl (5 mL). The mixture was extracted with CH_2Cl_2 (3 × 40 mL)

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and dried (Na_2SO_4), and the solvent was evaporated. The residue was purified by flash column chromatography (toluene/acetone, 6:1) to afford the pure compound: yield 71% (596.5 mg); yellow oil; $[\alpha]^{20}_D$ −139.3 (*c* 2.0, $CHCl_3$); IR ($CHCl_3$ solution) 3018, 2977, 1522, 1476, 1438, 1424, 1213 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.81 (d, 1H, *J* = 7.6 Hz), 7.55−6.95 (m, 12H), 4.25 (AB system, 2H, *J* = 12.6 Hz), 2.37 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 141.5, 134.1, 131,0 130.5, 129.9, 129.1, 128.4, 127.8, 129.1, 125.9, 125.8, 28.1, 21.3; ^{77}Se (38 MHz, $CDCl_3$) δ 383.28 ppm, MS (TOF+) *m*/*z* 387(100) [M + H^+], 231 (26), 229 (44), 149 (60); HRMS (TOF+) calcd for $C_{20}H_{19}OSeS$ 387.0317, found 387.0305.

General Procedure for the Synthesis of ***3a−f, 4g−i, and 5j.*** To a solution of *i*-Pr_2NH (0.74 mmol, 74.7 mg, 1.8 equiv) in anhydrous THF (2 mL) at 0 °C under argon atmosphere was added a solution of *n*-BuLi (2.3 M in hexane, 0.54 mmol, 1.4 equiv). After of 10 min stirring, the mixture was cooled at −98 °C, and then a solution of 2-[(*S*)-2-(*p*-tolylsulfinyl)benzyl]phenylselenide (**1**) (0.38 mmol, 146.4 mg, 1.0 equiv) in anhydrous THF (2 mL) was added. The mixture was stirred at rt for 10 min, and then 0.76 mmol (1.4 equiv) of the corresponding (*S*)-*N*-sulfinylimine was added quickly. When the reaction was complete (5−10 min), the mixture was hydrolyzed with saturated aqueous NH_4Cl (3 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography employed as solvent the indicated in each case.

*[1R,2S,(S)S]-N-[1-Phenyl-2-(phenylselanyl)-2-[2(S)-(p-tolylsulfinyl)phenyl]ethyl]-p-toluenesulfinamide (**3a**).* (*S*)-*N*-Benzylidene-4-methylbenzenesulfinamide **2a** (0.14 mmol, 35.4 mg, 1.4 equiv) was used as the electrophile, and the reaction was stirred at −98 °C for 10 min to give a diastereoisomeric >98:2 mixture of **3a**, which was purified by flash column chromatography (eluent hexane/EtOAc, 1:1): yield 69% (39.2 mg); white solid; mp 95−96 °C; $[\alpha]^{20}_D$ −8.5 (*c* 0.4, $CHCl_3$); IR (KBr) 3600−3000 (broad band), 1650, 1080, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, 1H, *J* = 8.4 Hz), 7.59−6.80 (m, 21H), 4.96 (d, 1H, *J* = 10.8 Hz), 4.77 (dd, 1H, *J* = 10.8 and 8.1 Hz), 4.28 (d, 1H, *J* = 8.1 Hz) 2.31 (s, 3H), 2.24 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 142.1, 141.4, 141.3, 140.9, 140.7, 140.5, 139.5, 135.8, 131.7, 130.2, 130.1, 128.8, 128.4, 128.2, 128.1, 127.8, 127.4, 126.4, 126.0, 125.4, 66.1, 47.2, 21.4, 21.2; MS (ESI+) *m*/*z* 629 (9) [M^+], 473 (98), 334 (23), 227 (77), 197 (10); HRMS (ESI+) calcd for $C_{34}H_{32}NO_2S_2Se$ 629.0958, found 629.0746.

*[1R,2S,(S)S]-N-[1-(4-Methylphenyl)-2-(phenylselanyl)-2-[2(S)-(p-tolylsulfinyl)phenyl]ethyl]-p-toluenesulfinamide (**3b**).* (*S*)-*N*-4-Methylbenzylidene-4-methylbenzenesulfinamide **2b** (0.14 mmol, 37.5 mg, 1.4 equiv) was used as the electrophile, and the reaction was stirred at −98 °C for 10 min to give a diastereoisomeric >98:2 mixture of **3b**, which was purified by flash column chromatography (eluent hexane/EtOAc, 1:1): yield 65% (43.4 mg); yellow oil; $[\alpha]^{20}_D$ +8.5 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$ solution) 3018, 2924, 1518, 1438, 1219, 1124 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.89 (d, 1H, *J* = 8.4 Hz), 7.60−6.87 (m, 18H), 6.78 (d, 2H *J* = 8.2 Hz), 4.95 (d, 1 H, *J* = 10.6 Hz) 4.77 (dd, 1H, *J* = 10.6 and 8.0 Hz), 3.98 (d, 1H, *J* = 8.0), 2.32 (s, 3 H), 2.29 (s, 3 H), 2.21 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 142.0, 140.6, 139.3, 137.4, 136.0, 131.4, 129.9, 129.0, 128.8, 128.3, 128.0, 127.7, 127.2, 126.5, 125.6, 125.3, 63.4, 47.4, 29.8, 21.5, 21.3; MS (EI) *m*/*z* 489 (100), 332 (28), 227 (75), 149 (47); HRMS (ESI+) calcd for $C_{28}H_{25}OSSe$ 489.0787, found 489.0770.

