Asymmetric Induction in the Oxidation of [2.2]Paracyclophane-Substituted Selenides. Application of Chirality Transfer in the Selenoxide [2,3] Sigmatropic Rearrangement

Hans J. Reich* and Kenneth E. Yelm[1]

S. M. McElvain Laboratories of Organic Chemistry, Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706

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When selenides derived from [2.2]paracyclophane systems were oxidized, the chiral aryl substituent provided for asymmetric induction to the new selenoxide chiral center. The ratio of diastereomeric selenoxides obtained depended upon whether the oxidation was performed under kinetic conditions or whether the selenoxides were allowed to equilibrate. Thus 4-(methylseleno)[2.2]paracyclophane (**10**) gave a 1:1 kinetic ratio of selenoxides **11** and **12** on oxidation with *m*-chloroperbenzoic acid and a 30:1 ratio at equilibrium (thermodynamic ratio). The more hindered 4-(methylseleno)-15-(*p*-toluenesulfonyl)[2.2]paracyclophane (**23**) was prepared in almost optically pure form. It gave a better kinetic ratio of selenoxides **24** and **25** (4.5:1) but a poorer thermodynamic one (1.5:1). The relative configuration of **11** and **12** and the absolute configuration of **24** and **25** were assigned. A geranyl selenide substituted with a resolved [2.2]paracyclophane substituent was oxidized and allowed to undergo a selenoxide [2,3] sigmatropic rearrangement to linalool. This sequence proves that the [2,3] sigmatropic rearrangement of γ,γ-dialkylallyl selenoxides proceeds through an endo transition state and illustrates the use of asymmetric induction during oxidation followed by chirality transfer by rearrangement to prepare optically active allylic alcohols.

Selenoxides serve as valuable synthetic intermediates in modern organic chemistry.[2] Although they are chiral, only occasionally have useful levels of enantiomeric excess been achieved in the preparation of simple optically active selenoxides (Se only chiral center) by enantioselective oxidation,[3] kinetic resolution methods,[3ab,4] or chromatography on chiral substrates.[5] The highest level of ee achieved by using these techniques is 83% by oxidation with a chiral oxaziridine.[3b] Optically pure selenoxides have been obtained by separation of diastereomers of the sterically hindered 2,4,6-triisopropylphenyl 4'-((*l*-menthyloxy)carbonyl)phenyl selenoxide and subsequent conversion to an optically active methyl ester having Se as the only chiral center.[6] Optically pure *complexes* of selenoxides with 2,2'-dihydroxy-1,1'-binaphthol or 1,6-bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol have also been reported.[7] No subsequent application of these highly optically pure materials toward chiral synthesis have appeared.

In contrast, nonracemic sulfoxides have been prepared with high enantiomeric excesses by chemical[8] and enzymatic oxidations[9] as well as by synthesis from menthyl sulfinates[10] and other auxiliaries.[11a] Recently several sulfoxides that are diasteromerically pure by virtue of stereoselective oxidation[11b] or thermodynamic preference[11b,c] have been prepared. These sulfoxides have been exploited in synthetic procedures in which asymmetry at sulfur was transferred to carbon.[9a,12]

A major reason that optically active selenoxides have not been used extensively is their poor configurational stability. Whereas sulfoxides are configurationally stable at sulfur under normal conditions,[12] selenoxides are so labile that the process can sometimes be studied by dynamic NMR techniques.[13] Alkyl aryl and dialkyl selenoxides are especially easy to equilibrate.[3a,b,7,13b] The source and extent of this lability is not clear; all of the published studies have been anecdotal in character, without systematic study of pH, temperature, or solvent effects. The inherent configurational stability of selenoxides is probably high, but they are easily equilibrated by reversible acid-catalyzed formation of hydrates **1**, as has been demonstrated by ^{18}O-labeling experiments.[14] Addition of water to anhyd-

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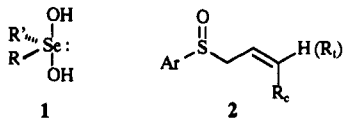
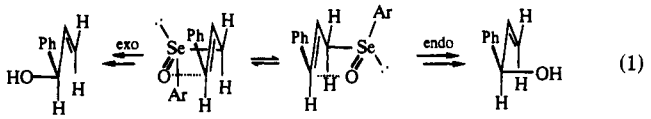


1 2

rous solvents has been variously reported to cause very rapid,[3b,4] moderate,[15] or negligible[14c,16] increases in the rate of equilibration. Thus Davis and co-workers report that phenyl methyl selenoxide and 2,4,6-triisopropylphenyl methyl selenoxide do not lose optical activity over 1 or 2 days at 60 °C in dry solvent.[4] The phenyl selenoxide racemizes in less than 10 s when water is added; the triisopropyl selenoxide is only slowly affected by water, but racemizes in less than 10 s with a trace of acid. On the other hand, Shimizu and co-workers[14c] report that the half-life for racemization of several chiral selenoxides in methanol decreased from 32 to 6 h on going to 4/1 methanol/water. They also found rapid racemization with acid. In these cases steric effects are crucial in slowing down configurational equilibration.

In related work, several diastereomeric selenoxides have been prepared in isomerically pure form.[6,16] Jones, Mundy, and Whitehouse were able to separate diastereomeric steroidal selenoxides by chromatography (alumina, −50 °C) and found that the two isomers (dissolved in water-immiscible solvents) did not interconvert in the presence of water between −78 and 25 °C.[16a] In other cases, equilibration in aqueous media was observed.[15,17]

The [2,3] sigmatropic rearrangement of selenoxides provides a path for transferring selenium chirality to carbon, a process already well studied for sulfoxides.[18] For selenoxides there is little information on the two key parameters that control asymmetry transfer: the relative rate of [2,3] sigmatropic rearrangement vs selenoxide epimerization and the exo/endo ratio. The $H_2{}^{18}O$ exchange of an allylic selenoxide competes with a selenoxide [2,3] sigmatropic rearrangement in one case, suggesting that racemization could be competitive with the rearrangement.[14a] On the other hand, Davis and co-workers[3a] have obtained 1-phenyl-2-propen-1-ol with 12% ee by asymmetric oxidation of cinnamyl phenyl selenide (eq 1). Since



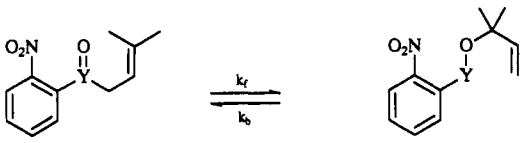
3-S 3-R (1)

the optical purity of the precursor allylic selenoxide was not known (it could only be extrapolated from the results of the oxidation of the methyl selenoxide, 10% ee), this experiment provides only approximate information about the extent of racemization prior to rearrangement, or the exo/endo ratio, which defines the fidelity of asymmetry transfer.

