178. Stereoselectivity of the Radical Reductive Alkylation of Enamines: Importance of the Allylic 1,3-Strain Model

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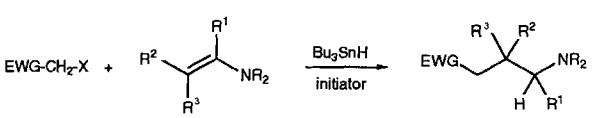
Radical addition to enamines using Bu_3SnH as reducing agent are reported (*Schemes 2* and *4*). The diastereoselectivity of these reactions was examined in different systems (*Tables 1* and *2*). Enamines derived from cyclic ketones such as cyclohexanone were alkylated with high diastereoselectivity with preferential formation of the *cis*-disubstituted cycloalkanes. In acyclic systems such as enamines derived from propiophenone and diethyl ketone, moderate to high stereoselectivities were observed in the H-abstraction step. A model based principally on minimization of allylic 1,3-strain ($A^{1,3}$ strain) was deduced from the experimental results and semi-empirical (AM1) calculations.

Introduction. – The work of *Stork* and coworkers [1] in 1954 on the alkylation and acylation of enamines has generated a strong interest in this field of chemistry. Reactions with a wide range of electrophiles [2a] and cycloadditions [2b] were reported. The amino moiety is usually used as an activating group and is removed during the final workup. However, hydride reduction of iminium intermediates [3] is possible and leads to tertiary amines. We recently reported an alternative method for performing the reductive alkylation of enamines (*Scheme 1*) in a one-step procedure *via* a radical-chain mechanism [4–6]. Radical additions to enamines *via* a SET mechanism [7] [8] and a group-transfer mechanism [9] [10] were also published.

Scheme 1



EWG = electron-withdrawing group

In this paper, we focus on the different factors governing the diastereoselectivity of the radical-mediated reductive alkylation of enamines. Enamines derived from cyclic and acyclic carbonyl compounds were investigated.

Results. – The enamines **1**–**12** were either commercially available (**1**, **2**, and **5**) or prepared from the corresponding ketones and secondary amines by either azeotropic

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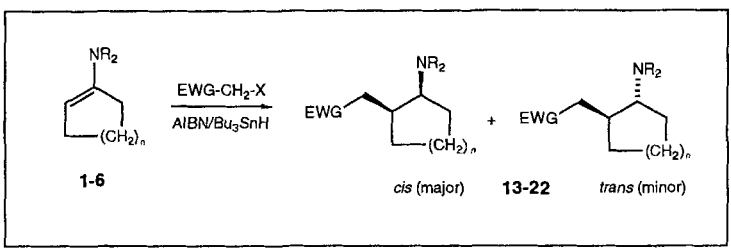
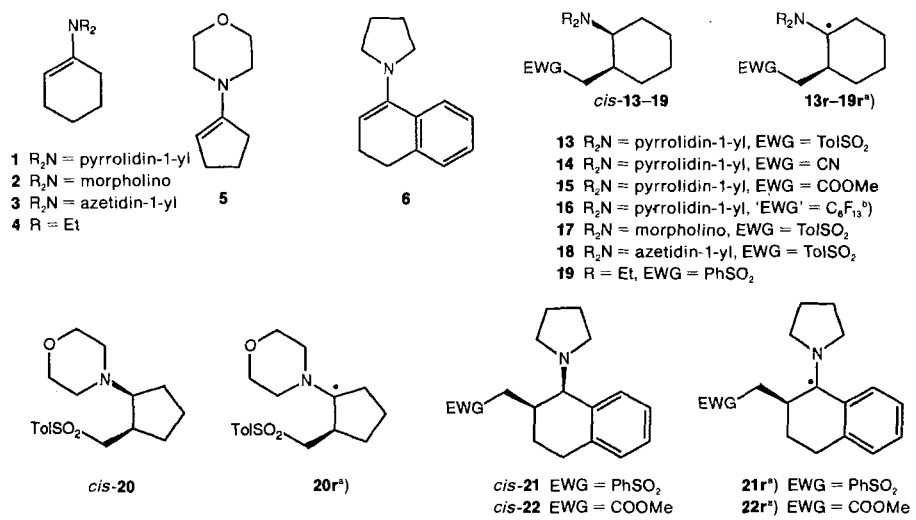
removal of H_2O (**6** and **8**), by the *Weingarten* method [11] with $TiCl_4$ (**3**, **4**, **7**, **9**, and **10**), or by treatment with K_2CO_3 in Et_2O (**11**–**12**). The radical precursors were either commercially available or prepared in a straightforward manner (see *Exper. Part*). The results of the reductive alkylation of the cyclic enamines **1**–**6** (*Scheme 2*) are reported in *Table 1*. In

Scheme 2





a) **r** for radical, see *Discussion*. b) 'EWG' means $EWGCF_2$ instead of $EWGCH_2$ in *Formula*.

Table 1. *Reductive Alkylation of Cyclic Enamines* (*Scheme 2*)

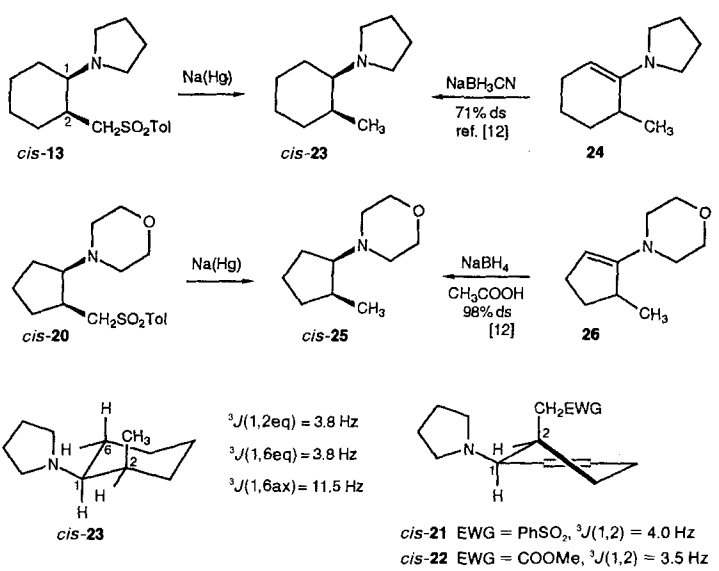
Entry	Enamine	$EWGCH_2X$	Product	Yield [%]	*cis*/*trans*
1	**1**	$TolSO_2CH_2Cl$	**13**	57	97:3
2	**1**	$CNCH_2SPh$	**14**	88	92:8
3	**1**	$MeOOCCH_2SPh$	**15**	74	98:2
4	**1**	$C_6F_{13}STol$ [a])	**16**	58	90:10
5	**2**	$TolSO_2CH_2Cl$	**17**	62	96:4
6	**3**	$TolSO_2CH_2Cl$	**18**	10	> 95: < 5
7	**4**	$PhSO_2CH_2Cl$	**19**	76	91:9
8	**5**	$TolSO_2CH_2Cl$	**20**	54	84:16
9	**6**	$PhSO_2CH_2Cl$	**21**	52	75:25
10	**6**	$MeOOCCH_2SPh$	**22**	63	91:9

[a]) 'EWG'X instead of $EWGCH_2X$.

all cases, the formation of the *cis*-disubstituted compounds was favored (see **13**–**22**). High diastereoselectivities were obtained for enamines **1**–**4** derived from cyclohexanone with all radical precursors tested (*Entries 1–7*). Moderate diastereoselectivities were observed for cyclopentanone derivative **5** (*Entry 8*, *cis*/*trans* 84:16) and α-tetralone derivative **6** (*Entries 9* and *10*, *cis*/*trans* 75:25 and 91:9).

The *cis*-configuration of the major isomer of **13** was deduced from its ^{1}H-NMR spectra by looking at the coupling constant of H–C(1) with the three vicinal protons. Due to the relative complexity of the spectrum, we reductively desulfonylated (Na/Hg) *cis*-**13** to *cis*-**23** (*Scheme 3*) to assign this signal unambiguously. Thus, we deduced the configuration of *cis*-**23** and established that *cis*-**23** lies in the expected chair conformation as shown in *Scheme 3*. For comparison, *cis*-**23** was also prepared according to *Hutchins*' procedure [12] by reduction of enamine **24** with $NaBH_3CN$ in AcOH (*Scheme 3*). The structure of the major isomer of **20** was established by desulfonylation to *cis*-**25** and comparison with an authentic sample of *cis*-**25** prepared by *Hutchins*' method from **26**. The *cis*-configurations of the main isomers of **21** and **22** were deduced from the small $J(1,2)$ of 4.0 and 3.5 Hz, respectively. This attribution is based on the assumption that *cis*-**21** and *cis*-**22** lie in the conformation depicted in *Scheme 3*.

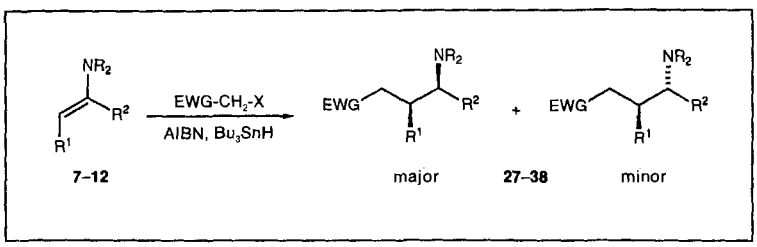
Scheme 3

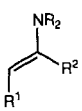


The results of the reductive alkylation of acyclic enamines (*Scheme 4*) are reported in *Table 2*. Enamines **7**–**9** prepared from propiophenone reacted with modest stereoselectivities (60–66% ds) with cyanomethyl (→**27**; *Entry 1*) and (alkoxycarbonyl)methyl radicals (→**28**; *Entries 2* and *3*) at 80°. At 10°, the stereoselectivity raised to 77% for the reaction with (phenylthio)acetonitrile (*Entry 1*). With bulkier electron-withdrawing groups such as phenylsulfonyl and (*tert*-butyl)sulfonyl, better selectivities (→**29**–**32**; *Entries 4–7*) of 80–88% ds were obtained with enamines derived from cyclic amines. Reactions with enamine **9** prepared from Et_2NH were less diastereoselective (→**33** and **34**; *Entries 8* and

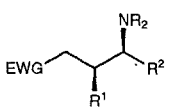
9, 68 and 76% ds, resp.). As can be seen, the size of the electron-withdrawing (EWG) group is critical for high diastereoselectivity, and, therefore, we decided to complex the sulfones with $LiClO_4$ (*Entries 4* and *5*) in order to increase their steric bulk. A pronounced enhancement of the stereoselectivity was observed in the case of the $PhSO_2$ group (88% ds), however, no effect was observed with the *t*-$BuSO_2$ group. The relative configuration of the major isomer of **29** and **31** was proved by X-ray analysis[2]) (*Fig. 1*). In both cases, the major isomer was *like*(*l*)-configurated.

Scheme 4

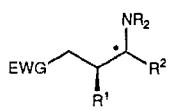




7 R^1 = Me, R^2 = Ph, R_2N = pyrrolidin-1-yl
8 R^1 = Me, R^2 = Ph, R_2N = morpholino
9 R^1 = Me, R^2 = Ph, R = Et
10 R^1 = Me, R^2 = Et, R_2N = morpholino
11 R^1 = $PhCH_2$, R^2 = H, R_2N = pyrrolidin-1-yl
12 R^1 = i-Pr, R^2 = H, R_2N = 1,4-dioxa-8-azaspiro[4.5]decan-8-yl

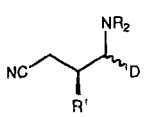


27–37 (major)

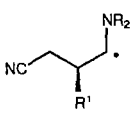


27r–37r[a])

27 R^1 = Me, R^2 = Ph, R_2N = pyrrolidin-1-yl, EWG = CN
28 R^1 = Me, R^2 = Ph, R_2N = pyrrolidin-1-yl, EWG = COOMe
29 R^1 = Me, R^2 = Ph, R_2N = pyrrolidin-1-yl, EWG = $PhSO_2$
30 R^1 = Me, R^2 = Ph, R_2N = pyrrolidin-1-yl, EWG = *t*-$BuSO_2$
31 R^1 = Me, R^2 = Ph, R_2N = morpholino, EWG = $PhSO_2$
32 R^1 = Me, R^2 = Ph, R_2N = morpholino, EWG = *t*-$BuSO_2$
33 R^1 = Me, R^2 = Ph, R = Et, EWG = $PhSO_2$
34 R^1 = Me, R^2 = Ph, R = Et, EWG = *t*-$BuSO_2$
35 R^1 = Me, R^2 = Et, R_2N = morpholino, EWG = $PhSO_2$
36 R^1 = Me, R^2 = Et, R_2N = morpholino, EWG = CN



37 R = $PhCHz$, R_2N = pyrrolidin-1-yl
38 R = i-Pr, R_2N = 1,4-dioxa-8-azaspiro[4.5]decan-8-yl



37r[a]) R^1 = $PhCH_2$, R_2N = pyrrolidin-1-yl
38r[a]) R^1 = i-Pr, R_2N = 1,4-dioxa-8-azaspiro[4.5]decan-8-yl

[a]) **r** for radical, see *Discussion*.