*[1R,2S,(S)S]-N-[1-(4-Methoxyphenyl)-2-(phenylselanyl)-2-[2(S)-(p-tolylsulfinyl)phenyl]ethyl]-p-toluenesulfinamide (**3c**).* (*S*)-*N*-4-Methoxybenzylidene-4-methylbenzenesulfinamide **2c** (0.14 mmol, 39.8 mg, 1.4 equiv) was used as the electrophile, and the reaction was stirred at −98 °C for 10 min to give a diastereoisomeric >98:2 mixture of **3c**, which was purified by flash column chromatography (eluent hexane/EtOAc, 1:1): yield 66% (45.2 mg); colorless oil; $[\alpha]^{20}_D$ −7.0 (*c* 2.2, $CHCl_3$); IR ($CHCl_3$ solution) 3019, 2976, 1514, 1423, 1212 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, 1H, *J* = 7.5 Hz), 7.60−6.78 (m, 18H), 6.67 (d, 2H, *J* = 8.1 Hz), 4.95 (d, 1H, *J* = 10.5 Hz), 4.75 (dd, 1H, *J* = 10.5 and 8.1 Hz), 4.10 (d, 1H, *J* = 8.1 Hz), 3.76 (s, 3H), 2.31 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 158.9, 141.9, 140.5, 139.3, 135.8, 132.5, 131.5, 130.2, 129.9, 128.4, 128.1, 127.9, 127.7, 126.4, 125.9, 125.3, 124.8, 113.6, 62.9, 55.2, 47.6, 21.5, 21.3; MS (ESI+) *m*/*z* 660 (10) [M − H^+], 505 (100), 149 (18); HRMS (ESI+) calcd for $C_{35}H_{34}NO_3S_2Se$ 660.1142, found 660.1161.

*[1R,2S,(S)S]-N-[1-(4-Bromophenyl)-2-(phenylselanyl)-2-[2(S)-(p-tolylsulfinyl)phenyl]ethyl]-p-toluenesulfinamide (**3d**).* (*S*)-*N*-4-Bromobenzylidene-4-methylbenzenesulfinamide **2d** (0.14 mmol, 45.1 mg, 1.4 equiv) was used as the electrophile, and the reaction was stirred at −98 °C for 10 min to give a diastereoisomeric >98:2 mixture of **3d**, which was purified by flash column chromatography (eluent hexane/EtOAc, 1:1): yield 70% (51.5 mg); white solid; mp 75−77 °C; $[\alpha]^{20}_D$ +13.6 (*c* = 1.25, $CHCl_3$); IR ($CHCl_3$ solution) 3500, 3056, 2997, 2920, 1593, 1488, 1437, 1069, 1010 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.87 (d, 1H, *J* = 7.4 Hz), 7.64−6.83 (m, 15H), 6.76 (d, 3H, *J* = 8.6 Hz), 6.57 (d, 2H, *J* = 6.8 Hz), 5.02 (d, 1H, *J* = 7.4 Hz), 4.88 (d, 1H, *J* = 10.6 Hz), 4.71 (dd, 1H, *J* = 10.6 and 7.4 Hz), 2.31 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 141.8, 140.7, 139.8, 135.1, 132.2, 130.8, 130.4, 130.1, 129.3, 128.7, 128.3, 127.8, 127.7, 127.3, 125.9, 125.4, 121.4, 61.8, 47.2, 21.5, 21.3; MS (ESI+) *m*/*z* 708 (21) [M − H^+], 552 (100), 396 (5), 227 (19); HRMS (ESI+) calcd for $C_{34}H_{31}BrNO_2S_2Se$ 708.0139; found 708.0139.