In summary, acid catalysis is probably an important element in the stereoisomerizations of selenoxides, and weakly basic conditions are required to prevent facile equilibration. It also appears that intentionally causing the equilibration of selenoxides should be easy. This led us to construct a system in which a chiral auxiliary attached to selenium could influence the selenoxide configuration.[19] If diastereomeric selectivity was not obtained kinetically during selenide oxidation, it might be possible to equilibrate to a predominant configuration at selenium. In either case chirality at selenium can be transferred to carbon by a [2,3] sigmatropic rearrangement or some other chiral induction process.

Chirality Transfer Using a Selenoxide [2,3] Sigmatropic Rearrangement

Preliminary Considerations. Our results from the 2-nitrophenyl prenyl sulfoxide (**4-S** and **5-S**) system[1b] showed that the rearrangement of 4 had a very high preference for one transition state over the other (k_{endo}/k_{exo} = 275). If this transition state preference could be completely transferred by using a sulfoxide to allylic alcohol sequence starting with an optically pure allylic sulfoxide system, optically active allylic alcohols (99.6% ee) could be obtained. On the basis of the system **4-S**/**5-S** and the known effects of various substituents in other sulfoxide systems,[18,21] the important features present in **4-S** are the lack of substituents at C-1 and C-2 and the cis substituent at C-3 (see **2**). Thus, a framework that should lead to a high endo/exo selectivity (and thus high S to C-3 chirality transfer) will have this cis substituent. An additional trans substituent at C-3 should not detract from its suitability.



4 5

Y = S ΔG = 1.5 kcal/mol k_{endo}/k_{exo} = 275

Y = Se ΔG ~ -11 kcal/mol

Hoffmann and co-workers recognized that a system such as **2** was well suited for chirality transfer, but their synthetic methodology (isomerization of an optically active vinyl sulfoxide to a β,γ-unsaturated sulfoxide) did not allow the selective production of (*Z*)-allylic sulfoxides.[18,22] The oxidation of prochiral sulfides has been achieved with enantiomeric excesses as high as 93% by chemical means[8a-c] and sometimes 100% by enzymatic oxidations.[9] High optical purity alcohol products would be anticipated if an enantioselective oxidation of an appropriate geometrically uniform allylic sulfide could be achieved and the resulting optically active allylic sulfoxide converted to allylic alcohol before racemization of the sulfoxide ($t_{1/2}$ = 62 min for rearrangement of phenyl allyl sulfoxide in benzene at 50 °C[23]).

Assuming a comparable endo/exo preference for selenoxides, a similar scenario can be envisioned beginning with

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(20) This effect can also be achieved for the special case of allylic sulfoxides, where the [2,3] sigmatropic rearrangement equilibrates the configuration at the sulfoxide center.[11b,c] However, such equilibration also of necessity equilibrates stereochemistry of the double bond.

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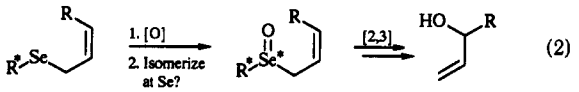
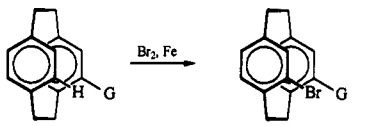
an allylic selenide. However, the complications of facile racemization exist. An alternative approach would be to attach chiral group (R*) to the selenium atom to influence the oxidation at this site (asymmetric induction). If the group is homochiral, any diastereomeric preference translates into a configurational excess at selenium (eq 2).



(2)

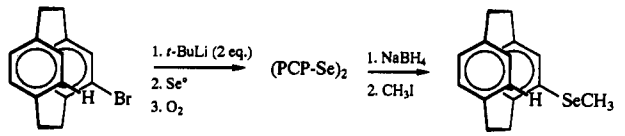
The selenium-based system has certain advantages over sulfur. With a selenoxide we have the choice of accepting the kinetically determined ratio of diastereomers or causing the equilibration at selenium to a thermodynamically determined ratio.[20] This equilibration would have to be performed at low temperature (<−50 °C) to avoid the facile [2,3] sigmatropic rearrangement.

We have investigated this approach by employing [2.2]paracyclophane as the chiral group R*.[24] This group offers a highly asymmetric environment and a key element of regiochemical control in the pseudo-gem aromatic bromination of certain derivatives (e.g., preparation of **7** from **6**, G = NO_2, COMe, CO_2Me),[25] which provides a degree of flexibility for the modification and design of this chiral group.



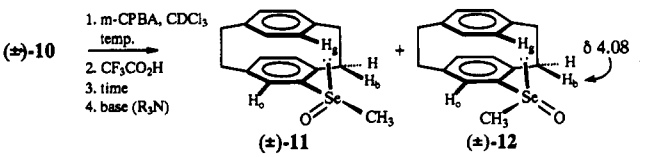
6 **7** pseudo-gem

Oxidation of 4-(Methylseleno)[2.2]paracyclophane. The diastereomer ratio of selenoxides obtained in the oxidation of an allylic selenide would be hard to measure. NMR analysis is complicated by the diasterotopic and highly coupled α-methylene protons, and the selenoxide would have to be analyzed at low temperature to avoid rearrangement (which typically occurs between −45 °C and −30 °C for allyl phenyl selenoxides[1b,26]). 4-(Methylseleno)[2.2]paracyclophane (**10**) (easily prepared from the bromide **8**) provided a convenient model for an allylic selenide. The methyl selenide **10** and the corresponding selenoxides **11** and **12** had distinct methyl singlets by ^1H NMR and no facile decomposition pathways.