Reductive alkylation of enamine **10**, prepared from diethyl ketone and morpholine, is more diastereoselective than the preceding examples. *E.g.*, chloromethyl phenyl sulfone gave the amine **35** with 93% diastereoselectivity (*Entry 10*). Even with nitrile group, a modest diastereoselectivity of 74% ds (*Entry 11*) was observed. The reductive alkylation of the enamines **11** and **12** (derived from aldehydes) using tributyltin deuteride as reducing agent was not stereoselective (*Entries 12* and *13*).

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[2]) The determination of the structure of both compounds by X-ray crystal-structure analysis was necessary, since there was a complete lack of similarity between the ^{1}H-NMR spectra of the major isomers of **29** and **31**.

Table 2. *Reductive Alkylation of Acyclic Enamines (Scheme 4)*

Entry	Enamine	$EWGCH_2X$	Product	Yield [%]	ds [%]
1	**7**	$CNCH_2SPh$	**27**	81	66[a]), 77[b])
2	**7**	$MeOOCCH_2SPh$	**28**	53	64[a])
3	**7**	t-$BuOOCCH_2SPh$	**28**[c])	27	60[a])
4	**7**	$PhSO_2CH_2Cl$	**29**	52	72[a]), 81[b]), 88[b])[c])
5	**7**	t-$BuSO_2CH_2Cl$	**30**	58	74[a]), 85[b]), 87[b])[c])
6	**8**	$PhSO_2CH_2Cl$	**31**	41	80[b])
7	**8**	t-$BuSO_2CH_2Cl$	**32**	48	87[b])
8	**9**	$PhSO_2CH_2Cl$	**33**	20	68[b])
9	**9**	t-$BuSO_2CH_2Cl$	**34**	20	76[b])
10	**10**	$PhSO_2CH_2Cl$	**35**	76	93[b])
11	**10**	$CNCH_2SPh$	**36**	78	74[a])
12	**11**	$CNCH_2SPh$	**37**	60	50[a])[e])
13	**12**	$CNCH_2SPh$	**38**	60	50[a])[e])

[a]) 80°. [b]) 10°. [c]) Transesterification occurred during the workup procedure (see *Exper. Part*). [d]) 1 Equiv. of $LiClO_4$. [e]) Bu_3SnD.

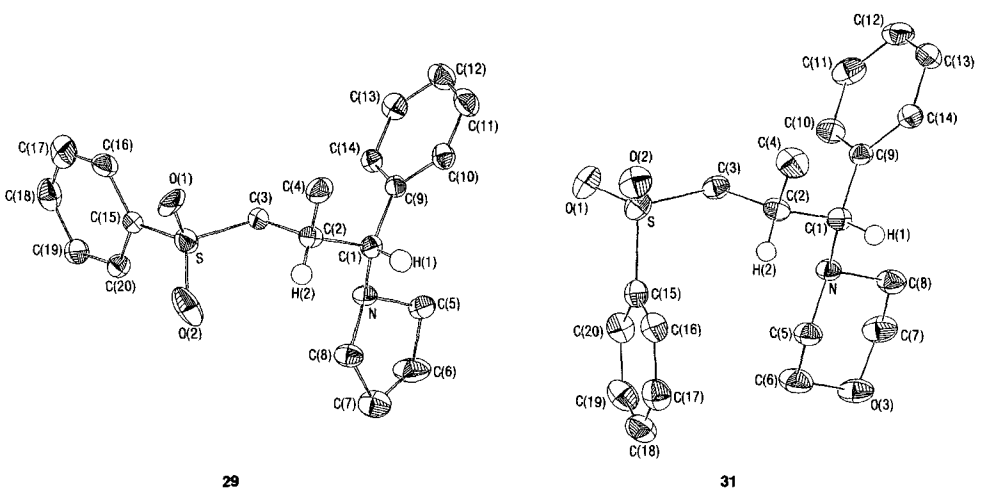


Fig. 1. *X-Ray crystal structure of the major isomer of* **29** *and* **31** (ORTEP plots). H-Atoms are omitted for reasons of clarity, except at the asymmetric centers. Arbitrary numbering.

Discussion. – Our rationalization of the observed diastereoselectivities is based on the hypothesis that an early transition state is operative for the H-abstraction step[3]). Thus, the conformational preference of the radical intermediate should strongly influence the stereoselectivity. Amino-substituted radicals are stabilized by interaction with the electron lone pair on the N-atom, and, therefore, the ·C–N bond possesses partial double-bond character. We calculated the rotational barrier using *ab initio* methods (6-31G**) for the simple aminomethyl radical (*Fig. 2*) and found a value of 6.6 kcal/mol. As a consequence, a close analogy exists between dialkylamino-substituted radicals (see **I**) and allylic systems (see **II**). Investigation of the conformations of cyclic [13] and acyclic [14]

[3]) Similar approaches were successfully applied to numerous other radical reactions [15] [16].

allylic systems led to the concept of allylic 1,3-strain ($A^{1,3}$ strain). The same concept was applied, with success, to conjugated radicals [15] [16]. It is likely that type-**I** radicals adopt a conformation where the smallest substituent on the C-atom adjacent to the radical center eclipses the pseudodouble bond to minimize $A^{1,3}$ strain. Changes in the dihedral angle around C(1) and C(2) of ±30° is possible with only small energy cost [14]. As a consequence, the two faces of the radical are differently shielded by L and M (*Fig. 2*), the steric bulk of these substituents controlling the direction of attack[4]).

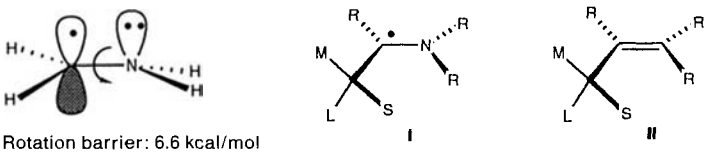
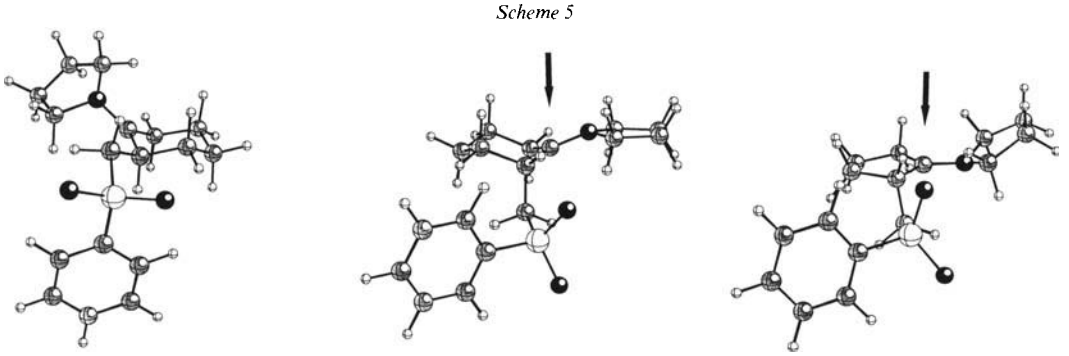


Fig. 2. *Rotation barrier of amino-substituted radicals and analogy with an allylic system*

To confirm this hypothesis, we performed AM1 semiempirical calculations on several cyclic and acyclic systems. We calculated the relative heat of formation of the two possible radical conformers **13r(ii)** and **13r(v)** (*Scheme 5*) possessing the $PhSO_2CH_2$ group in axial and equatorial position, respectively. As expected, **13r(v)** is less stable by *ca.* 4.6 kcal/mol than **13r(ii)** due to $A^{1,3}$-strain. The high stereoselectivity observed for the formation of **13** is caused by H-abstraction from the less hindered face (black arrow) of **13r(ii)**. For the radical adduct **20r**, only one minimum-energy conformation was found by calculation. This conformer, **20r(ii)**, is depicted in *Scheme 5* and possesses a H–C(2)–C˙–N dihedral angle of 57°.

Scheme 5

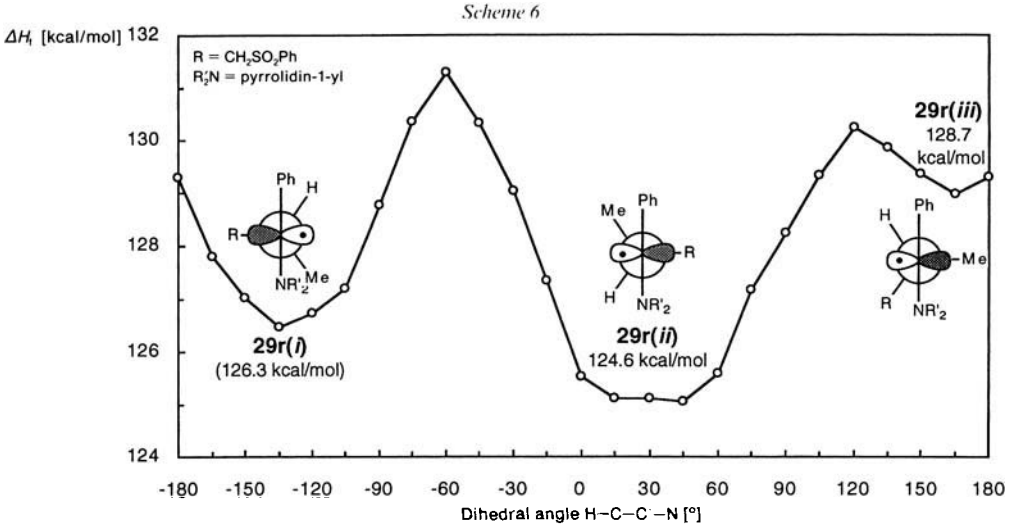


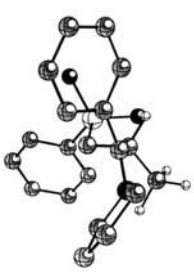
For radical **29r**, we calculated the relative heat of formation for fixed values of the dihedral angle (H–C(2)–C˙–N). Three minima, **29r(i–iii)**, were found (*Scheme 6*). H-Abstraction from the less hindered face of the more stable conformer **29r(ii)** (black arrow) is expected to give the observed major isomer (*l*)-**29**. Conformer **29r(i)** is 1.7 kcal/mol higher in energy and leads to the minor isomer (*u*)-**29**. Conformer **29r(iii)** is

[4]) This model was already presented in a preliminary communication [6] and also proved to be valuable for reactions based on phenylselenenyl-group transfer [10].