*[1R,2S,(S)S]-N-[1-(4-Cyanophenyl)-2-(phenylselanyl)-2-[2(S)-(p-tolylsulfinyl)phenyl]ethyl]-p-toluenesulfinamide (**3e**).* (*S*)-*N*-4-Cyanobenzylidene-4-methylbenzenesulfinamide **2e** (0.14 mmol, 37.6 mg, 1.4 equiv) was used as the electrophile, and the reaction was stirred at −98 °C for 10 min to give a diastereoisomeric >98:2 mixture of **3e**, which was purified by flash column chromatography (eluent hexane/EtOAc, 1:1): yield 75% (51.0 mg); white solid; $[\alpha]^{20}_D$ −29.5 (*c* 2.0, $CHCl_3$); mp 85−87 °C; IR ($CHCl_3$ solution) 3500, 3056, 2997, 2920, 2219, 1593, 1531, 1437, 1070, 1014 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, 1H, *J* = 7.9 Hz), 7.75−6.65 (m, 18H), 6.24 (d, 2H, *J* = 8.1 Hz), 5.99 (d, 1H, *J* = 7.2 Hz), 4.90 (d, 1H, *J* = 10.5 Hz), 4.74 (dd, 1H, *J* = 10.5 and 7.2 Hz), 2.33 (s, 3H), 2.28 (s, 3H); ^{13}C NMR δ 147.3, 141.9, 140.5, 140.4, 134.3, 133.0, 131.2, 130.3, 128.9, 128.7, 128.5, 128.2, 128.0, 127.5, 125.6, 118.2, 110.3, 61.3, 46.4, 21.4, 21.2; MS (ESI) *m*/*z* 653 (7) [M − H^+], 623 (33), 607 (49), 593 (100), 551(27), 493 (17); MS (ESI+) *m*/*z* 654 (32) [M + H^+], 500 (100), 149 (17); HRMS (ESI+) calcd for $C_{35}H_{31}N_2O_2S_2Se$ 655.0988, found 655.0984.

*[1R,2S,(S)S]-N-1-[4-(Trifluoromethyl)phenyl]-2-(phenylselanyl)-2-[2(S)-(p-tolylsulfinyl)phenyl]ethyl]-p-toluenesulfinamide (**3f**).* (*S*)-*N*-4-(Trifluoromethyl)benzylidene-4-methylbenzenesulfinamide **2f** (0.14 mmol, 43.6 mg, 1.4 equiv) was used as the electrophile, and the reaction was stirred at −98 °C for 10 min to give a diastereoisomeric >98:2 mixture of **3f**, which was purified by flash column chromatography (eluent hexane/EtOAc, 1:1): yield 73% (52.9 mg); white solid; $[\alpha]^{20}_D$ +8.2 (*c* 1.3, $CHCl_3$); IR ($CHCl_3$ solution) 3010, 2950, 1620, 1324, 1217, 1167, 1067 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, 1H, *J* = 9.0 Hz), 7.68−6.77 (m, 18H), 6.38 (d, 2H, *J* = 7.8 Hz), 5.51 (d, 1H, *J* = 6.6 Hz), 4.89 (d, 1H, *J* = 10.8 Hz), 4.80 (dd, 1H, *J* = 10.8 and 6.6 Hz), 2.33 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 144.9, 141.8, 140.6, 140.1, 134.7, 132.7, 130.6, 130.2, 128.6, 128.2, 128.1, 127.9, 127.6, 125.8, 125.5, 124.4, 61.1, 46.8, 21.5, 21.2; MS (ESI) *m*/*z* 698 (30) [M + H^+], 543 (100), 149 (24); HRMS (FAB+) calcd for $C_{35}H_{31}F_3NO_2S_2Se$ 698.0910, found 698.0914.

*[1S,2S,(S)S]-N-[1-(Phenylselanyl)-1-[2-(S)-(p-tolylsulfinyl)phenyl]-pentan-2-yl]-p-toluenesulfinamide (**4g**).* (*S*)-*N*-Butylidene-4-methylbenzenesulfinamide **2g** (0.22 mmol, 45.6 mg, 1.4 equiv) was used as the electrophile, and the reaction was stirred at −98 °C for 10 min to give a diastereoisomeric >98:2 mixture of **4g**, which was purified by flash column chromatography (eluent hexane/EtOAc, 1:1): yield 60% (55.5 mg); $[\alpha]^{20}_D$ +22.5 (*c* 0.6, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.98−7.92 (m, 1H), 7.50−7.16 (m, 10H), 7.01 (d, 2H, *J* = 8.4 Hz), 6.71 (d, 2H, *J* = 8.0 Hz), 6.60 (d, 2H, *J* = 8.4 Hz), 4.53 (d, 1H, *J* = 9.8 Hz), 3.95−3.77 (m, 1H), 2.66 (d, 1H, *J* = 9.8 Hz), 2.34 (s, 3H), 2.14 (s, 3H), 2.05−1.80 (m, 2H), 1.58−1.32 (m, 2H), 0.85 (t, 3H, *J* = 7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 142.4, 142.2, 142.0, 140.9, 140.8, 139.7, 136.3, 130.9, 129.6, 129.3, 128.9, 128.7, 127.5, 126.6, 125.9, 125.0, 61.5, 46.9, 37.4, 21.4, 21.3, 17.9, 14.0; MS (ESI) *m*/*z* 596 (61)

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[M + H$^+$], 458 (15), 300 (14), 162 (100); HRMS (FAB+) calcd for $C_{31}H_{34}NO_2S_2Se$ 596.1192, found 596.1201.