8 (PCP-Br) (±)-**9** (±)-**10**

Room temperature oxidation of **10** with *m*-chloroperbenzoic acid (*m*-CPBA) provided two new methyl singlets corresponding to the diastereomeric selenoxides **11** (δ 2.40) and **12** (δ 2.69) in a ratio of about 30:1. Low temperature *m*-CPBA oxidation in $CDCl_3$ followed by the addition of amine base (to retard equilibration) before warming gave the selenoxides in a 1:1 ratio (Figure 1), which we believe



Run	Temp.	Eq. CF_3CO_2H	Time (min)	11/12
1	25	0		30
2	-50	0	5	1
3	-60	1	30	2.9
4	-60	5	30	13
5	-50	0.5	240	32

Figure 1. Formation and stereochemical equilibration of diastereomeric paracyclophane selenoxides. The time refers to the contact time between trifluoroacetic acid and selenoxide before quench with amine.

is the kinetic ratio. The NMR spectrum of this mixture helped to confirm the identity of **12**. From this spectrum, ^{77}Se side bands were seen for both of the methyl singlets ($^2J_{Se-H}$ = 12.0 Hz for **11** and 12.5 Hz for **12**). Thus this oxidation of **10** was unselective kinetically. A similar low diastereoselectivity is usually seen in the oxidation of sulfides with *m*-CPBA and other oxidants,[9b,27] although there are exceptions.[11c] The spectrum was essentially unchanged after 24 h, even when on special precautions were used to exclude moisture. However, after 17 days the mixture had reverted to the 30:1 thermodynamic ratio of **11**:**12**. A chiral allylic sulfoxide with thermodynamic diastereomer ratios as high as 11.5:1 has been reported.[11b]

The assignment of the relative configurations of **11** and **12** was based upon the downfield benzylic proton (δ 4.08) or **12** in the NMR spectrum. The diastereomeric selenoxide **11** has no such downfield proton, and the reason for this striking (0.8 ppm) shift was rationalized on the basis of reasonable conformations. It is apparent from models that the most severe steric interaction for a substituent on the aryl ring of [2.2]paracyclophane is with the pseudo-gem proton (H_g) on the facing ring. If we assume that the smallest group at selenium (the lone pair) points toward the facing ring, steric interactions with H_g (as well as with H_b and H_o) can be avoided as shown in Figure 1.[24,28] The proton shifted downfield in **12** is presumably H_b due to its proximity to the selenoxide oxygen. Evidence for the validity of this argument came from an optically active sulfoxide system where the absolute configuration of the paracyclophane unit and the configuration at sulfur were both known (see the following section).

The results of attempts to equilibrate the selenoxides at low temperature are summarized in Figure 1. The presence of *m*-CPBA did not immediately equilibrate the selenoxides (run 2). Greater amounts of a stronger acid (trifluoroacetic acid, runs 3 vs 4) and extended time at a higher temperature (run 5) predictably led to more isomerization. Unfortunately, the required times and temperatures were close to our predicted half-life of a [2,3] sigmatropic rearrangement ($t_{1/2}$ = 44 min at −51 °C[26b]). The acid-catalyzed isomerization was much slower in CD_2Cl_2/CD_3OD (2:3) than in $CDCl_3$. These results encouraged us to believe that high asymmetric induction could be achieved and that selenoxide configuration could be equilibrated faster than [2,3] sigmatropic rearrangement, should this be necessary. Attempts to resolve a

(24) For reviews on [2.2]paracyclophanes: (a) Cram, D. J.; Hornby, R. B.; Truesdale, E. A.; Reich, H. J.; Delton, M. H.; Cram, J. M. *Tetrahedron* **1974**, *30*, 1757. (b) Vogtle, F.; Neumann, P. *Top. Curr. Chem.* **1974**, *48*, 67. (c) Boekelheide, V. *Top. Curr. Chem.* **1983**, *113*, 89. (d) Kleinschroth, J.; Hopf, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 469.

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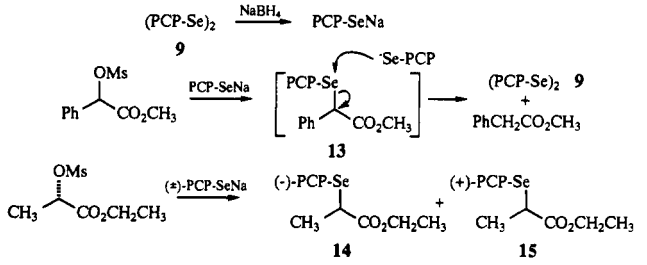
(26) (a) Reich, H. J. in *Organoselenium Chemistry*; Liotta, D., Ed.; Wiley: New York, 1987; p 365. (b) Wollowitz, S., Ph.D. Thesis, University of Wisconsin—Madison, 1980.

(27) Rigau, J. J.; Bacon, C. C.; Johnson, C. R. *J. Org. Chem.* **1970**, *35*, 3655.

(28) The benzene rings are shown as planar for artistic convenience. They are in fact bent considerably. Hope, H.; Bernstein, J.; Trueblood, K. N. *Acta Crystallogr. B* **1972**, *28*, 1733.