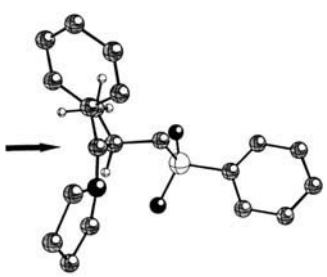
higher in energy (+4.1 kcal/mol) and contributes only slightly to the formation of the major isomer (*l*)-**29**. The difference in energy between **29r(ii)** and **29r(i)** is responsible for the observed stereoselectivity. Careful examination of the structure of **29r(ii)** and **29r(i)** showed that the former radical is stabilized exclusively by the N-atom. The Ph ring is orthogonal to the radical center and no delocalization of the radical to the aromatic ring is possible. In the case of conformer **29r(i)**, the radical is stabilized by both the amino and the Ph groups (*Scheme 6*). Replacement of the stabilizing Ph group by an alkyl residue is

Scheme 6

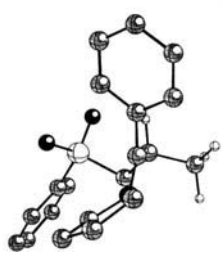




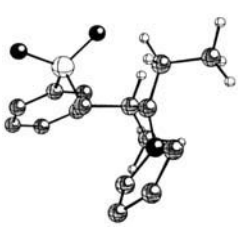
29r(i) (ΔH_f = 126.3 kcal/mol)



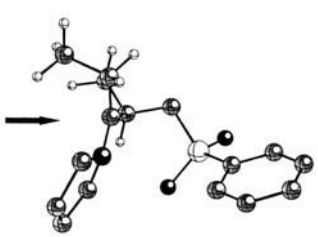
29r(ii) (ΔH_f = 124.6 kcal/mol)



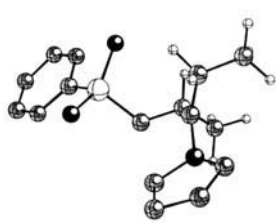
29r(iii) (ΔH_f = 128.7 kcal/mol)



35r(i) (ΔH_f = 86.6 kcal/mol)



35r(ii) (ΔH_f = 84.0 kcal/mol)



35r(iii) (ΔH_f = 87.6 kcal/mol)

expected to increase the energy difference between conformers **ii** and **i** and to enhance the diastereoselectivity of the reductive alkylation. This happens with enamine **10** (*Table 2, Entry 10*, 93% ds) derived from diethyl ketone. Calculations showed that **35r(i)** is 2.6 kcal/mol less stable than **35r(ii)**. Conformer **35r(iii)** is destabilized by 3.6 kcal/mol relative to **35r(ii)**.

Based on the above results, the following rules may be deduced for predicting the stereoselectivity of reactions based on dialkylamino-substituted radicals. For cyclic radicals, the minimum-energy conformation has the structure depicted in *Fig. 3*, and preferential attack occurs '*anti*' to the group L. High diastereoselectivities are expected when the relative size of the two substituents L and S is very different. This is always the case when S is a H-atom and L a substituted methyl group[5]).

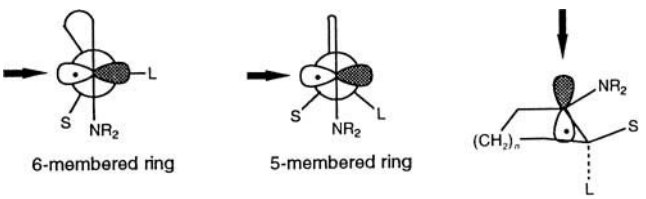


Fig. 3. *1,2-Transfer of chirality: general model for cyclic radicals.* Black arrows represent the preferential approach of Bu_3SnH.

For acyclic radicals (*Fig. 4*), the global minimum energy conformation **ii** is expected to be favored. However, four conformers have to be considered (**i–iv**). High diastereoselectivity may only be obtained when the three groups L, M, and S are sterically well differentiated. However, this condition is not sufficient, the group R′ is also playing a crucial role. When R′ is a H-atom (see radical **37r** and **38r**, *Table 2, Entries 12* and *13*), no stereoselection is observed. Bigger R′ such as alkyl groups are necessary for good stereoselection.

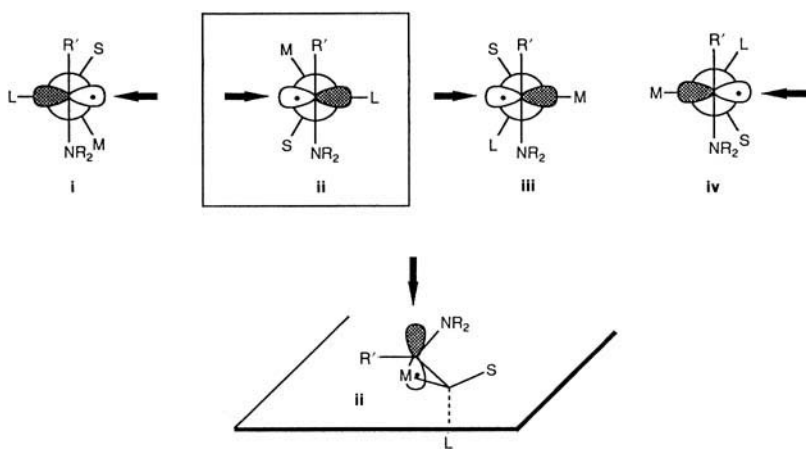


Fig. 4. *1,2-Transfer of chirality: general model for acyclic radicals.* Black arrows represent the preferential approach of Bu_3SnH.

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[5]) A similar model based on $A^{1,3}$ strain was reported for the reduction of cyclic iminium salts by metal hydrides [12].

The model depicted in *Figs. 3* and *4* for the transfer of chirality in dialkylamino-substituted radicals is very similar to the one recently published for other stabilized radicals such as ester-[16a–e] and phenyl-substituted [10] [17] radicals. This demonstrates further the unique importance of allylic 1,3-strain effects in radical reactions involving delocalized radicals.

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Experimental Part

General. THF was freshly distilled from K under N_2, CH_2Cl_2 from P_2O_5, and benzene from CaH_2 under N_2. Lithium diisopropylamide (LDA; 1M) was prepared by treating at −78° a soln. of $(i\text{-Pr})_2NH$ (15 ml, 105 mmol; distilled from CaH_2) in THF (22.5 ml) with 1.6M BuLi (62.5 ml, 100 mmol, in hexane) and stored in a brown bottle in a freezer. Irradiations were conducted using a sunlamp *Osram Ultra-Vitalux 300W*. Flash column chromatography (FC): *Merck* silica gel *60* (70–230 mesh), AcOEt and petroleum ether (p.e.) as solvent for elution. TLC: *Merck* silica gel *60* F_{254} anal. plates; detection either with UV, I_2, or by spraying with a soln. of 25 g of phosphomolybdic acid, 10 g of $Ce(SO_4)_2 \cdot 4\ H_2O$, 60 ml of conc. H_2SO_4, and 940 ml of H_2O with subsequent heating. Bulb-to-bulb distillations: *Büchi-GKR-50* apparatus; b.p.'s refer to air-bath temp. GC: *Carlo-Erba, DB-1*, 50 m (capillary column). M.p.: not corrected; *Büchi-Tottoli* apparatus. IR: *Perkin-Elmer-297* spectrophotometer; in cm^{-1}. NMR: *Bruker AC-200 FT* (200 MHz, ^2H) and *AC-250 FT* (250 MHz, ^1H, ^{13}C); unless otherwise indicated, $CDCl_3$ solns.; chemical shifts δ in ppm rel. to Me_4Si (= 0 ppm). MS: *Finnigan 1020* and *Nermag R10-10C*. Elemental analysis: *Ilse Beetz, Mikroanalytisches Laboratorium*, D–8640 Kronach.

Calculations. The semi-empirical AM1 calculations [18a] were performed on a *Silicon-Graphics-4D-320* workstation with the software MOPAC 5.0 (QCPE N° 445) *via* the *SYBYL* interface (*Tripos Associates, Ltd.*, Saint-Louis, USA) for the construction of input geometries and for the graphical analysis of results. All the geometry optimizations for isolated conformers and along a given reaction path were performed with the keyword PRECISE. The UHF Hamiltonian was used to calculate the open-shell species. The standard convergence criteria were used in optimization. The *ab initio* calculations were performed with the GAUSSIAN 90 software on a *Silicon-Graphics-4D-320* workstation [18b]. Here again, the geometry optimizations were performed with the standard convergence criteria and the open-shell species calculated with the UHF Hamiltonian. The direct-SCF option was used in all *ab initio* calculations.

Radical Precursors. – (Phenylthio)acetonitrile, chloromethyl phenyl sulfone, and methyl (phenylthio)acetate are commercially available. Chloromethyl tol-4-yl sulfone [19], tol-4-yl tridecafluorohexyl sulfide [20], and *tert*-butyl (phenylthio)acetate [21] [22] were prepared according to reported methods.

tert-Butyl (Phenylselenenyl)methyl Sulfone. A soln. of *t*-BuSMe (2.0 g, 19 mmol) in H_2O/MeOH 2:3 (250 ml) was treated at 0° with 48% *Oxone*® (35 g, 57 mmol). The mixture was stirred for 12 h at r.t. Filtration over *Celite* and evaporation gave a residue which was dissolved in CH_2Cl_2 (200 ml) and washed with H_2O (2 × 50 ml). Drying ($MgSO_4$), evaporation, and recrystallization (CH_2Cl_2/p.e.) gave *t*-BuS(O_2)Me as a white solid (1.3 g, 51%). M.p. 80–82° ([23]: 78–79°). To a cooled (−78°) soln. of *t*-BuS(O_2)Me (1.0 g, 7.3 mmol) in THF was added 1M LDA (14.7 ml, 14.7 mmol). After 30 min stirring at −78°, a soln. of phenylselenenyl chloride (1.4 g, 7.4 mmol) in THF (10 ml) was added dropwise. The mixture was allowed to warm up to r.t. After 2 h at r.t., it was poured into Et_2O (50 ml) and washed with 10% aq. NH_4Cl soln. Drying ($MgSO_4$), evaporation, and FC (AcOEt/p.e. 1:1) gave the desired product (1.9 g, 89%). White solid. M.p. 98.5–100°. IR (film): 2920, 2850, 1455, 1260, 1020, 800. ^1H-NMR: 1.39 (*s*, *t*-Bu); 4.13 (*s*, CH_2); 7.25–7.70 (*m*, 5 arom. H). ^{13}C-NMR: 23.48 (*q*); 42.47 (*t*); 59.00 (*s*); 128.19 (*d*); 129.02 (*d*); 133.81 (*d*). MS: 292 (13, M^+), 171 (17), 91 (47), 84 (33), 78 (10), 77 (18), 71 (33), 57 (100), 55 (22), 50 (11). Anal. calc. for $C_{11}H_{16}O_2SSe$ (291.27): C 45.36, H 5.54, S 11.01; found: C 45.27, H 5.51, S 10.97.

Enamines. – Enamines **1**, **2**, and **5** are commercially available and were distilled prior to use.

General Procedure 1 [24]. A soln. of the ketone (0.10 mol) and the amine (0.60 mol) in heptane (200 ml) was treated at 0° (N_2) with a soln. of $TiCl_4$ (6.6 ml, 60 mmol) in heptane (20 ml). The mixture was stirred for 12 h at r.t. Filtration and evaporation gave the crude product.

General Procedure 2 [25]. A soln. of the ketone (10 mmol), the amine (20 mmol), and TsOH (15 mg) in benzene or toluene (20 ml) was heated under reflux (*Dean-Stark*) until no more H_2O was produced (12 h). Evaporation gave the crude product.

General Procedure 3 [26]. Anh. K_2CO_3 (24 g, 174 mmol) was added to a soln. of the aldehyde (50 mmol) and the amine (50 mmol) in Et_2O (150 ml). The mixture was stirred for 12 h at r.t. Filtration and evaporation of the solvent gave the crude product.

1-(Cyclohex-1-en-1-yl)azetidine (**3**). From azetidine (2.4 g, 37 mmol), cyclohexanone (4.1 g, 42 mmol), and $TiCl_4$ (2.5 ml, 23 mmol) according to *General Procedure 1*. Bulb-to-bulb distillation of the crude product gave **3** (0.76 g, 13%). Pale yellow oil. B.p. 125°/15 Torr. Physical and spectral data: in accordance with [29].

N,N-*Diethyl(cyclohex-1-en-1-yl)amine* (**4**). From Et_2NH (44 g, 0.60 mol), cyclohexanone (9.8 g, 0.10 mol), and $TiCl_4$ (6.0 ml, 57 mmol) according to *General Procedure 1*. Distillation of the crude product gave **4** (12.1 g, 79%). Pale yellow oil. B.p. 75–77°/10 Torr. Physical and spectral data: in accordance with [27].

1-(3,4-Dihydronaphth-1-yl)pyrrolidine (**6**). From 3,4-dihydronaphthalen-1(2*H*)-one (= α-tetralone; 6.0 g, 40 mmol), pyrrolidine (8.2 ml, 100 mmol), and TsOH (100 mg) in toluene according to *General Procedure 2*. Bulb-to-bulb distillation of the crude product gave **6** (5.8 g, 73%). Pale yellow oil. B.p. $100°/10^{-2}$ Torr. Physical and spectral data: in accordance with [28].