*[1S,2S,(S)S]-N-[4-Methyl-1-(phenylselanyl)-1-[2-(S)-(p-tolylsulfinyl)phenyl]pentan-2-yl]-p-toluenesulfinamide (**4h**).* (*S*)-*N*-3-Methylbutylidene-4-methyl-benzenesulfinamide **2h** (0.22 mmol, 49.1 mg, 1.4 equiv) was used as the electrophile, and the reaction was stirred at −98 °C for 10 min to give a diastereoisomeric >98:2 mixture of **4h**, which was purified by flash column chromatography (eluent hexane/EtOAc, 1:1): yield 80% (73.0 mg); colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.98−7.90 (m, 1H), 7.55−7.12 (m, 10H), 7.03 (d, 2H, J = 8.0 Hz), 6.76 (d, 2H, J = 7.8 Hz), 6.67 (d, 2H, J = 8.2 Hz), 4.55 (d, 1H, J = 9.0 Hz), 3.91−3.76 (m, 1H), 2.58 (d, 1H, J = 9.8 Hz), 2.35 (s, 3H), 2.16 (s, 3H), 2.00−1.84 (m, 1H), 1.79−1.66 (m, 1H), 1.18−1.04 (m, 1H), 0.94 (d, 3H, J = 6.4 Hz), 0.87 (d, 3H, J = 6.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 142.8, 142.3, 142.0, 141.0, 140.8, 139.6, 136.1, 130.8, 129.6, 129.4, 129.0, 128.6, 127.6, 126.6, 125.0, 124.3, 59.9, 48.9, 45.1, 24.0, 23.7, 22.9, 21.4, 21.2; MS (ESI+) m/z 610 (100), 455 (9), 213 (20), 149 (17); HRMS (ESI+) calcd for $C_{32}H_{36}NO_2S_2Se$ 610.1348, found 610.1351.

*[1S,2S,(S)S]-N-[3-Methyl-1-(phenylselanyl)-1-[2-(S)-(p-tolylsulfinyl)phenyl]butan-2-yl]-p-toluenesulfinamide (**4i**).* (*S*)-*N*-2-Methylpropylidene-4-methylbenzenesulfinamide **2i** (0.22 mmol, 45.6 mg, 1.4 equiv) was used as the electrophile and the reaction was stirred at −98 °C for 10 min to give a diastereoisomeric >98:2 mixture of **4i**, which was purified by flash column chromatography (eluent hexane/EtOAc, 1:1); Yield: 65% (58.0 mg); white solid; mp: 99−101 °C; $[\alpha]^{20}_D$ +24.7 (c 2.0, $CHCl_3$); IR (KBr): 3019, 2980, 1730, 1595, 1492, 1475, 1438, 1261 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97−7.91 (m, 1H), 7.55−7.13 (m, 10H), 6.94 (d, 2H, J = 7.2 Hz), 6.66 (d, 2H, J = 8.7 Hz), 6.38 (d, 2H, J = 8.1 Hz), 4.55 (d, 1H, J = 11.1 Hz), 3.84 (ap.td, 1H, J = 10.8 and 1.8 Hz), 2.72 (bd, 1H, J = 10.5 Hz), 2.64−2.52 (m, 1H), 2.32 (s, 3H), 2.13 (s, 3H), 1.16 (d, 3H, J = 6.4 Hz), 0.60 (d, 3H, J = 6.9 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 142.2, 140.1, 136.9, 131.2, 129.7, 129.2, 129.1, 128.9, 127.5, 126.7, 125.0, 124.7, 67.4, 44.7, 29.1, 24.9, 21.2, 14.8; MS (ESI+) m/z 596 (100) [M − H$^+$], 456 (17), 284 (27), 149 (35); HRMS (ESI+) calcd for $C_{31}H_{34}NO_2S_2Se$ 596.1192, found 596.1195.

*[1R,2S,(S)S]-N-[3,3-Dimethyl-1-(phenylselanyl)-1-[2-(S)-(p-tolylsulfinyl)phenyl]butan-2-yl]-p-toluenesulfinamide (**5j**).* (*S*)-*N*-2-Methylpropylidene-4-methylbenzenesulfinamide **2i** (0.22 mmol, 49.1 mg, 1.4 equiv) was used as the electrophile, and the reaction was stirred at −98 °C for 5 min to give a diastereoisomeric >98:2 mixture of **5j**, which was purified by flash column chromatography (eluent hexane/EtOAc, 1:1): yield 51% (46.6 mg); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.25 (bd, 1H, J = 8.4 Hz), 7.83−6.88 (m, 16 H), 5.24 (bd, 1H, J = 1.6 Hz), 4.17 (bd, 1H, J = 10.8 Hz), 3.66 (dd, 1H, J = 10.8 and 1.6 Hz), 2.41 (s, 3H), 2.37 (s, 3H), 0.80 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.5, 143.1, 141.6, 141.3, 137.2, 136.6, 135.9, 132.4, 131.4, 130.1, 129.6, 128.7, 126.1, 125.7, 124.8, 70.7, 44.2, 37.7, 27.7, 21.5, 21.4.