4-seleno[2.2]paracyclophane for this purpose were not successful. Our strategy was to attach a resolved chiral group to selenium, separate diastereomers, and then cleave the originally formed C–Se bond to provide the resolved selenium reagent. Two candidates for this resolution were envisioned that would use the mesylates of methyl mandelate and ethyl lactate (both alcohols commercially available in optically active form) as sources of a resolved chiral group:

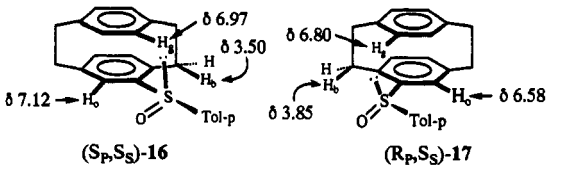


However, diselenide **9** was immediately formed upon addition of methyl 2-(methylsulfonoxy)mandelate to a solution of selenolate. Presumably **13** was deselenated by selenolate anion as it was formed. This sort of behavior is known for α-carbonyl selenides in which the resulting enolate has additional stabilization.[29] Selenides **14** and **15** derived from L-ethyl lactate were prepared as outlined, but these diastereomers could not be easily separated. Attempts using preparative TLC or HPLC resulted in less than a 10% enrichment of the diastereomers. The distance between asymmetric centers and the conformational "flexibility" of the selenide evidently leads to the lack of diastereomer differentiation. We thus turned our attention toward a more highly substituted paracyclophane system that would be more amenable to resolution and provide a greater kinetic (and thermodynamic) selectivity in the selenide oxidations.

Pseudo-gem *p*-Tolylsulfonyl-Substituted [2.2]-Paracyclophanes. A substituent placed on the opposite ring directly across from our selenium substituent should have a considerable influence on the chemistry there since this pseudo-gem orientation would crowd the site greatly. Certain substituents allow for the convenient introduction of a pseudo-gem substituent by bromination[25] or chloromethylation.[30] In both of these substitutions proton transfer is rate-limiting, and thus the orientation of the new substituent is determined by the site that most readily loses a proton. Pseudo-gem bromination is observed either exclusively or in great preference for the 4-carboxy-, 4-carbomethoxy-, 4-acetyl-, and 4-nitro[2.2]paracyclophanes **7**.[25] These groups have basic oxygen atoms that can accept the transannular proton from the pseudo-gem position and direct the bromination there.

The above-mentioned groups all have a degree of incompatibility with subsequent functionalization via Li/Br exchange. This is unfortunate since the introduction of a selenium substituent would be achieved most conveniently from a lithium reagent. Protection of some of these groups would be a viable alternative, but we instead sought a group that could serve as an efficient director for the pseudo-gem bromination and that would be inert to further transformations.

The sulfone group is stable to strong base conditions and it possesses oxygen atoms that might be sufficiently basic

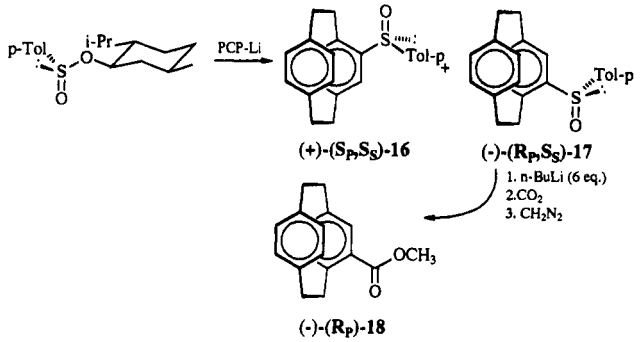


(S_P,S_S)-**16** (R_P,S_S)-**17**

Figure 2. Probable conformations of *p*-(toluenesulfinyl)paracyclophanes.

to provide direction for the bromination. Preliminary results in the bromination of 4-(methylsulfonyl)[2.2]-paracyclophane were encouraging, providing a single product upon bromination. However, deprotonation of the methyl sulfone is a likely problem when lithium reagents are used.[31] An arylsulfonyl group is likely to be more tolerant of anticipated reaction conditions and offered another important advantage. (–)-Menthyl (–)-(*S*)-*p*-toluenesulfinate is a conveniently prepared and resolved precursor for optically active sulfoxides.[10] In our case it provided diastereomeric sulfoxides **16** and **17**, which were separated by chromatography allowing for the resolution of the paracyclophane group before conversion to the sulfone **19**.

Since the reaction with sulfinate is known to occur with inversion,[10c] **16** and **17** have the *S* configuration at sulfur and differ only in the chirality of the paracyclophane portions. The diastereomer with the downfield shifted benzylic proton in its ^{1}H NMR spectrum, **17**, was chemically correlated to (–)-(*R*)-4-carbomethoxy[2.2]paracyclophane (**18**), whose absolute configuration has been determined.[32] This correlation was performed by a slight modification of Johnson's procedure for preparing optically active dialkyl sulfoxides from optically active aryl alkyl sulfoxides.[33] Treatment of (–)-**17** with 6 equiv of *n*-butyllithium in THF (30 min, –78 °C) was followed by the addition of carbon dioxide to trap all the organolithium species (PCP-Li, Tol-Li and excess *n*-BuLi). Treating the mixture of acids with diazomethane and purification gave a methyl ester with the *R* configuraiton shown: (–)-(*R*)-**18**,[34] thus completing the assignment.



Arguments similar to those presented with respect to the conformations and resulting relative configuration assignments of the methyl selenoxides **11** and **12** also apply to these sulfoxides. However, since the absolute configurations are known for the paracyclophane units as well as at sulfur, we can discuss the differences in the observed NMR spectra of **16** and **17** in terms of conformational evidence (as opposed to the conformational assumptions made for **11** and **12**). Conformations for **16** and **17** (Figure 2) are similar to those illustrated for **11** and **12** earlier. The