(E)-1-(1-Phenylprop-1-en-1-yl)pyrrolidine (**7**). From 1-phenylpropan-1-one (2.7 g, 20 mmol), pyrrolidine (5.7 g, 80 mmol), and $TiCl_4$ (0.9 ml, 8 mmol) according to *General Procedure 1*. Bulb-to-bulb distillation of the crude product gave **7** (3.4 g, 90%). Pale yellow oil. B.p. 75–78°/0.5 Torr. Physical and spectral data: in accordance with [29].

(E)-4-(1-Phenylprop-1-en-1-yl)morpholine (**8**). From 1-phenylpropan-1-one (13.4 g, 100 mmol), morpholine (35 g, 0.40 mol), and TsOH (100 mg) in toluene according to *General Procedure 2*. Distillation of the crude product gave **8** (18.3 g, 90%). Colorless oil. B.p. 77–78°/0.5 Torr. Physical and spectral data: in accordance with [30].

*(E)- and (Z)-*N,N-*Diethyl(1-phenylprop-1-en-1-yl)amine* (**9**). From 1-phenylpropan-1-one (13.4 g, 100 mmol), Et_2NH (36 g, 0.60 mol), and $TiCl_4$ (7.0 ml, 57 mmol) in benzene according to *General Procedure 1*. Distillation of the crude product gave **9** (15.6 g, 82%; (*E*/*Z*) 90:10). Yellow oil. B.p. 93–102°/1 Torr. Physical and spectral data: in accordance with [31].

(E)-4-(Pent-2-en-3-yl)morpholine (**10**). From pentan-3-one (1.7 g, 20 mmol), morpholine (7.0 g, 80 mmol), and $TiCl_4$ (0.9 ml, 8 mmol) in benzene according to *General Procedure 1*. Bulb-to-bulb distillation of the crude product gave **10** (2.5 g, 80%). Colorless oil. B.p. 120–122°/10 Torr. Physical and spectral data: in accordance with [32].

(E)-1-(3-Phenylprop-1-en-1-yl)pyrrolidine (**11**). From 3-phenylpropanal (24.2 g, 180 mmol), pyrrolidine (12.8 g, 180 mmol), and K_2CO_3 (24.0 g, 170 mmol) according to *General Procedure 3*. Distillation gave **11** (28.7 g, 85%). Colorless oil. B.p. 120–124°/1 Torr. IR (film): 2960, 1650, 1360, 695. ^{1}H-NMR: 1.95 (*m*, CH_2CH_2N); 3.13 (*m*, CH_2N); 3.46 (*d*, *J* = 7.5, $PhCH_2$); 4.42 (*dt*, *J* = 14.0, 7.5, CH=CHN); 6.39 (*d*, *J* = 14.0, CH=CHN); 7.35 (*m*, 5 arom. H). ^{13}C-NMR: 24.78 (*t*); 38.74 (*t*); 48.96 (*t*); 96.88 (*d*); 125.38 (*d*); 136.66 (*d*); 143.25 (*s*). Anal. calc. for $C_{13}H_{17}N$ (187.28): C 83.37, H 9.15, N 7.48; found: C 83.49, H 9.22, N 7.51.

(E)-8-(3-Methylbut-1-en-1-yl)-1,4-dioxa-8-azaspiro[4.5]decane (**12**). From 1,4-dioxa-8-azaspiro[4.5]decane (1.4 g, 10 mmol), 3-methylbutanal (1.3 g, 15 mmol), and K_2CO_3 (1.3 g, 9.6 mmol) according to *General Procedure 3*: **12** (2.0 g, 97%). Colorless oil. The crude product was used without purification for the reductive alkylation. IR (film): 2960, 1650, 1464, 1360, 1340, 1145, 1100, 945, 915, 800. ^{1}H-NMR: 0.84 (*d*, *J* = 7.0, Me_2CH); 1.57 (*m*, CH_2N); 2.10 (*m*, Me_2CH); 2.75 (*m*, CH_2CH_2N); 3.80 (*s*, CH_2O); 4.25 (*dd*, *J* = 14.0, 7.0, CHN); 5.68 (*d*, *J* = 14.0, CHCHN). ^{13}C-NMR: 23.89 (*q*); 29.18 (*d*); 33.74 (*t*); 46.81 (*t*); 63.86 (*t*); 106.94 (*s*); 110.00 (*d*); 126.23 (*d*).

1-(6-Methylcyclohex-1-en-1-yl)pyrrolidine (**24**). From pyrrolidine (13 g, 0.18 mol), 2-methylcyclohexanone (7.0 g, 62 mmol), and TsOH (0.2 g) in benzene (60 ml) according to *General Procedure 2*. Bulb-to-bulb distillation of the crude product gave **24** (7.0 g, 67%). Pale yellow liquid. B.p. 135°/15 Torr. Physical and spectral data: in accordance with [12].

1-(5-Methylcyclopent-1-en-1-yl)morpholine (**26**). From morpholine (16 g, 0.18 mol), 2-methylcyclopentanone (8.2 g, 83 mmol), and TsOH (0.2 g) according to *General Procedure 2*. Bulb-to-bulb distillation of the crude product gave **26** (11.2 g, 80%). Colorless oil. B.p. 125°/15 Torr. Physical and spectral data: in accordance with [12].

Radical Reactions. – *General Procedure 4*. A soln. of Bu_3SnH (5.5 mmol), radical precursor (5 mmol), enamine (10 mmol), and 2,2′-azobis(isobutyronitrile) (= 2,2′-dimethyl-2,2′-azobis(propanenitrile); AIBN, 30 mg) in benzene (30 ml) was heated under reflux (TLC monitoring). AIBN was added every 5 h until complete disappearance of the radical precursor. The mixture was poured into Et_2O and extracted with 1M HCl. The aq. phase was washed (3 ×) with Et_2O/toluene 1:1, neutralized with 3M NaOH, and extracted with CH_2Cl_2 (3 ×). Drying ($MgSO_4$) and

evaporation gave the crude product. Diastereoselectivity of the reaction was determined from ^{1}H-NMR and ^{13}C-NMR spectra of the crude product.

General Procedure 5. Identical to *General Procedure 4*, except that the mixture was irradiated (sunlamp, 300 W) at 10° instead of being heated under reflux.

General Procedure 6. A soln. of Bu_3SnH (5.5 mmol) and AIBN (50 mg) in benzene (10 ml) was added over 6 h (automatic syringe) to a refluxing soln. of enamine (10 mmol) and radical precursor (5 mmol) in benzene (20 ml). The mixture was maintained under reflux for 2 h and treated as in *General Procedure 4*.

General Procedure 7. A soln. of Bu_3SnH (5.5 mmol), radical precursor (5 mmol), enamine (10 mmol), $LiClO_4$ (10 mmol), and AIBN (30 mg) in THF (30 ml) was irradiated (sunlamp, 300 W) at 10° for 6 h. The workup procedure was similar to *General Procedure 4*.

cis-*1-{2-[(Tolu-4-ylsulfonyl)methyl]cyclohexyl}pyrrolidine* (*cis*-**13**). From **1** (0.23 g, 1.5 mmol), chloromethyl tol-4-yl sulfone (0.61 g, 3.0 mmol), and Bu_3SnH (1.31 g, 4.5 mmol) according to *General Procedure 4*. FC (AcOEt/p.e. 1:2) of the crude product (*cis*/*trans* 97:3) gave diastereoisomerically pure *cis*-**13** (0.55 g, 57%). White solid. M.p. 110–111°. IR (KBr): 3060, 2920, 2860, 2780, 2760, 1600, 1450, 1290, 1140, 1080, 760, 660. ^{1}H-NMR 0.90–1.50 (*m*, 5 H); 1.53–1.80 (*m*, 6 H); 1.88–2.00 (*m*, 1 H); 2.03–2.12 (*m*, 1 H); 2.25–2.38 (*m*, CH_2CH_2N); 2.42 (*s*, Me); 2.50–2.60 (*m*, $CHCH_2SO_2$); 3.12 (*dd*, J = 11.0, 14.0, 1 H, CH_2SO_2); 3.54 (*d*, J = 14.0, 1 H, CH_2SO_2); 7.32 (*m*, 2 arom. H); 7.80 (*m*, 2 arom. H). ^{13}C-NMR: 144.15; 137.47; 129.65; 127.80; 66.36; 52.31; 51.23; 32.09; 27.39; 27.14; 25.11; 24.77; 23.05; 19.60. MS: 321 (2, M^+), 166 (100), 124 (2), 110 (6), 97 (5), 91 (25), 77 (2), 65 (11), 55 (7). Anal. calc. for $C_{18}H_{27}NO_2S$ (321.49): C 67.25, H 8.47, N 4.36, S 9.97; found: C 67.32, H 8.44, N 4.39, S 9.90.

1-[2-(Cyanomethyl)cyclohexyl]pyrrolidine (= *2-(Pyrrolidin-1-yl)cyclohexane-1-acetonitrile*; **14**). From **1** (0.15 g, 1.0 mmol), (phenylthio)acetonitrile (0.30 g, 2.0 mmol), and Bu_3SnH (0.73 g, 2.5 mmol) according to *General Procedure 6*. Bulb-to-bulb distillation of the crude product (*cis*/*trans* 92:8) gave **14** (0.17 g, 88%). Inseparable mixture of isomers. Colorless oil. B.p. 90–100°/0.1 Torr. IR (film): 3018, 2933, 2862, 2792, 2246, 1452, 1219, 1214, 885. ^{1}H-NMR: 1.04–1.33 (*m*, 3 H); 1.51 (*m*, 2 H); 1.74 (*m*, 6 H); 2.00 (*m*, 1 H); 2.06 (*dt*, J = 3.5, 11.0, CHN); 2.35 (*m*, 2 H); 2.47 (*m*, 4 H); 2.52 (*m*, 1 H, CH_2CN). ^{13}C-NMR: 13.95 (*t*); 19.39 (*t*); 23.04 (*t*); 24.08 (*t*); 26.30 (*t*); 27.74 (*t*); 34.74 (*t*); 51.50 (*t*); 65.30 (*d*); 120.58 (*s*). MS: 192 (8, M^+), 152 (4), 124 (1), 110 (100), 97 (17), 84 (4), 70 (5), 55 (3). Anal. calc. for $C_{12}H_{20}N_2$ (192.30): C 51.30, H 5.50, N 56.62; found: C 51.20, H 5.45, N 16.54.

1-{2-[(Methoxycarbonyl)methyl]cyclohexyl}pyrrolidine (= *Methyl 2-(Pyrrolidin-1-yl)cyclohexane-1-acetate*; **15**). From **1** (0.15 g, 1.0 mmol), methyl (phenylthio)acetate (0.36 g, 2.0 mmol), and Bu_3SnH (0.73 g, 2.5 mmol) according to *General Procedure 6*. After washing with Et_2O/toluene 1:1, the aq. acidic phase was evaporated. The residue was dissolved in MeOH (20 ml), treated with Me_3Si (0.30 ml, 2.4 mmol) and allowed to stand at r.t. for 12 h. After evaporation, the residue was treated with 3M NaOH (30 ml) and extracted with CH_2Cl_2 (3 × 40 ml). Drying ($MgSO_4$) and evaporation gave the crude product (*cis*/*trans* 98:2) [35]. Bulb-to-bulb distillation gave **15** (0.17 g, 74%). Inseparable mixture of isomers. B.p. 95–110°/0.2 Torr. IR (film): 2930, 2685, 1740, 1450, 1290, 1170, 1130, 1020, 830. ^{1}H-NMR: 1.16–1.49 (*m*, 5 H); 1.60–1.82 (*m*, 7 H); 1.93–2.06 (*dt*, J = 3.75, 11.5, CHN); 2.36 (*dd*, J = 11.1, 1 H, CH_2COOMe); 2.41–2.53 (*m*, CH_2N, $CHCH_2COOMe$); 2.63 (*dd*, J = 2.1, 1 H, CH_2COOMe); 3.66 (*s*, MeO). ^{13}C-NMR: 19.86 (*t*); 23.13 (*t*); 25.24 (*t*); 26.91 (*t*); 28.45 (*t*); 30.54 (*t*); 34.18 (*d*); 51.30 (*d*); 51.71 (*t*); 66.56 (*d*); 174.88 (*s*). MS: 225 (13, M^+), 224 (2), 194 (4), 182 (2), 124 (2), 110 (100), 97 (10), 84 (6), 70 (8), 55 (9). Anal. calc. for $C_{13}H_{23}NO_3$ (225.33): C 69.29, H 10.29, N 6.22; found: C 69.32, H 10.26, N 6.17.