General Procedure of C−S Desulfinylation. To a solution of the corresponding *N*-sulfinylphenylselenylamine (0.08 mmol, 1.0 equiv) in anhydrous THF (2 mL) at −78 °C was added a solution of *t*-BuLi (2.3 M in pentane, 146 μL, 0.34 mmol, 4 equiv). The reaction mixture was stirred at −78 °C until complete transformation of the starting material (20 min). The mixture was hydrolyzed with saturated aqueous NH_4Cl solution (2 mL) and extracted with CH_2Cl_2 (3 × 4 mL). The combined organic layers were dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (eluent hexane/EtOAc, 3:1).

*[1S,2S,(S)S]-N-[3-Methyl-1-phenyl-1-(phenylselanyl)butan-2-yl]-p-toluenesulfinamide (**8i**).* Compound **8i** was obtained from 47.6 mg (0.08 mmol) of [1S,2S,(S)*S*]-*N*-3-methyl-1-(phenylselanyl)-1-[2-(*S*)-(*p*-tolylsulfinyl)phenyl)butan-2-yl]-*p*-toluensulfinamide (**4i**): yield 72% (26.3 mg); $[\alpha]^{20}_D$ +129.9 (c 1.3, $CHCl_3$); IR ($CHCl_3$ solution) 3018, 2976, 1522, 1476, 1423 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (bd, 2H, J = 6.9 Hz), 7.27−7.13 (m, 12H), 4.36 (d, 1H, J = 7.2 Hz), 3.83 (ddd, 1H, J = 3.9, 9.3, and 13.5 Hz), 3.80 (bs, 1H), 2.36 (s, 3H), 2.25−2.13 (m, 1H), 1.08 (d, 3H, J = 6.6 Hz), 0.86 (d, 3H, J = 6.9 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 143.2, 141.0, 140.4, 135.5, 129.2, 129.0, 128.8, 128.3, 128.0, 127.1, 125.4, 66.3, 53.9, 30.4, 21.3, 20.9, 16.9; MS (ESI) m/z 458 (15), 300 (14), 162 (100), 149 (17); HRMS (ESI+) calcd for $C_{24}H_{28}NOSSe$ 458.1052, found 458.1038.

*[1R,2S,(S)S]-N-[1-(4-Bromophenyl)-2-phenyl-2-(phenylselanyl)-ethyl]-p-toluenesulfinamide (**6d**).* Compound **6d** was obtained from 56.6 mg (0.08 mmol) of [1R,2S,(S)*S*]-*N*-[1-(4-bromophenyl)-2-(phenylselanyl)-2-[2-(*S*)-(*p*-tolylsulfinyl)phenyl]ethyl]-*p*-toluenesulfinamide (**3d**): yield 69% (31.4 mg); $[\alpha]^{20}_D$ = +135.1 (c 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.07 (m, 16H), 6.84 (d, 2H, J = 8.4 Hz), 4.91 (dd, 1H, J = 6.3 and 7.8 Hz), 4.67 (d, 1H, J = 6.3 Hz), 4.56 (d, 1H, J = 7.8 Hz), 2.32 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 141.1, 138.7, 138.3, 135.1, 134.9, 130.9, 129.4, 129.0, 128.8, 128.4, 127.8, 127.6, 125.4, 121.5, 60.3, 56.0, 21.4; MS (ESI+) m/z 569 (5) [M + H$^+$], 473 (13), 335 (23), 259 (34), 180 (100); HRMS (ESI+) calcd for $C_{27}H_{25}NOSSeNa$ 514.0715, found 514.0717.

General Procedure of N−S Desulfinylation. To a solution of the corresponding product of C−S desulfinylation (**6d** or **8i**) (45.5 mg or 36.5 mg, respectively, 0.08 mmol, 1.0 equiv) in anhydrous methanol (1 mL) at rt was added TFA (0.24 mmol, 3.0 equiv). The mixture was stirred for 4 h at rt, and then the solvent was removed under reduced pressure. The residue was purified by SCX column chromatography to afford the corresponding amine.