(29) (a) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434. (b) Miyashita, M.; Suzuki, T.; Yoshikoshi, A. *Tetrahedron Lett.* **1987**, *28*, 4293.
(30) Gilb, W.; Menke, K.; Hopf, H. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 191.
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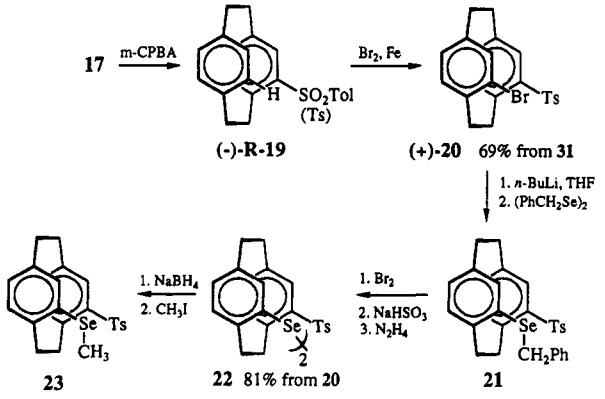
(33) Johnson, C. R.; Lockard, J. P.; Schroeck, C. W. *Synthesis* **1973**, 485.
(34) Reich, H. J.; Cram, D. J. *J. Am. Chem. Soc.* **1969**, *91*, 3517.

downfield chemical shift (δ 3.85) observed for one of the benzylic protons of **17** was attributable to the proximity of the sulfoxide oxygen and was 0.35 ppm further downfield than any benzylic proton of **16**. This observation lent credibility to the conformations and assignments presented for the methyl selenoxides **11** and **12**. The conformations shown for **16** are also supported by NMR evidence. A downfield doublet (δ 7.12, J = 1.8 Hz) was observed for **16** corresponding to the proton ortho to the sulfoxide (H_o) and near the sulfoxide oxygen. The corresponding ortho proton of **17** appears at 6.58, some 0.5 ppm further upfield. Both **16** and **17** had a paracyclophane aromatic doublet (J = 8 Hz), which was downfield from the other paracyclophane aromatic protons (δ 6.97 and 6.80, respectively). These can be assigned to the pseudo-gem protons (H_g).

With the resolved *R* and *S* configurations of the [2.2]paracyclophanes in the form of the diastereomeric sulfoxides **16** and **17** in hand, oxidation (*m*-CPBA) of each separately gave enantiomeric sulfones. The remaining transformations will be illustrated for the *R* enantiomers derived from **17**.

The bromination of sulfone **19** proceeded very well under conditions similar to those used for the bromination of 4-nitro[2.2]paracyclophane.[25] No other isomers were seen by HPLC analysis: only 1 or 2% of **19** contaminated the crude product and was removed by recrystallization. Assignment of the product as the pseudo-gem brominated sulfone **20** was readily apparent from the ^{1}H NMR spectrum. Protons pseudo-gem to bromine in [2.2]paracyclophanes show a considerable downfield shift (e.g., the pseudo-gem proton of 4-bromo[2.2]paracyclophane comes at δ 7.16, the aromatic resonance of [2.2]paracyclophane is δ 6.37).[35] The only significantly downfield paracyclophane aromatic proton in **20** came at δ 7.38. This doublet (J = 2 Hz) was at nearly the same chemical shift as the proton ortho to the sulfonyl group in the starting material. If the pseudo-ortho isomer has been formed, the proton ortho to the sulfonyl group should have moved downfield 0.5 to 0.75 ppm.[35] Thus, as expected, the selectively produced monobromination product was **20**.

The conversion of **20** to diselenide **22** was first attempted by Li/Br exchange and reaction of the anion with elemental selenium,[36] followed by air oxidation of the resulting selenolate. This generally reliable reaction did not work well; therefore we used dibenzyl diselenide as a more reactive selenium source. After cleavage of the benzyl selenide **21** with bromine, reduction of the resulting selenenyl bromide and column chromatography, the diselenide **22** was obtained in an 81% yield.



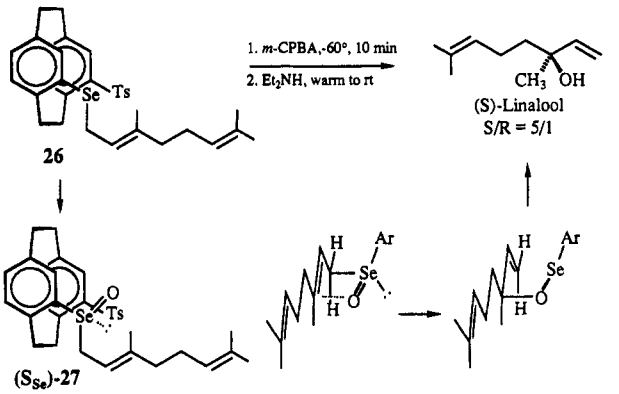
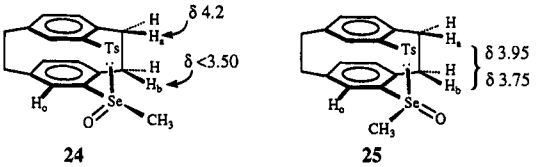


Figure 3. Optically active linalool by [2,3] sigmatropic rearrangement of (S_{Se})-**27**.

Reduction of **22** with sodium borohydride provided the substituted paracyclophaneselenolate (ArSeNa), which was methylated to give the methyl selenide **23**. The effect of having the bulky *p*-toluenesulfonyl group[37]) pseudo-gem to the selenium substituent can be seen upon oxidation with *m*-CPBA. Unlike the unselective oxidation of **10**, similar treatment of **23** (*m*-CPBA/−60 °C/$CDCl_3$/3 min, then addition of 2,2,6,6-tetramethylpiperidine before warming) produced selenoxides **24** and **25** in a ratio of ~4.5:1. However, allowing these selenoxides to equilibrate by acidifying the solution (CD_3CO_2D) resulted in an equilibrium ratio of ~1.5:1 **24**:**25** (assignments of **24** and **25** made as earlier for **11**, **12**, **16**, and **17**). The kinetic preference for the formation of **24** can be rationalized in terms of the selenide **23** favoring a conformation in which the methyl group was pointed away from the pseudo-gem sulfonyl group. Oxidation would then occur from the most accessible side of the selenium atom to form **24** preferentially. The sulfonyl-substituted paracyclophane thus behaves in a quite unexpected and disappointing fashion. When compared to the systems with a pseudo-gem proton (**10**, **11**, and **12**) this system offers a more selective kinetic ratio of products but a lower thermodynamic preference.