1-[2-(Tridecafluorohexyl)cyclohexyl]pyrrolidine (**16**). From **1** (1.30 g, 8.5 mmol), tol-4-yl tridecafluorohexyl sulfide (4.0 g, 9.0 mmol), and Bu_3SnH (3.8 g, 13 mmol) according to *General Procedure 4*. FC (AcOEt/p.e. 1:1) of the crude product (*cis*/*trans* 90:10 by GC) gave **16** (2.3 g, 58%). Inseparable mixture of isomers. IR (film): 2960, 2880, 1460, 1250, 1160, 810, 790, 740, 730, 700, 660. ^{1}H-NMR: 1.35–2.10 (*m*, 14 H); 2.45–2.70 (*m*, CH_2N). ^{13}C-NMR: 23.28 (*t*); 29.31 (*t*); 41.45 (*dm*); 52.35 (*t*); 62.68 (*d*). MS: 471 (3, M^+), 452 (3), 202 (5), 11 (8), 110 (100), 108 (2), 98 (2), 97 (23), 96 (9), 82 (2), 81 (2), 77 (3), 71 (2), 70 (14), 69 (13), 68 (4), 56 (2), 55 (6), 54 (3). Anal. calc. for $C_{16}H_{18}F_{13}N$ (471.31): C 40.78, H 3.85, N 2.97; found: C 40.69, H 3.90, N 3.08.

4-{2-[(Tol-4-ylsulfonyl)methyl]cyclohexyl}morpholine (**17**). From **2** (0.33 g, 2.0 mmol), chloromethyl tol-4-yl sulfone (0.19 g, 0.90 mmol), and Bu_3SnH (0.58 g, 2.0 mmol) according to *General Procedure 4*. FC (AcOEt/p.e. 1:1) of the crude product (*cis*/*trans* 96:4) gave **17** (0.42 g, 62%). White solid. M.p. 110–111°. IR (KBr): 3060, 2940, 2880, 2810, 1600, 1460, 1300, 1290, 1140, 1115, 1090. ^{1}H-NMR: 0.70–0.90 (*qd*, J = 12.5, 3.5, 1 H); 1.10–1.55 (*m*, 4 H); 1.70–1.85 (*m*, 2 H); 1.95–2.10 (*m*, 2 H); 2.20–2.35 (*m*, CH_2N); 2.45 (*s*, Me); 2.52–2.62 (*m*, H–C(2)); 3.08 (*dd*, J = 10.5, 14.0, 1 H, CH_2SO_2); 3.52 (*m*, CH_2O); 3.62 (*d*, J = 14.0, 1 H, CH_2SO_2); 7.37 (*m*, 2 arom. H); 7.80 (*m*, 2 arom. H). ^{13}C-NMR: 19.57; 21.48; 24.43; 24.85; 27.41; 29.80; 50.19; 52.47; 64.81; 67.14; 127.90; 129.76; 137.15; 144.32. MS: 337 (2, M^+), 182 (100), 139 (1), 124 (6), 113 (1), 98 (1), 91 (4), 81 (1), 67 (2), 55 (5). Anal. calc. for $C_{18}H_{27}NO_3S$ (337.49): C 64.06, H 8.06, N 4.15, S 9.50; found: C 64.09, H 8.06, N 4.20, S 9.59.

1-{2-[(Tol-4-ylsulfonyl)methyl]cyclohexyl}azetidine (**18**). From **3** (0.16 g, 1.1 mmol), chloromethyl tol-4-yl sulfone (0.30 g, 1.4 mmol), and Bu_3SnH (0.29 g, 1.0 mmol) according to *General Procedure 4*. Filtration of the crude product through silica gel (AcOEt/p.e. 1:2) gave **18** (0.32 g, 10%). Mixture of isomers (*cis/trans* > 95:5). ^{1}H-NMR: 0.60–1.00 (*m*, 1 H); 1.10–2.20 (*m*, 10 H); 2.30–2.45 (*m*, 1 H); 2.46 (*s*, Me); 2.85–3.05 (*m*, CH_2N); 3.04 (*dd*, *J* = 10.5, 14.5, 1 H, CH_2SO_2); 3.44 (*d*, *J* = 14.5, 1 H, CH_2SO_2); 7.34 (*m*, 2 arom. H); 7.80 (*m*, 2 arom. H). ^{13}C-NMR: 144.18; 137.27; 129.63; 127.85; 68.75; 52.83; 52.57; 29.47; 27.21; 24.14; 23.99; 21.48; 19.63; 16.88. Anal. calc. for $C_{17}H_{25}NO_2S$ (307.46): C 66.41, H 8.20, N 4.56, S 10.43; found: C 66.35, H 8.08, N 4.62, S 10.37.

cis-N,N-*Diethyl{2-[(phenylsulfonyl)methyl]cyclohexyl}amine* (**19**). From **4** (0.61 g, 4.0 mmol), chloromethyl phenyl sulfone (0.38 g, 2.0 mmol), and Bu_3SnH (0.64 g, 2.2 mmol) according to *General Procedure 4*. FC (AcOEt/p.e. 1:2) of the crude product (*cis/trans* 91:9) gave diastereoisomerically pure *cis*-**19** (0.47 g, 76%). IR (film): 2920, 1450, 1300, 1150, 1090. ^{1}H-NMR: 0.77 (*t*, *J* = 6.0, Me); 0.90 (*m*, 1 H); 1.10–1.49 (*m*, 4 H); 1.7 (*m*, 2 H); 2.10 (*m*, 1 H); 2.30–2.48 (*m*, 5 H); 2.55 (*m*, CHN); 3.08 (*dd*, *J* = 11.0, 14.0, 1 H, CH_2SO_2); 3.55 (*d*, *J* = 14.0, 1 H, CH_2SO_2); 7.49–7.91 (*m*, 5 arom. H). ^{13}C-NMR: 10.65 (*q*); 19.54 (*t*); 25.25 (*t*); 25.53 (*t*); 27.37 (*t*); 30.88 (*d*); 40.93 (*t*); 52.26 (*t*); 60.59 (*d*); 127.71 (*d*); 129.02 (*d*); 133.20 (*d*); 140.17 (*s*). MS: 308 (2, M^+), 169 (10), 168 (100), 86 (11), 84 (22), 77 (47), 71 (19), 67 (10), 56 (22), 51 (21). Anal. calc. for $C_{17}H_{27}NO_2S$ (309.47): C 65.98, H 8.79, N 4.53, S 10.36; found: C 65.97, H 8.74, N 4.54, S 10.40.

4-{2-[(Tol-4-ylsulfonyl)methyl]cyclopentyl}morpholine (**20**). From **5** (0.77 g, 5.0 mmol), chloromethyl tol-4-yl sulfone (0.19 g, 0.9 mmol), and Bu_3SnH (0.44 g, 1.5 mmol) according to *General Procedure 4*. FC (AcOEt/p.e. 1:2) of the crude product (*cis/trans* 84:16) gave diastereoisomerically pure *cis*-**20** (1.70 g, 54%). M.p. 114–115°. IR (KBr): 2950, 2840, 1595, 1450, 1290, 1140, 1120, 1080, 890. ^{1}H-NMR: 1.20 (*m*, 1 H); 1.60–1.85 (*m*, 5 H); 2.20–2.40 (*m*, 5 H); 2.45 (*s*, Me); 2.55 (*m*, 1 H); 2.70 (*dd*, *J* = 10.0, 14.0, 1 H, CH_2SO_2); 3.60 (*m*, CH_2O); 7.30–7.80 (*m*, 5 arom. H). ^{13}C-NMR: 19.92; 27.08; 28.54; 34.96; 52.48; 54.36; 66.86; 69.38; 71.95; 128.04; 129.83; 137.03; 144.48. MS: 323 (0.4, M^+), 169 (11), 168 (100), 126 (28), 91 (33), 86 (7), 65 (12), 55 (11). Anal. calc. for $C_{17}H_{24}NO_3S$ (323.45): C 63.32, H 7.50, N 4.34, S 9.94; found: C 63.37, H 7.56, N 4.33, S 9.78.

Isomer *trans*-**20** was also isolated. M.p. 103–105°. ^{1}H-NMR: 1.20–1.70 (*m*, 5 H); 1.90–2.20 (*m*, 2 H); 2.30–2.40 (*m*, 5 H); 2.45 (*s*, Me); 2.95 (*dd*, *J* = 10.0, 14.0, 1 H, CH_2SO_2); 3.45 (*dd*, *J* = 2.0, 14.0, 1 H, CH_2SO_2); 3.60 (*m*, CH_2O); 7.30–7.80 (*m*, 5 arom. H).

cis-*1-{1,2,3,4-Tetrahydro-2-[(phenylsulfonyl)methyl]naphth-1-yl}pyrrolidine* (*cis*-**21**). From **6** (0.20 g, 1.0 mmol), chloromethyl phenyl sulfone (0.38 g, 2.0 mmol), and Bu_3SnH (0.73 g, 2.5 mmol) according to *General Procedure 6*. FC (AcOEt/p.e. 1:3) of the crude product (*cis/trans* 75:25) gave diastereoisomerically pure *cis*-**21** (0.18 g, 52%). IR (KBr): 3020, 2960, 1450, 1300, 1150, 1090, 890. ^{1}H-NMR: 1.50–1.70 (*m*, CH_2N); 1.72–1.95 (*m*, 2 H); 2.30–2.90 (*m*, 7 H); 3.06 (*dd*, *J* = 6.0, 14.5, 1 H, CH_2SO_2); 3.82 (*dd*, *J* = 6.0, 14.5, 1 H, CH_2SO_2); 3.98 (*d*, *J* = 4.0, CHN); 7.05–8.00 (*m*, 9 arom. H). ^{13}C-NMR: 23.75 (*t*); 24.78 (*t*); 28.04 (*t*); 35.48 (*d*); 52.36 (*t*); 59.21 (*t*); 59.97 (*d*); 125.03 (*d*); 126.99 (*d*); 127.73 (*d*); 128.64 (*d*); 129.14 (*d*); 129.49 (*d*); 133.34 (*d*); 135.51 (*s*); 136.31 (*s*); 140.16 (*s*). MS: 356 (1, M^+), 215 (29), 214 (100), 172 (13), 145 (13), 144 (11), 143 (15), 130 (12), 129 (12), 128 (30), 117 (12), 115 (14), 77 (18), 70 (13). Anal. calc. for $C_{21}H_{25}NO_2S$ (355.50): C 70.95, H 7.09, N 3.94, S 9.02; found: C 70.89, H 7.00, N 4.01, S 9.03.

cis-*1-{1,2,3,4-Tetrahydro-2-[(methoxycarbonyl)methyl]naphth-1-yl}pyrrolidine* (= *Methyl* cis-*1,2,3,4-Tetrahydro-1-(pyrrolidin-1-yl)naphthalene-2-acetate*; *cis*-**22**). From **6** (0.20 g, 1.0 mmol), methyl (phenylthio)acetate (0.36 g, 2.0 mmol), and Bu_3SnH (0.73 g, 2.5 mmol) according to *General Procedure 6*. After washing with Et_2O/toluene 1:1, the aq. acidic phase was evaporated. The residue was dissolved in MeOH (20 ml), treated with Me_3SiCl (0.30 ml, 2.4 mmol), and allowed to stand at r.t. for 12 h [33]. Evaporation, heating under reflux with methyloxirane (40 ml) for 4 h, evaporation, and FC (AcOEt/p.e. 1:5) of the crude product (*cis/trans* 91:9) gave diastereoisomerically pure *cis*-**22** (0.50 g, 63%). IR (film): 2940, 1740, 1435, 1350, 1170. ^{1}H-NMR: 1.50–1.80 (*m*, 6 H); 2.20–2.90 (*m*, 9 H); 3.67 (*s*, MeO); 3.89 (*d*, *J* = 3.5, CHN); 7.05–7.20 (*m*, 4 arom. H). ^{13}C-NMR: 23.89; 24.57; 28.51; 37.36; 37.54; 51.21; 52.52; 60.32; 124.82; 126.67; 128.67; 129.67; 136.72; 136.90; 174.04. MS: 273 (19, M^+), 173 (40), 172 (100), 158 (18), 145 (11), 144 (31), 143 (12), 130 (31), 129 (50), 128 (97), 117 (12), 116 (10.1), 115 (16), 104 (13), 72 (39), 70 (14). Anal. calc. for $C_{23}H_{26}N_4O_9$ (502.49): C 54.98, H 5.22, N 11.15; found: 54.89, H 5.18, N 11.11.