*(1R,2S)-1-(4-Bromophenyl)-2-phenyl-2-(phenylselanyl)-ethanamine (anti-**7d**):* yield 68% (23.5 mg); colorless oil; $[\alpha]^{20}_D$ +80.1 (c 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.03 (m, 14H), 4.53 (bd, 1H, J = 9 Hz), 4.47 (bd, 1H, J = 8.7 Hz), 3.60−2.80 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1, 135.0, 131.3, 129.3, 128.6, 128.5, 127.7, 125.7, 60.0, 54.3; MS (ESI+) m/z 414 (5) [M$^+$ − NH_2], 337 (46), 259 (40), 180 (100); HRMS (ESI+) calcd for $C_{20}H_{19}BrNSe$ [M$^+$ − NH_2] 414.9593, found 414.9576.

*(1S,2S)-3-Methyl-2-phenyl-2-(phenylselanyl)butan-2-amine (syn-**9i**):* yield 70% (17.8 mg); white solid; mp 104−106 °C; $[\alpha]^{20}_D$ + 45.1 (c 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD) δ 7.40−7.15 (m, 10H), 4.39 (d, 1H, J = 8.4 Hz), 3.16 (dd, 1H, J = 4.4 and 8.4 Hz), 2.11−2.30 (m, 1H), 1.07 (d, 3H, J = 7.0 Hz), 0.93 (d, 3H, J = 7.0 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 138.1, 137.0, 130.4, 130.1, 129.8, 129.7, 129.1, 129.5, 60.1, 30.0, 20.0, 16.8; MS (ESI+) m/z 320 (6) [M + H$^+$], 303 (44), 246 (80), 145 (100); HRMS (ESI+) calcd for $C_{17}H_{22}NSe$ 320.0913, found 320.0904.

*[1S,(S)S]-N-[1-(4-Bromophenyl)-2-[(S)-2-(p-tolylsulfinyl)phenyl]-ethyl]-p-toluenesulfinamide (**10d**).* To a solution of [1R,2S,(S)*S*]-*N*-1-(4-bromophenyl)-2-(phenylselanyl)-2-[2-(*S*)-(*p*-tolylsulfinyl)-phenyl)ethyl]-*p*-toluensulfinamide (**3d**) (42.4 mg, 0.06 mmol, 1 equiv) in anhydrous THF (2 mL) at rt was added activated Raney Ni (750 mg). The reaction mixture was stirred for 90 min, and then it was filtered over Celite. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc, 1:1): yield 73% (24.2 mg); white solid; mp 77−79 °C; $[\alpha]^{20}_D$ +12.5 (c 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, 1H, J = 7.8 Hz), 7.56−7.12 (m, 11H), 7.02 (d, 2H, J = 8.1 Hz), 6.91 (d, 2H, J = 8.4 Hz), 5.79 (d, 1H, J = 6.3 Hz), 4.52 (ddd, 1H, J = 6.0, 9.9, and 14.1 Hz), 3.34 (dd, 1H, J = 9.9 and 14.1 Hz), 2.78 (dd, J = 5.4 and 14.1 Hz), 2.33 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 142.0, 141.3, 141.1, 140.8, 137.5, 132.3, 132.0, 131.3, 129.9, 128.9, 128.4, 127.7, 127.6, 125.7, 125.1, 120.8, 56.4, 39.1, 21.2, 21.2; MS (ESI+) m/z 554 (100) [M + H$^+$], 414 (55), 183 (51); HRMS (ESI+) calcd for $C_{28}H_{27}BrNO_2S_2$ 554.0643, found 554.0625.

*[2R,(S)S]-N-[3-Methyl-1-[(S)-2-(p-tolylsulfinyl)phenyl]butan-2-yl]-p-toluenesulfinamide (**11i**).* To a solution of [1S,2S,(S)*S*]-*N*-[3-methyl-1-(phenylselanyl)-1-[2-(*S*)-(*p*-tolylsulfinyl)phenyl]butan-2-yl]-*p*-toluenesulfinamide (**4i**) (35.7 mg, 0.06 mmol, 1 equiv) in anhydrous THF (2 mL) was added at rt activated Raney Ni (750 mg). The reaction mixture was stirred for 90 min, and then it was filtered over Celite. The solvent was removed under vacuum. The residue was purified by flash column chromatography (hexane/EtOAc, 2:1): yield 68% (17.9 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, 1H, J = 8.0 Hz), 7.07−7.61 (m, 11H), 4.23 (bd, 1H, J = 8.7 Hz), 3.53−3.64 (m, 1H), 2.94 (dd, 1H, J = 9.9 and 14.1 Hz), 2.80 (dd, 1H, J = 5.1 and 14.1 Hz), 2.38 (s, 3H), 2.32 (s, 3H), 1.81−1.93 (m, 1H), 0.97 (d, 3H, J = 6.9 Hz), 0.89 (d, 3H J = 6.6 Hz).

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR for compounds **3a−f**, **4g−i**, **5j**, **6d**, **7d**, **8i**, and **9i**, and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: (J.L.G.R.) joseluis.garcia.ruano@uam.es, (A.D.) alessandro.deglinnocenti@unifi.it.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Mugesh, G.; du Mont, W. W.; Sies, H. *Chem. Rev.* **2001**, *101*, 2125. (b) Nogueria, C. W.; Zeni, G.; Roch, J. B. T. *Chem. Rev.* **2004**, *104*, 6255.