Optically Active Linalool by Chirality Transfer. The results of the oxidation of the methyl selenide **23** suggested that an oxidation of an allylic pseudo-gem-(*p*-tolylsulfonyl)[2.2]paracyclophanyl selenide would probably exhibit a fair diastereomeric selectivity. The geranyl selenide **26** was chosen since the substitution pattern of the allylic portion has the features necessary for high endo selectivity in the [2,3] sigmatropic rearrangement (see above) and because the rearrangement product is linalool, a naturally occurring alcohol for which the absolute configurations is known.

Figure 3 presents the results of the oxidation of **26** and subsequent [2,3] sigmatropic rearrangement of the resulting selenoxides. Before warming the reaction mixture to room temperature, diethylamine was added as a scavenger for selenic acid (ArSeOH) derivatives to avoid any undesired side reactions, such as addition to the double bonds of the product.[38] Addition of hydrazine to the

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(37) The *A* value for $PhSO_2$ is 2.5 kcal/mol. Corey, E. J.; Feiner, N. F. *J. Org. Chem.* **1980**, *45*, 765.

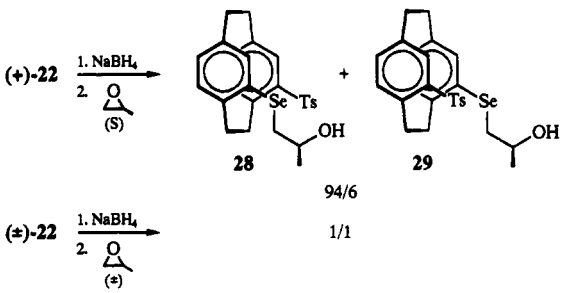
reaction mixture reduced the selenium species present to diselenide **22**, which could be recovered in high yield.

The results of Figure 3 seem to agree well with results of the oxidation of the methyl selenide **23**. Under conditions where the selenoxides **27** and its epimer are not expected to equilibrate, a 5:1 ratio of (*S*)/(*R*)-linalool was obtained, whereas a 4.5:1 ratio of methyl selenoxides **24** and **25** was obtained from **23**. Allowing the selenoxides **27** and its epimer to stir with trifluoroacetic acid before addition of amine produced linalool with S/R = 3.5 (CH_2Cl_2) and S/R = 2.1 (wet acetone). If one accepts the assignment of the relative configurations of **24** and **25** and assumes an analogous diastereomeric preference in the oxidation of **26**, the absolute configuration of **27** is as shown. This assignment is also consistent with the endo transition state predicted for this rearrangement based upon related sulfoxides.[18,22]

The minimum stereospecificity of our rearrangement can only be estimated since the ratio of **27** to its epimer is not known. If the kinetic ratio in the oxidation was approximately the same as that for the methyl selenoxides **24** and **25** (4.5:1), the rearrangement occurred with complete chirality transfer. On the other hand, if the oxidation is 100% stereoselective, this 5:1 ratio requires a minimum of 83% chirality transfer, assuming that only (*E*)-**26** was formed (no *Z*) and 100% configurational purity of the paracyclophane group. We also assume that the diastereomers prefer the same rearrangement transition state (endo) and there is no kinetic resolution (one diastereomer rearranging faster than the other). The last condition seems to be assured since the reaction was allowed to warm to room temperature and any selenoxide present should have rearranged at this temperature. A difference in the preferred transition state for the two diastereomers seems highly improbable on the basis of the rationalizations generally applied. The geometric purity of the selenide starting material **26** was observed to be >95% by ^{13}C NMR, so only a few percent of the (*R*)-linalool formed could possibly be attributed to (*Z*)-**26**. The configurational purity of the paracyclophane unit was assessed by reducing the recovered diselenide **22** to selenoate and alkylating with (*S*)-propylene oxide to form the hydroxy selenides **28** and **29** in a 94:6 ratio. It was also shown that racemic **22** under the same conditions reacted with racemic propylene oxide without preferential formation of one diastereomer over the other. Thus the paracyclophane portion of the geranyl selenide was at most 94% configuraitonally pure (assuming the propylene oxide was enantiomerically pure) and the highest (*S*)/(*R*)-linalool ratio that could have been achieved in a totally stereospecific rearrangement is 94:6. Our 5:1 (83:17) ratio found therefore represents a minimum stereoselectivity of 88% (k_{endo}/k_{exo} = 7). This indicates that the original oxidation of **24** must also be *at least* this selective. This rearrangement selectivity would correspond to a 0.9 kcal preference for the endo transition state at −40 °C (the temperature at which the rearrangement occurs is not known).

On the basis of the meager kinetic oxidation preferences for the methyl selenide **23**, a lack of complete selectivity in the oxidation of the geranyl selenide **26** is probably responsible for the major portion of the (*R*)-linalool obtained. However, this is speculation and was not proven by the above results.

Other Asymmetric Induction Probes. As noted above, the reaction of the tosyl-substituted selenolate anion with propylene oxide failed to show any preferential formation of one diastereomer over the other. Unsubstituted paracyclophanyl selenolate (from **9**) reacted with a similar lack of selectivity. This is in contrast to the reaction of binaphthyl selenolates with epoxides[39a] or selenenyl halides with olefins,[39b] which show considerable diastereoselectivity. Several other reactions with selenium reagents derived from the racemic unsubstituted paracyclophane system were also examined for the possibility of using the paracyclophane substituent to provide asymmetric induction. In each case racemic materials were used. The reaction of PCP-selenyl chloride with both *cis*- and *trans*-2-butene to provide β-chloro selenides and the alkylation of PCP-benzyl selenide (LDA, MeI) were performed. In each case, examination by NMR showed the formation of essentially 1:1 mixtures of diastereomers.



Experimental Section

General. Ozonizations were performed with a Welsbach ozonator. Optical rotations were measured with a Perkin-Elmer Model 241 polarimeter in an unthermostated cell. All reactions involving lithium reagents or selenolate anions were performed under an atmosphere of dry nitrogen. HPLC analyses were performed on an Ultrasphere Si 5 μm 4.6 × 250 mm column, usually using 20% ethyl acetate–hexane as eluent. Ratios from such an analysis were approximate and were not corrected for the relative responses of the components.