1-(2-Methylcyclohexyl)pyrrolidine [34] (**23**). A soln. of *cis*-**13** (0.64 g, 2.0 mmol), anh. Na_2HPO_4 (1.15 g, 8.1 mmol), and 6% Na/Hg amalgam (3 g) in abs. MeOH (20 ml) was stirred at r.t. for 2 days. MeOH was evaporated, the residue dissolved in CH_2Cl_2 (50 ml), and the soln. washed with 1M NaOH (20 ml), dried ($MgSO_4$), and evaporated. Bulb-to-bulb distillation gave *cis*-**23** (0.02 g, 6%). Colorless oil. B.p. 100°/10 Torr. GC (100°): 10.1 min. Physical and spectral data: in accordance with [12]. ^{1}H-NMR: 0.93 (*d*, *J* = 7.0, Me); 1.1–1.6 (*m*, 7 H); 1.70 (*m*, 1 H); 1.65–1.82 (*m*, CH_2CH_2N); 1.90 (*dt*, *J* = 11.0, 3.8, CHN); 2.07 (*m*, MeC*H*); 2.40–2.60 (*m*, 4 H, CH_2N).

A *cis/trans* (65:35) mixture **23** was prepared by reduction of enamine **24** ($NaBH_3CN$) according to [12]. GC (100°): 10.1 (*cis*), 8.5 min (*trans*).

1-(2-Methylcyclopentyl)morpholine [34] (**25**). As described for **23**, with *cis*-**20** (59 mg, 0.2 mmol), anh. Na_2HPO_4 (0.1 g, 0.8 mmol), 6% Na/Hg amalgam (0.5 g), abs. MeOH (10 ml; stirring until no *cis*-**20** left; workup with CH_2Cl_2 (20 ml) and 1M NaOH (10 ml)): *cis*-**25** (37 mg, 90%). Colorless oil. B.p. 100°/10 Torr. Physical and spectral data: in accordance with [12]. GC (100°): 10.0 min. ^{1}H-NMR: 0.82 (*d*, *J* = 7.0, Me); 1.30–1.90 (*m*, 6 H); 2.15 (*sext.*, *J* = 6.5–7.0, MeC*H*); 2.28 (*ddd*, *J* = 10.8, 7.0, 5.5, CHN); 2.43 (*m*, CH_2O). ^{13}C-NMR: 13.60 (*q*); 20.11 (*t*); 20.39 (*t*); 31.21 (*t*); 34.07 (*d*); 53.33 (*t*); 66.91 (*t*); 70.46 (*d*).

Similar treatment of *trans*-**20** gave *trans*-**25**. GC (100°): 9.5 min. A *cis/trans* (98:2) mixture **25** was prepared by reduction of enamine **26** ($NaBH_4$/AcOH) according to [12]. GC (100°): 10.0 (*cis*), 9.5 min (*trans*).

(1)- and (u)-3-Methyl-4-phenyl-4-(pyrrolidin-1-yl)butanenitrile (**27**). *a*) From **7** (3.8 g, 20 mmol), (phenylthio)acetonitrile (1.50 g, 10 mmol), and Bu_3SnH (3.2 g, 11 mmol) according to *General Procedure 6*. FC (AcOEt/p.e. 1:3) of the crude product (66% ds) gave **27** (1.8 g, 77%). Inseparable mixture of isomers.

b) From **7** (3.8 g, 20 mmol), (phenylthio)acetonitrile (1.50 g, 10 mmol), and Bu_3SnH (3.2 g, 11 mmol) according to *General Procedure 5*. FC (AcOEt/p.e. 1:3) of the crude product (77% ds) gave **27** (1.4 g, 62%). By analogy to **29** and **31**, the rel. configuration (*u*) was attributed to the major isomer. IR (film): 2970, 2800, 2250, 1490, 1455, 1425, 1360, 1140, 1115, 760, 710. ^{1}H-NMR: 0.95 (*d*, *J* = 7.0, Me); 1.63–1.78 (*m*, CH_2CH_2N); 1.84 (*m*, 1 H, CH_2CN, (*u*)); 2.15–2.33 (*m*, CH_2CN, (*l*)); 2.35–2.57 (*m*, CH_2CH_2); 2.86 (*dd*, *J* = 16.5, 3.0, 1 H, CH_2CN, (*u*)); 3.14 (*d*, *J* = 5.0, CHN, (*u*)); 3.35 (*d*, *J* = 7.5, CHN, (*l*)); 7.10–7.49 (*m*, 5 arom. H). ^{13}C-NMR: 15.37 (*t*); 17.57 (*q*, (*u*)); 18.70 (*q*, (*l*)); 23.00 (*t*, (*l*)); 23.26 (*t*, (*u*)); 32.96 (*d*, (*l*)); 33.68 (*t*, (*u*)); 50.21 (*t*, (*l*)); 52.09 (*t*, (*u*)); 70.94 (*d*, (*l*)); 73.51 (*d*, (*u*)); 119.44 (*s*, (*l*)); 120.01 (*s*, (*u*)); 127.49 (*d*, (*l*)); 127.96 (*d*, (*u*)); 129.03 (*d*, (*u*)); 129.31 (*d*, (*l*)); 136.41 (*s*, (*l*)); 137.80 (*s*, (*u*)). MS: 228 (0.5, M^+), 161 (12), 160 (100), 118 (2), 117 (4), 115 (3), 104 (3), 103 (2), 92 (2), 91 (23), 89 (2), 79 (2), 78 (2), 77 (5), 70 (2), 65 (3), 55 (3), 51 (2). Anal. calc. for $C_{15}H_{20}N_2$ (228.34): C 78.90, H 8.83, N 12.27; found: C 78.92, H 8.73, N 12.20.

Methyl (1)- and (u)-3-Methyl-4-phenyl-4-(pyrrolidin-1-yl)butanoate (**28**). *a*) From **7** (1.9 g, 10 mmol), methyl (phenylthio)acetate (0.91 g, 5.0 mmol), and Bu_3SnH (1.6 g, 5.5 mmol) according to *General Procedure 4*. After washing with Et_2O/toluene 1:1, the aq. acidic phase was evaporated. The residue was dissolved in MeOH (40 ml), treated with Me_3Si (3.0 ml, 24 mmol), and allowed to stand at r.t. for 12 h [33]. After evaporation, the residue was treated with 3M NaOH (50 ml) and extracted with CH_2Cl_2 (3 × 50 ml). After drying ($MgSO_4$) and evaporation, FC (AcOEt/p.e. 1:3) of the crude product (64% ds) gave **28** (0.69 g, 53%).

b) From **7** (1.9 g, 10 mmol), *tert*-butyl (phenylthio)acetate (1.12 g, 5.0 mmol), and Bu_3SnH (1.6 g, 5.5 mmol) according to *General Procedure 4*. Workup as under *a*). FC of the crude product (60% ds) gave **28** (0.35 g, 27%). Inseparable mixture of isomers. IR (film): 2965, 2780, 1740, 1550, 1430, 1370, 1250, 1170, 1010, 890, 765, 710. ^{1}H-NMR: 0.77 (*d*, *J* = 7.0, Me, major); 0.86 (*d*, *J* = 6.5, Me, minor); 1.60–1.96 (*m*, CH_2CH_2N, 1 H of CH_2COOMe, major); 2.35–2.70 (*m*, CH_2N, CH_2COOMe, minor); 2.92 (*dd*, *J* = 15.0, 3.0, 1 H, CH_2COOMe, major); 3.06 (*d*, *J* = 4.5, CHN, major); 3.18 (*d*, *J* = 6.5, CHN, minor); 3.65 (*s*, MeO, major); 3.68 (*s*, MeO, minor); 7.20–7.35 (*m*, 5 arom. H). ^{13}C-NMR: 15.15 (*q*, minor); 17.95 (*q*, major); 23.08 (*t*, minor); 23.27 (*t*, major); 32.77 (*d*, minor); 33.21 (*d*, major); 35.28 (*t*, minor); 39.83 (*t*, minor); 50.97 (*q*, major); 51.39 (*q*, minor); 52.33 (*t*); 72.82 (*d*, minor); 74.67 (*d*, major); 126.93 (*d*); 127.59 (*d*); 129.17 (*d*); 129.43 (*d*); 138.20 (*s*, minor); 139.48 (*s*, major); 173.85 (*s*, minor); 174.55 (*s*, major). MS: 261 (0.3, M^+), 161 (12), 160 (100), 115 (3), 105 (2), 104 (3), 103 (2), 91 (23), 77 (4), 70 (2), 65 (2), 59 (3), 55 (4). Anal. calc. for $C_{16}H_{23}NO_2$ (261.37): C 73.53, H 8.87, N 5.36; found: C 73.66, H 8.80, N 5.47.

(1)- and (u)-1-[2-Methyl-1-phenyl-3-(phenylsulfonyl)propyl]pyrrolidine (**29**). *a*) From **7** (3.7 g, 20 mmol), chloromethyl phenyl sulfone (1.9 g, 10 mmol), and Bu_3SnH (3.2 g, 11 mmol) according to *General Procedure 4*. FC (AcOEt/p.e. 1:2) of the crude product (72% ds) and recrystallization (Et_2O/p.e.) gave diastereoisomerically pure (*l*)-**29** (1.8 g, 79%).

b) From **7** (3.7 g, 20 mmol), chloromethyl phenyl sulfone (1.9 g, 10 mmol), and Bu_3SnH (3.2 g, 11 mmol) to *General Procedure 5*. FC (AcOEt/p.e. 1:2) of the crude product (81% ds) and recrystallization (Et_2O/p.e.) gave diastereoisomerically pure (*l*)-**29** (1.1 g, 33%).

c) From **7** (3.7 g, 20 mmol), chloromethyl phenyl sulfone (1.9 g, 10 mmol), Bu_3SnH (3.2 g, 11 mmol), and $LiClO_4$ (2.1 g, 20 mmol) according to *General Procedure 7*. FC (AcOEt/p.e. 1:2) of the crude product (88% ds) gave (*l*)-**29** (1.1 g, 33%).

(*l*)-**29** (major): White solid. M.p. 168–169°. IR: 2970, 2800, 1455, 1450, 1300, 1090, 770, 750, 730, 710, 690, 645, 600. ^{1}H-NMR: 0.90 (*d*, *J* = 6.0, Me); 1.65–2.29 (*m*, CH_2CH_2N); 2.65 (*m*, 1 H, CH_2SO_2, MeC*H*); 3.00 (*d*, *J* = 4.0, CHN); 3.90 (*d*, *J* = 13.0, 1 H, CH_2SO_2); 7.08–7.97 (*m*, 10 arom. H). ^{13}C-NMR: 15.92 (*q*); 22.83 (*t*); 30.66 (*d*); 49.78 (*t*); 60.17 (*t*); 71.00 (*d*); 127.14 (*d*); 127.70 (*d*); 129.14 (*d*); 129.29 (*d*); 133.43 (*d*); 136.40 (*s*); 140.04 (*s*).

CI-MS: 344 (31, M^+), 218 (1), 161 (14), 160 (100), 131 (5), 104 (5), 91 (62), 77 (61). Anal. calc. for $C_{20}H_{25}NO_2S$ (343.49): C 69.94, H 7.34, N 4.08, S 9.33; found: C 69.89, H 7.27, N 4.04, S 9.27.

(*u*)-**29** (minor): Colorless oil. ^{1}H-NMR: 0.96 (*d*, *J* = 6.0, Me); 1.60–2.27 (*m*, 8 H, CH_2CH_2N); 2.69 (*m*, 1 H of CH_2SO_2, MeC*H*); 3.27 (*d*, *J* = 7.0, CHN); 3.64 (*m*, 1 H of CH_2SO_2); 7.10–7.93 (*m*, 10 arom. H). ^{13}C-NMR: 17.83 (*q*); 23.13 (*t*); 31.20 (*d*); 52.21 (*t*); 57.07 (*t*); 74.82 (*d*); 127.22 (*d*); 127.76 (*d*); 128.67 (*d*); 129.13 (*d*); 133.40 (*d*); 138.71 (*s*); 140.16 (*s*).