(2) Miniejew, C.; Outurquin, F; Pannecoucke, X. *Tetrahedron* **2005**, *61*, 447.

(3) Sehnem, J. A.; Vargas, F.; Milani, P.; Nascimento, V.; Braga, A. L. *Synthesis* **2008**, 1262.

(4) (a) Braga, A. L.; Schneider, P. H.; Paixão, M. W.; Deobald, A. M.; Peppe, C.; Bottega, D. P. *J. Org. Chem.* **2006**, *71*, 4305. (b) Degl'Innocenti, A.; Capperucci, A.; Castagnoli, G.; Malesci, I.; Tiberi, C.; Innocenti, B. *Phosphorus, Sulfur, Silicon* **2008**, *183*, 966. (c) Ganesh, V.; Chandrasekaran, S. *Synthesis* **2009**, 3267.

(5) For comprehensive reviews about the use of chiral organo-selenium in asymmetric catalysis, see: (a) Wirth, T. *Tetrahedron* **1999**, *55*, 1. (b) Wirth, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 3741. (c) Braga, A. L.; Lüdtke, D. S.; Vargas, F.; Braga, R. C. *Synlett* **2006**, 1453. (d) Braga, A. L.; Lüdtke, D. S.; Vargas, F. *Curr. Org. Chem.* **2006**, *10*, 1921.

(6) (a) Braga, A. L.; Lüdtke, D. S.; Paixao, M. W.; Alberto, E. E.; Stefani, H. A.; Juliano, L. *Eur. J. Org. Chem.* **2005**, 4260. (b) Tiecco, M.; Testaferri, L.; Bagnoli, L.; Scarponi, C.; Temperini, A.; Marini, F.; Santi, C. *Tetrahedron: Asymmetry* **2007**, *18*, 2758.

(7) (a) Braga, A. L.; Schneider, P. H.; Paixao, M. W.; Deobald, A. M.; Peppe, C.; Bottega, D. P. *J. Org. Chem.* **2006**, *71*, 4305. (b) Sureshkumar, D.; Gunasundari, T.; Saravan, V.; Chandrasekaran, S. *Tetrahedron Lett.* **2007**, *48*, 623. (c) Braga, A. L.; Schwab, R. S.; Alberto, E. E.; Salman, S. M.; Vargas, J.; Arezedo, J. B. *Tetrahedron Lett.* **2009**, *50*, 2309. (d) Ganesh, V.; Chandrasekaran, S. *Synthesis* **2009**, *19*, 3267. (e) Senatore, M.; Lattanzi, A.; Santoro, S.; Claudio Santi, C.; Della Sala, G. *Org. Biomol. Chem.* **2011**, *9*, 6205.

(8) Schneider, A.; Rodrigues, O. E. D.; Paixão, M. W.; Appelt, H. R.; Braga, A. L.; Wessjohan, L. A. *Tetrahedron Lett.* **2006**, *47*, 1019.

(9) Cao, J.; Huang, X. *Synth. Commun.* **2009**, *39*, 205.

(10) Other seleno derivatives bearing the selenium atom bonded to one stereocenter have been recently reported. See: (a) Tiecco, M.; Carlone, A.; Sternativo, S; Marina, F.; Bartoli, G.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 6882. (b) Sundén, H.; Rios, R.; Córdova, A. *Tetrahedron Lett.* **2007**, *48*, 7865. (c) Marcos, V.; Alemán, J.; García Ruano, J. L.; Marini, F.; Tiecco, M. *Org. Lett.* **2011**, *13*, 3052.

(11) (a) Capperucci, A.; Tiberi, C.; Pollicino, S.; Degl'Innocenti, A. *Tetrahedron Lett.* **2009**, *50*, 2808. (b) Degl'Innocenti, A.; Capperucci, A.; Acciai, M.; Tiberi, C. *Phosphorus Sulfur Silicon Relat. Elem.* **2009**, *184*, 1621. (c) Temperini, A.; Capperucci, A.; Degl'Innocenti, A.; Terlizzi, R.; Tiecco, M. *Tetrahedron Lett.* **2010**, *51*, 4121. (d) Temperini, A.; Capperucci, A.; Degl'Innocenti, A.; Terlizzi, R.; Tiecco, M. *Phosphorus Sulfur Silicon Relat. Elem.* **2011**, *186*, 1137. (e) Torrente, E.; García Ruano, J. L.; Martín Castro, A. M.; Degl'Innocenti, A.; Capperucci, A.; Frateschi, L. *Phosphoru, Sulfur Silicon Relat. Elem.* **2011**, *186*, 1268.