Dry dichloromethane was washed successively with concd H_2SO_4, water, saturated aqueous $NaHCO_3$, and water, predried with $CaCl_2$, distilled from CaH_2, and stored over 4A molecular sieves. Triethylamine was distilled from CaH_2, and pyridine was distilled from KOH. Both were stored under nitrogen. *N*,*N*-Dimethylacetamide was dried over BaO and distilled under reduced pressure.

Eu(facam)$_3$[40] was obtained from Alfa Products (Eu-Opt). 4-Bromo[2.2]paracyclophane[41] and dibenzyl diselenide[42] were prepared by literature procedures. (−)-Menthyl (−)-(*S*)-*p*-toluenesulfinate was prepared by the procedure of Estep and Tavares[10a] and recrystallized from acetone: mp 103.8–105.3 °C (lit. 108–109 °C,[10a] 110 °C[10b]); $[\alpha]^{23}_D$ −200° (0.02017 g/mL in acetone) (lit. $[\alpha]^{22}_D$ −210°,[10a] $[\alpha]^{20}_D$ −202°[10b]). Geranyl chloride was prepared according to the method of Collington and Meyers[43] and shown to be >95% one isomer by ^{13}C NMR: ^1H NMR (270 MHz) δ 1.60 (s, 3 H), 1.68 (s, 3 H), 1.73 (s, 3 H), 2.0–2.2 (m, 4 H), 4.10 (d, *J* = 8 Hz, 2 H), 5.10 (m, 1 H), 5.44 (td, *J* = 8, 1.2 Hz, 1 H); ^{13}C NMR (15 MHz, C_6D_6) δ 15.8, 17.6, 25.6, 26.5, 39.5, 40.6, 120.6, 123.7, 131.2, 141.7.

Di[2.2]paracyclophan-4-yl Diselenide (9). A dry 50-mL 2-neck flask was equipped with a 7-in. tube, the system was flushed with nitrogen, and at −78 °C 15 mL of THF and 2 equiv of *t*-BuLi (3.93 mL of a 2.0 M solution, 7.86 mmol) were added. A solution of 1.128 (3.93 mmol) of 4-bromo[2.2]paracyclophane in 7 mL of THF was transferred into the flask by cannula over 15 min. After the gold-brown solution was stirred for 1 h at −78 °C, 310 mg (3.93 mmol) of grey selenium powder was added through the 7-in. tube

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(with a stream of nitrogen flowing through). The cold bath was pulled down to the point where it was just touching the bottom of the flask. The black suspension gradually changed to an orange solution. After 1.7 h, the solution was stirred at rt for another 75 min. Water (10 mL) was added and air was bubbled through the solution for 16 h. The yellow solid that precipitated was filtered and air dried to give 0.942 g (1.64 mmol, 84%) of crude di[2.2]paracyclophan-4-yl disenelide, mp 197–202 °C.

The diselenide was dissolved in 30 mL of CH_2Cl_2 and filtered to remove a small amount of selenium. The CH_2Cl_2 was removed, and the solid was recrystallized from 30 mL of CCl_4 to yield 0.383 g (0.67 mmol, 34%) of orange-yellow diselenide, mp 208.4–208.9 °C: NMR (270 MHz) δ 2.8–3.6 (m, 8 H), 6.1–6.8 (m, 7 H); IR (KBr) 2962, 2939, 2900, 2862, 733 cm^{-1}; MS M^+ 574.0677 (calcd for $C_{32}H_{30}{}^{80}Se_2$, 574.06775). Concentration of the mother liquor produced an additional 0.42 g (38%) of diselenide, mp 200.0–200.5 °C. The melting points given are of questionable value due to the uncertainty of diastereomer composition.

4-(Methylseleno)[2.2]paracyclophane (10). Di[2.2]paracyclophan-4-yl diselenide (**9**) (0.573 g, 1.0 mmol) in 12 mL of 1:1 THF–absolute EtOH was treated under nitrogen with 87 mg (2.3 mmol) of $NaBH_4$ in small portions. The suspension of diselenide changed to a light yellow solution. After stirring for 2 h at rt, 0.150 mL (2.41 mmol) of methyl iodide was added. After 20 min the reaction mixture was poured into 25 mL of 1.2 N HCl and 10 mL of CH_2Cl_2. The organic layer was washed with 7% $NaHCO_3$ solution and brine and filtered through a cone of Na_2SO_4. Solvent removal yielded 0.544 g (1.8 mmol, 90%) of the crude yellowish white selenide: mp 80–83 °C; NMR (100 MHz) δ 2.28 (s, 3 H, $^2J_{Se-H}$ = 11.4 Hz), 2.8–3.6 (m, 8 H), 6.4–7.0 (m, 6 H), 7.36 (dm, J = 8 Hz, 1 H). This material was generally used without purification, but it can be recrystallized from 1:1 ether–pentane to give a white solid: mp 98.3–98.4 °C; ^{13}C NMR (15 MHz, 14 of 17 signals resolved) δ 140.1, 139.8, 139.1, 134.9, 134.2, 133.2, 132.7, 131.7, 130.6, 128.6, 35.4, 35.1, 33.6, 6.4; MS M^+ 302.0567 (calcd for $C_{17}H_{18}Se$, 302.0574); IR (KBr) 2925, 2890, 2850, 1580, 1050, 840, 718 cm^{-1}.