*(l)- and (u)-1-{3-[(*tert*-Butyl)sulfonyl]-2-methyl-1-phenylpropyl}pyrrolidine* (**30**). *a*) From **7** (0.37 g, 2.0 mmol), *tert*-butyl (phenylselenenyl)methyl sulfone, and Bu_3SnH (0.32 g, 1.1 mmol) according to *General Procedure 4*. FC (AcOEt/p.e. 1:2) of the crude product (74% ds) gave diastereoisomerically pure (*l*)-**30** (0.19 g, 58%).

b) From **7** (0.37 g, 2.0 mmol), *tert*-butyl (phenylselenenyl)methyl sulfone, and Bu_3SnH (0.32 g, 1.1 mmol) according to *General Procedure 5*. FC (AcOEt/p.e. 1:2) of the crude product (85% ds) gave (*l*)-**30** (0.10 g, 30%).

c) From **7** (0.37 g, 2.0 mmol), *tert*-butyl (phenylselenenyl)methyl sulfone, Bu_3SnH (0.32 g, 1.1 mmol), and $LiClO_4$ (0.21 g, 2.0 mmol) according to *General Procedure 7*. FC (AcOEt/p.e. 1:2) of the crude product (87% ds) and recrystallization (CH_2Cl_2/p.e.) gave (*l*)-**30** (80 mg, 26%).

(*l*)-**30** (major): M.p. 154–155.5°. IR (film): 2945, 2760, 1670, 1445, 1270, 1100, 755, 700. ^{1}H-NMR: 0.93 (*d*, *J* = 6.5, Me); 1.33 (*s*, *t*-Bu); 1.65 (*m*, CH_2CH_2N); 2.19–2.53 (*m*, CHN, 1 H of CH_2SO_2); 2.85 (*m*, MeC*H*); 3.03 (*d*, *J* = 5.0, CHN); 3.70 (*d*, *J* = 13.0, 1 H, CH_2SO_2); 7.10–7.28 (*m*, 5 arom. H). ^{13}C-NMR: 18.35 (*q*); 23.18 (*q*); 23.18 (*t*); 29.69 (*d*); 45.24 (*t*); 52.24 (*t*); 59.03 (*s*); 74.65 (*d*); 127.17 (*d*); 127.75 (*d*); 128.57 (*d*); 139.19 (*s*). CI-MS: 324 (23, M^+), 161 (13), 160 (100), 104 (5), 91 (37), 77 (6). Anal. calc. for $C_{18}H_{29}NO_2S$ (323.50): C 66.83, H 9.04, N 4.33, S 9.91; found: C 66.96, H 9.02, N 4.38, S 9.88.

(*u*)-**30** (minor): Colorless oil. ^{1}H-NMR: 1.00 (*d*, *J* = 6.5, Me); 1.33 (*s*, *t*-Bu); 1.57 (*m*, CH_2CH_2N); 2.35 (*m*, CH_2N, 1 H of CH_2SO_2); 2.90 (*m*, MeC*H*); 3.34 (*d*, *J* = 7.0, CHN); 3.38 (*dd*, *J* = 13.0, 4.0, 1 H, CH_2SO_2); 7.10–7.28 (*m*, 5 arom. H). ^{13}C-NMR: 16.54 (*q*); 23.24 (*q*); 23.24 (*t*); 29.22 (*d*); 48.70 (*t*); 49.88 (*t*); 52.32 (*s*); 71.08 (*d*); 127.14 (*d*); 127.70 (*d*); 128.63 (*d*); 129.45 (*d*); 136.85 (*s*).

(l)-4-[2-Methyl-1-phenyl-3-(phenylsulfonyl)propyl]morpholine (**31**). From **8** (2.03 g, 10 mmol), chloromethyl phenyl sulfone (0.95 g, 5.0 mmol), and Bu_3SnH (1.60 g, 5.5 mmol) according to *General Procedure 5*. FC (AcOEt/p.e. 1:2) of the crude product (80% ds) and recrystallization (CH_2Cl_2/p.e.) gave diastereoisomerically pure (*l*)-**31** (0.74 g, 41%). White solid. M.p. 138.5–140°. IR (film): 2960, 2930, 1730, 1450, 1305, 1145, 1120. ^{1}H-NMR: 0.95 (*d*, *J* = 6.0, Me); 2.20 (*m*, CH_2N); 2.70 (*m*, MeC*H*, CH_2SO_2); 3.01 (*d*, *J* = 7.0, CHN); 3.56 (*m*, CH_2O); 7.00–7.90 (*m*, 10 arom. H). ^{13}C-NMR: 17.88 (*q*); 28.01 (*d*); 50.89 (*t*); 57.38 (*t*); 66.84 (*t*); 74.17 (*d*); 127.45 (*d*); 127.73 (*d*); 127.99 (*d*); 128.79 (*d*); 129.14 (*d*); 133.46 (*d*); 136.43 (*s*); 139.75 (*s*). CI-MS: 360 (24, M^+), 243 (4), 177 (11), 176 (100), 117 (4), 105 (6), 91 (23), 78 (7), 77 (27). Anal. calc. for $C_{20}H_{25}NO_3S$ (359.49): C 66.82, H 7.01, N 3.90, S 8.92; found: C 66.69, H 7.02, N 3.94, S 8.73.

*(l)- and (u)-4-{3-[(*tert*-Butyl)sulfonyl]-2-methyl-1-phenylpropyl}morpholine* (**32**). From **8** (0.81 g, 4.0 mmol), *tert*-butyl (phenylselenenyl)methyl sulfone (0.58 g, 2.0 mmol), and Bu_3SnH (0.64 g, 2.2 mmol) according to *General Procedure 5*. FC (AcOEt/p.e. 1:2) of the crude product (87% ds) gave **32** (0.33 g, 48%). Inseparable mixture of isomers. IR (film): 2970, 2850, 1450, 1280, 1120. ^{1}H-NMR: 0.95 (*d*, *J* = 6.5, Me, minor); 1.03 (*d*, *J* = 6.5, Me, major); 1.29 (*s*, *t*-Bu, major); 1.50 (*s*, *t*-Bu, minor); 2.25–2.50 (*m*, CH_2N, 1 H of CH_2SO_2); 2.98 (*m*, MeC*H*); 3.12 (*d*, *J* = 7.0, CHN, major); 3.43 (*d*, *J* = 13.0, 1 H of CH_2SO_2, major); 3.60 (*m*, CH_2O); 7.00–7.30 (*m*, 5 arom. H). ^{13}C-NMR: 18.31 (*q*, minor); 18.43 (*q*, major); 22.95 (*q*, major); 32.10 (*q*, minor); 26.29 (*d*); 45.45 (*t*); 50.89 (*t*); 58.85 (*s*); 66.86 (*t*, major); 67.09 (*t*, minor); 73.71 (*d*, minor); 74.09 (*d*, major); 127.40 (*d*); 127.78 (*d*, minor); 127.96 (*d*, major); 128.70 (*d*, major); 128.92 (*d*, minor); 134.33 (*s*, minor); 136 (*s*, major). CI-MS: 218 (1), 177 (11), 176 (100), 105 (9), 91 (23), 86 (42), 84 (52), 77 (10). Anal. calc. for $C_{18}H_{29}NO_3S$ (339.50): C 63.68, H 8.61, N 4.13, S 9.44; found: C 63.58, H 8.50, N 4.15, S 9.37.

(l)- and (u)-N,N-Diethyl[2-methyl-1-phenyl-3-(phenylsulfonyl)propyl]amine (**33**). From **9** (1.89 g, 10 mmol), chloromethyl phenyl sulfone (0.95 g, 5.0 mmol), and Bu_3SnH (1.60 g, 5.5 mmol) according to *General Procedure 5*. FC (AcOEt/p.e. 1:4) of the crude product (68% ds) gave **33** (0.35 g, 20%). Inseparable mixture of isomers. IR (film): 2970, 2930, 1450, 1380, 1150, 1090. ^{1}H-NMR: 0.93 (*t*, *J* = 7.0, *Me*CH_2); 1.12 (*d*, *J* = 6.0, *Me*CH); 1.91 (*m*, MeCH_2N, minor); 2.18, 2.46 (*m*, MeCH_2N, major); 2.68 (*m*, 1 H of CH_2SO_2, CHN, MeC*H*, major); 3.31 (*m*, 1 H of CH_2SO_2, major); 4.28 (*d*, *J* = 13.0, 1 H of CH_2SO_2, minor); 6.90–8.00 (*m*, 10 arom. H). ^{13}C-NMR: 11.66 (*q*, major); 13.62 (*q*, minor); 18.09 (*q*); 29.07 (*d*, minor); 29.20 (*d*, major); 41.87 (*t*, major); 42.48 (*t*, minor); 58.72 (*t*, major); 59.92 (*t*, minor); 67.88 (*d*, minor); 68.59 (*d*, major); 127.13 (*d*, minor); 127.82 (*d*, major); 127.86 (*d*); 128.82 (*d*); 128.93 (*d*, minor); 129.11 (*ds*, major); 133.38 (*d*); 137.11 (*s*); 139.90 (*s*). CI-MS: 257 (32), 256 (9), 113 (7), 112 (100), 91 (18), 84 (4), 70 (4). Anal. calc. for $C_{20}H_{27}NO_2S$ (345.52): C 69.53, H 7.88, N 4.05, S 9.28; found: C 69.66, H 7.80, N 4.08, S 9.21.

*(1)- and (u)-*N,N-*Diethyl{3-[(*tert*-butyl)sulfonyl]-2-methyl-1-phenylpropyl}amine* (**34**). From **9** (0.76 g, 4.0 mmol), *tert*-butyl (phenylselenenyl)methyl sulfone (0.58 g, 2.0 mmol), and Bu_3SnH (0.74 g, 2.2 mmol) according to *General Procedure 5*. FC (AcOEt/p.e. 1:3) of the crude product (76% ds) gave **34** (0.13 g, 20%). Inseparable mixture of isomers. IR (film): 2980, 2940, 1460, 1450, 1290, 1120, 755, 660. ^{1}H-NMR: 0.96 (*t*, *J* = 7.0, *Me*CH_2); 1.17 (*d*, *J* = 6.0, *Me*CH); 1.26 (*s*, *t*-Bu, major); 1.43 (*s*, *t*-Bu, minor); 1.98 (*m*, CH_2, minor); 2.28 (*m*, 1 H, CH_2N, major); 2.61 (*m*, 1 H, CH_2NC, major); 2.95 (*m*, MeC*H*); 3.19 (*dd*, *J* = 13.0, 1.0, 1 H, CH_2SO_2, major); 3.34 (*d*, *J* = 11.0, CHN, minor); 3.46 (*d*, *J* = 8.0, CHN, major); 4.13 (*dd*, *J* = 13.0, 2.0, 1 H, CH_2SO_2, minor); 7.00–7.40 (*m*, 5 arom. H). ^{13}C-NMR: 11.72 (*q*, major); 13.78 (*q*, minor); 18.65 (*d*); 23.02 (*q*, major); 23.25 (*q*, minor); 27.48 (*q*, minor); 27.59 (*q*, major); 41.98 (*t*, major); 42.62 (*t*, minor); 47.16 (*t*, major); 48.44 (*t*, minor); 58.95 (*s*); 68.32 (*d*, minor); 68.68 (*d*, major); 126.98 (*d*, minor); 127.11 (*d*, major); 127.73 (*d*, minor); 127.82 (*d*, major); 128.88 (*d*, major); 129.03 (*d*, minor); 135.88 (*s*, minor); 137.61 (*s*, major). CI-MS: 326 (26, M^+), 163 (12), 162 (100), 105 (4), 91 (20), 79 (8). Anal. calc. for $C_{18}H_{31}NO_2$ (325.52): C 66.42, H 9.60, N 4.30, S 9.85; found: C 66.44, H 9.65, N 4.26, S 9.83.