(12) García Ruano, J. L.; Carreño, M. C.; Toledo, M. A; Aguirre, J. M.; Aranda, M. T.; Fischer, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2736.

(13) Recent references: (a) Arroyo, Y.; Meana, A.; Sanz-Tejedor, M. A.; Alonso, I.; García Ruano, J. L. *Chem.—Eur. J.* **2010**, *16*, 9874. (b) García Ruano, J. L.; Schopping, C.; Alvarado, C.; Alemán, J. *Chem.—Eur. J.* **2010**, *16*, 8968. (c) García Ruano, J. L.; Martín-Castro, A. M.; Tato, F.; Torrente, E.; Poveda, A. *Chem.—Eur. J.* **2010**, *16*, 6317. (d) García Ruano, J. L.; Parra, A.; Marcos, V.; del Pozo, C.; Catalán, S.; Monteagudo, S.; Fustero, S. *J. Am. Chem. Soc.* **2009**, *131*, 9432.

(14) (a) Davis, F. A. *J. Org. Chem.* **2006**, *71*, 8993. (b) Ellman, J. A.; Owens, T. D.; Tang, T. P. *Acc. Chem. Res.* **2002**, *35*, 984.

(15) García Ruano, J. L.; Alemán, J.; Soriano, F. *Org. Lett.* **2003**, *5*, 677.

(16) Their characterization was not possible in our hands.

(17) Mikołajczyk, M.; Drabowicz, J.; Bujnicki, B. *J. Chem. Soc., Chem. Commun.* **1976**, 568.

(18) Selenoamines **3a−f**, **4g−i**, and **5j** readily decomposed upon standing in solution at room temperature for long periods of time.

(19) For clarity purposes in the discussion of the results, we maintain the same notation, i.e., C(1) for carbon atom bonded to nitrogen and C(2) for carbon atom bonded to selenium, for both aromatic (**3a−f**) and aliphatic (**4g−i**, **5j**) selenoamines. However, in Experimental Section, the correct IUPAC numbering for each series has been used for these compounds.

(20) (a) Perdew, J. P.; Chevary, S. H.; Vosko, K. A.; Jackson, K. A.; Pederson, M. R.; Singh, D. J.; Fiolhais, C. *Phys. Rev. B* **1992**, *46*, 6671. (b) Perdew, J. P.; Chevary, S. H.; Vosko, K. A.; Jackson, K. A.; Pederson, M. R.; Singh, D. J.; Fiolhais, C. *Phys. Rev. B* **1993**, *48*, 4978. (c) Perdew, J. P.; Burke, K.; Wang, Y. *Phys. Rev. B* **1996**, *54*, 16533. (d) Adamo, C.; Barone, V. *J. Chem. Phys.* **1998**, *108*, 664. It is proposed that the mPW1PW91 can account for the likely long-range dispersive interactions as well as hydrogen bonding (see Patil, M. P.; Sunoj, R. B. *Chem. Asian J.* **2009**, *4*, 714 and references therein). We have recently obtained excellent results modeling interactions between imines and other carbanions: Arroyo, Y.; Sanz-Tejedor, M. A.; Alonso, I.; García-Ruano, J. L. *Org. Lett.* **2011**, *13*, 4534.

(21) (a) Barone, V.; Cossi, M. *J. Phys. Chem. A* **1998**, *102*, 1995. (b) Cossi, M.; Rega, N.; Scalmani, G.; Barone, V. *J. Comput. Chem.* **2003**, *24*, 669.

(22) Gaussian 09, Revision B.01. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li,X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J. Fox, D. J. Gaussian, Inc., Wallingford, CT, 2010. See the Supporting Information for computational details.

(23) Geometries have been fully optimized by using the standard 6-31G(d) basis set for all the atoms except Se: (a) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1971**, *54*, 724. (b) Francl, M. M.; Petro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654. The LANL2DZ basis set supplemented with a d function of exponent 0.364 was used for selenium: (c) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.

(d) Höllwarth, A.; Böhme, M.; Dapprich, S.; Ehlers, A. W.; Gobbi, A.; Jonas, V.; Köhler, K. F.; Stegmann, R.; Veldkamp, A.; Frenking, G. *Chem. Phys. Lett.* **1993**, *208*, 237. Frequencies and zero-point energy (ZPE) were also computed at the same level of theory. Final energies have been obtained by using the more extended 6-311G(d,p) basis set for all atoms except Se: (e) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650. For Se, a basis set of similar quality (SDB-cc-pVTZ) was used: (f) Martin, J. M. L.; Sundermann, A. *J. Chem. Phys.* **2001**, *114*, 3408. Relative free energies (in kcal·mol^{-1}) were evaluated at the mPW1PW91/6-311G** and SDB-cc-pVTZ level with ZPE and entropy corrections evaluated at 298 K by using the frequencies previously calculated at the mPW1PW91/6-31G(d) and LANL2DZ* level.