(1)- and (u)-4-[2-Methyl-1-(phenylsulfonyl)pentan-3-yl]morpholine (**35**). From **10** (0.62 g, 4.0 mmol), chloromethyl phenyl sulfone (0.38 g, 2.0 mmol), and Bu_3SnH (0.64 g, 2.2 mmol) according to *General Procedure 5*. FC (AcOEt/p.e. 1:2) of the crude product (93% ds) gave **35** (0.47 g, 76%). Colorless oil. The rel. configuration (*u*) of the major isomer was attributed by analogy to **29** and **31**. IR (film): 2960, 1445, 1300, 1145, 1115, 1085, 995. ^{1}H-NMR: 0.80 (*t*, *J* = 7.0, *Me*CH_2); 0.95 (*d*, *J* = 7.0, *Me*CH, (*u*)); 1.05 (*d*, *J* = 7.0, *Me*CH, (*l*)); 1.20–1.50 (*m*, MeCH_2); 2.13–2.50 (*m*, 6 H); 2.70 (*dd*, *J* = 9.0, 14.0, 1 H, CH_2SO_2, (*l*)); 2.85 (*dd*, *J* = 7.0, 14.0, 1 H, CH_2SO_2, (*u*)); 3.50 (*m*, 5 H); 7.42–7.83 (*m*, 5 arom. H). ^{13}C-NMR ((*u*), colorless oil): 12.56 (*q*); 16.10 (*q*); 19.11 (*t*); 30.44 (*d*); 51.09 (*t*); 59.46 (*t*); 67.27 (*t*); 68.29 (*d*); 127.55 (*d*); 127.63 (*d*); 129.05 (*d*); 133.31 (*d*); 139.88 (*s*). ^{13}C-NMR (*l*): 13.38 (*q*); 17.67 (*q*); 19.57 (*t*); 30.44 (*d*); 44.88 (*t*); 59.81 (*t*); 67.27 (*t*); 69.47 (*d*); 127.55 (*d*); 127.63 (*d*); 129.05 (*d*); 133.31 (*d*); 139.88 (*s*). CI-MS: 312 (26, M^+), 140 (3), 129 (7), 128 (100), 78 (4), 77 (21). Anal. calc. for $C_{16}H_{25}NO_3S$ (311.45): C 61.71, H 8.09, N 4.50, S 10.30; found: C 61.74, H 8.06, N 4.59, S 10.21.

(1)- and (u)-3-Methyl-4-morpholinohexanenitrile (**36**). From **10** (0.62 g, 4.0 mmol), (phenylthio)acetonitrile (0.42 g, 2.8 mmol), and Bu_3SnH (0.58 g, 2.00 mmol) according to *General Procedure 4*. FC (AcOEt/p.e. 1:3) of the crude product (74% ds) gave **36** (0.21 g, 78%). Inseparable mixture of isomers. IR (film): 2960, 2240, 1450, 1290, 1250, 1120. ^{1}H-NMR: 0.85 (*t*, *J* = 9.0, *Me*CH_2, major); 0.87 (*t*, *J* = 9.0, *Me*CH_2, minor); 0.90 (*d*, *J* = 8.0, *Me*CH, major); 0.98 (*d*, *J* = 8.0, *Me*CH, minor); 1.20–2.07 (*m*, MeCH_2); 2.20 (*m*, 1 H); 2.37–2.78 (*m*, 5 H); 3.52 (*m*, 4 H). ^{13}C-NMR: 12.42 (*q*, major); 13.30 (*q*, minor); 15.22 (*t*, major); 17.06 (*t*, minor); 19.42 (*q*, major); 19.77 (*q*, minor); 21.80 (*t*, major); 22.42 (*t*, minor); 32.28 (*d*, minor); 33.17 (*d*, major); 49.03 (*t*, minor); 50.97 (*t*, major); 67.15 (*t*); 67.80 (*d*, major); 68.98 (*d*, minor); 119.29 (*s*). MS: 196 (7, M^+), 168 (5), 128 (100), 110 (5), 85 (8), 83 (11), 69 (15), 56 (27). Anal. calc. for $C_{11}H_{20}N_2O$ (196.30): C 67.31, H 10.27, N 14.27; found: C 67.38, H 10.28, N 14.25.

(1)- and (u)-3-Benzyl-4-pyrrolidino(4-^{2}H)butanenitrile (**37**). From **11** (1.9 g, 10 mmol), (phenylthio)-acetonitrile (0.75 g, 5.0 mmol), and Bu_3SnD (1.6 g, 5.5 mmol) according to *General Procedure 6*. FC (AcOEt/p.e. 1:4) of the crude product gave **37** (0.69 g, 60%). Inseparable 1:1 mixture of isomers. IR (film): 3250, 2960, 2920, 2790, 2240, 1680, 1600, 1495, 1455, 745, 700. ^{1}H-NMR: 1.78 (*m*, CH_2CH_2N); 2.06–2.71 (*m*, 9 H); 2.87 (*ddd*, *J* = 14.0, 6.0, 3.0, 1 H, CH_2CN); 7.10–7.40 (*m*, 5 arom. H). ^{2}H-NMR: 2.30, 2.70. ^{13}C-NMR: 19.20 (*t*); 23.39 (*t*); 36.52 (*d*); 37.73 (*t*); 53.98 (*t*); 58.42 (*dt*, *J*(^{13}C,^{2}H) = 20.0); 118.56 (*s*); 126.09 (*d*); 128.38 (*d*); 128.87 (*d*); 138.52 (*s*). MS: 229 (2, M^+), 118 (3), 91 (8), 86 (6), 85 (100), 84 (12), 78 (1), 65 (3), 56 (3), 55 (5), 51 (2).

The reaction was also run using Bu_3SnH to give *3-benzyl-4-pyrrolidinobutanenitrile*. Picrate derivative: M.p. 103–104°. Anal. calc. for $C_{21}H_{23}N_5O_7$ (457.45): C 55.14, H 5.07, N 15.31; found: C 55.13, H 4.99, N 15.28.

(1)- and (u)-3-[(1,4-Dioxa-8-azaspiro[4.5]decan-8-yl)($^2H_1$*)methyl]-4-methylpentanenitrile* (**38**). From **12** (0.80 g, 4.0 mmol), (phenylthio)acetonitrile (0.30 g, 2.0 mmol), and Bu_3SnD (0.64 g, 2.0 mmol) according to *General Procedure 6*. FC (AcOEt/p.e. 1:4) of the crude product gave **38** (0.35 g, 69%). Inseparable 1:1 mixture of isomers. IR (film): 2960, 2820, 1470, 1365, 1145, 1100, 1040, 965, 950, 920. ^{1}H-NMR: 0.88 (*d*, *J* = 7.0, *Me*CH); 0.90 (*d*, *J* = 7.0, *Me*CH); 1.60–1.80 (*m*, 6 H); 2.10–2.60 (*m*, 7 H); 3.90 (*s*, CH_2O). ^{13}C-NMR: 17.62 (*t*); 19.17 (*q*); 19.54 (*q*); 28.81 (*d*); 34.61 (*t*); 39.00 (*d*); 51.48 (*t*); 57.91 (*dt*, *J*(^{13}C,^{2}H) = 20.1); 63.94 (*t*); 106.96 (*s*); 119.40 (*s*). MS: 253 (100, M^+), 212 (11), 156 (55), 126 (5), 100 (4), 99 (27), 86 (9), 85 (2), 83 (4), 71 (10).

The reaction was also run using Bu_3SnH to give *3-[(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)methyl]-4-methylpentanenitrile*. Anal. calc. for $C_{14}H_{24}N_2O_2$ (252.36): C 66.63, H 9.59, N 11.10; found: C 66.51, H 9.53, N 11.02.

*X-Ray Structure Analysis of (1)-***29** *and (1)-***31**. Suitable crystals were obtained by slow crystallization from Et_2O/p.e. ((*l*)-**29**) or CH_2Cl_2/p.e. ((*l*)-**31**). Experimental parameters are given in *Tables 3* and *4*, resp. Atomic coordinates, bond lengths, and bond angles are deposited with the *Cambridge Crystallographic Data Centre*.

Table 3. *X-Ray Structure Determination of* (1)-**29**

Crystal Data		Standard reflections	3 measured every 97 reflections
Empirical formula	$C_{20}H_{25}NO_2S$		
Color, habit	colorless transparent platelets	Index ranges	$-10 < h < 10$, $-12 < k < 12$, $-22 < l < 22$
Crystal system	monoclinic	Reflections collected	8406
Space group	$P2_1/n$	Independent reflections	3214
Unit cell dimensions	$a = 9.181(4)$ Å	Observed reflections	2181 ($F > 5\sigma(F)$, $R_{int} = 3.2\%$)
	$b = 10.482(4)$ Å		
	$c = 19.341(8)$ Å	Absorption correction	*N/A*
	$\beta = 102.04(3)°$		
Volume	1820.3(2) Å^3	*Solution and Refinement*	
Z	4	System used	*Siemens* SHELXTL PLUS (VMS)
Formula weight	343.5		
Density (calc.)	1.253 Mg/m^3	Solution	direct methods
Absorption coefficient	1.89 cm^{-1}	Refinement method	full-matrix least-squares
$F(000)$	736	Quantity minimized	$\Sigma w(F_o - F_c)^2$
		Absolute structure	*N/A*
Data Collection		Extinction correction	*N/A*
Diffractometer used	*Siemens R3m/V*	H-Atoms	x,y,z, and U_{iso} refined
Radiation	MoK_α ($\lambda = 0.71073$ Å)	Weighting scheme	$w^{-1} = \sigma^2(F) + 0.0000F^2$
Temperature	293 K	Number of parameters refined	317
Monochromator	highly oriented graphite crystal	Final R indices (obs. data)	$R = 5.86\%$, $R_w = 3.28\%$
2θ Range	2.0–50.0°	Goodness-of-fit	2.01
Scan type	2θ–θ	Largest and mean D/σ	0.005, 0.001
Scan speed	variable; 2.00 to 10.00°/min in ω	Data-to-parameter ratio	10.1:1
		Largest difference peak	0.47 eÅ^{-3}
Scan range (ω)	2.00° plus K_α separation	Largest difference hole	−0.37 eÅ^{-3}
Background measurement	stationary crystal and stationary counter at beginning and end of scan, each for 50.0% of total scan time		

Table 4. *X-Ray Structure Determination of* (1)-**31**

Crystal Data		Monochromator	highly oriented graphite crystal
Empirical formula	$C_{20}H_{25}NO_3S$		
Color, habit	colorless transparent platelets	2θ Range	2.0–45.0°
		Scan type	2θ–θ
Crystal system	orthorhombic	Scan speed	variable; 0.25 to 4.00°/min in ω
Space group	*Pbca*		
Unit cell dimensions	$a = 8.6935(4)$ Å	Scan range	$0.66 + 0.34 \tan\theta$
	$b = 19.1768(9)$ Å	Background measurement	first and last 16 of the 96 profile steps
	$c = 22.698(1)$ Å		
Volume	3784.1(3) Å^3	Standard reflections	3 measured every 108 min
Z	8	Index ranges	$0 < h < 9$, $0 < k < 20$, $0 < l < 24$
Formula weight	359.5		
Density (calc.)	1.262 g/cm^3	Reflections collected	18976
Absorption coefficient	1.89 cm^{-1}	Independent reflections	2472
$F(000)$	1536	Observed reflections	1921 ($F > 6\sigma(F)$, $R_{int} = 1.8\%$)
Data Collection			
Diffractometer used	*Enraf-Nonius CAD4*	Reflections used in refinement	2324 (F excluded if $F \leq 0$)
Radiation	MoK_α ($\lambda = 0.71073$ Å)		
Temperature	293 K	Absorption correction	*N/A*

Table 4 (cont.)

Solution and Refinement		Number of parameters refined	326
System used	*Siemens* SHELXTL PLUS (VMS)	Final R indices (obs. data)	$R = 4.23\%$, $R_w = 2.16\%$
		Goodness-of-fit	3.23
Solution	direct methods	Largest and mean D/σ	0.002, 0.001
Refinement method	full-matrix least-squares	Data-to-parameter ratio	7.1:1
Quantity minimized	$\Sigma w(F_0 - F_c)^2$	Largest difference peak	0.15 eÅ^{-3}
Absolute structure	N/A	Largest difference hole	−0.26 eÅ^{-3}
Extinction correction	N/A		
H-Atoms	x,y,z, and U_{iso} refined		
Weighting scheme	$w^{-1} = \sigma^2(F) + 0.0000F^2$		

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