4-(Methaneseleninyl)[2.2]paracyclophanes (11 and 12). To a solution of 0.130 g (0.43 mmol) of 4-(methylseleno)[2.2]paracyclophane (**10**) in 2 mL of CH_2Cl_2 was added 91.4 mg (0.45 mmol) of 85% *m*-CPBA. After 50 min at rt the reaction mixture was poured into 10 mL of 1.5 M NaOH. The organic layer was washed with 10 mL of NaOH solution and brine and filtered through a cone of Na_2SO_4. Solvent removal afforded 0.126 g (0.40 mmol, 93%) of white solid: mp 128–131 °C; NMR (100 MHz) δ 2.40 and 2.69 (**11** and **12**) (singlets, ca 30:1, 3 H), 2.8–3.6 (m, 8 H), 6.4–7.0 (m, 6 H), 7.26 (d, J = 3 Hz, 1 H); ^{13}C NMR (15 MHz, $CDCl_3$, 15 of 17 signals resolved): δ 33.3, 34.7, 35.2, 36.0, 128.7, 131.0, 133.0, 133.3, 134.9, 135.9, 136.9, 138.3, 139.9, 142.5, 143.7; IR (KBr) 2940, 2870, 830, 731 cm^{-1}; MS M^+ 318.0523 (calcd for $C_{17}H_{18}OSe$, 318.0523). Further purification of the product can be achieved by preparative TLC (19:1 $CHCl_3$:MeOH).

The procedure for obtaining the data of Figure 2 can be illustrated by the following (run 3): A solution of 3.8 mg (0.013 mmol) of selenide **10** in 0.2 mL of $CDCl_3$ was cooled to −60 °C. A solution of 2.6 mg (0.013 mmol) of 85% *m*-CPBA in 0.3 mL of $CDCl_3$ was added dropwise to the cold selenide solution and stirred 10 min. The addition of 1.5 mg (0.0010 mL, 0.013 mmol) of trifluoroacetic acid was followed by 30 min of stirring at −60 °C before the addition of 5.1 mg (0.0070 mL, 0.050 mmol) of triethylamine. The solution was warmed to rt after 10 min. The NMR spectrum (200 MHz) showed a 2.9:1 ratio of the diastereomeric selenoxides **11** and **12** by comparison of their respective methyl singlets (200 MHz): δ 2.43 (J_{Se-H} = 12.0 Hz) and 2.72 (J_{Se-H} = 12.5 Hz). Other signals of **12** that were resolved from those of **11** included δ 4.07 (t, J = 9 Hz, 1 H) and δ 6.42 (d, J = 8 Hz, 1 H). The NMR of this solution remained essentially unchanged after 19 h at rt, but went to the ≈30:1 (**11**:**12**) equilibrium mixture upon extended times (≈2 weeks) or after workup (acid then base extractions).

(+)-(S_P,S_S)-4-(*p*-Toluenesulfinyl)[2.2]paracyclophane (16) and (−)-(R_P,S_S)-4-(*p*-Toluenesulfinyl)[2.2]paracyclophane (17). A solution of 1.29 g (4.49 mmol) of 4-bromo[2.2]paracyclophane in 20 mL of THF was cooled to −78 °C under N_2, and 2.58 mL of *n*-BuLi in hexane (1.74 M, 4.49 mmol) was added. After 15 min this solution was transferred by cannula into a −78 °C solution of (−)-menthyl (−)-(*S*)-*p*-toluenesulfinate (1.35 g, 4.58 mmol) in 20 mL of THF and stirred for 10 min. The cold bath was then removed. After 30 min the solution was poured into 20 mL of saturated NH_4Cl and 30 mL of water and extracted with ether. The organic layer was washed with water and brine and then dried over Na_2SO_4. Solvent removal provided 2.70 g of a yellow oil. The two diastereomers were separated and purified by preparative HPLC on silica (2:1 hexane–ethyl acetate) to provide 0.53 g (1.53 mmol, 34%) of **16** (t_R 7 min) and 0.52 g (1.50 mmol, 33%) of **17** (t_R 5 min).

16: mp 151–155 °C; NMR (270 MHz) δ 2.30 (s, 3 H), 2.88 (ddd, J = 13.5, 10.5, 5.4 Hz, 1 H), 3.0–3.24 (m, 5 H), 3.34 (ddd, J = 13, 10, 5 Hz, 1 H), 3.50 (ddd, J = 13, 10, 2.5 Hz, 1 H), 6.43 (d, J = 8 Hz, 1 H), 6.53 (s, 2 H), 6.61 (br d, J = 8 Hz, 2 H), 6.96 (d, J = 8 Hz, 1 H), 7.10 (d, J = 1.7 Hz, 1 H), 7.15 (d, J = 8 Hz, 2 H), 7.37 (d, J = 8 Hz, 2 H); IR (KBr) 2950, 2866, 1608, 1098, 1076, 1047, 825, 738 cm^{-1}; MS M^+ 346.1357 (calcd for $C_{23}H_{22}OS$, 346.13916), 346 (34), 330 (11, M^+ − 16), 242 (21, $C_{15}H_{14}OS^+$), 105 (100), 104 (61); $[\alpha]^{24}_D$ +85° (0.0040 g/mL in $CHCl_3$, sample for this measurement had ≈8% of **17** in it by HPLC).

17: mp 176–177 °C; NMR (270 MHz) δ 2.37 (s, 3 H), 2.79 (ddd, J = 13, 11, 5 Hz, 1 H), 2.90–3.32 (m, 5 H), 3.36 (ddd, J = 12.5, 10.5, 5 Hz, 1 H), 3.85 (ddd, J = 13, 10.5, 2.5 Hz, 1 H), 6.38 (d, J = 8 Hz, 1 H), 6.45 (d, J = 8 Hz, 1 H), 6.57 (m, 4 H), 6.80 (d, 8 Hz, 1 H), 7.26 (d, J = 8 Hz, 2 H), 7.40 (d, J = 8 Hz, 2 H); IR (KBr) 2945, 2875, 1600, 1095, 1052, 835, 735 cm^{-1}; MS M^+ 346.1388 (calcd for $C_{23}H_{22}OS$, 346.13916), 346 (100), 330 (29, M^+ − 16), 242 (48, $C_{15}H_{14}OS^+$), 105 (85), 104 (47); $[\alpha]^{23}_D$ −51° (0.0025 g/mL in $CHCl_3$).

Anal. Calcd for $C_{23}H_{22}OS$: C, 79.73; H, 6.40. Found: C, 79.50; H, 6.51.

4-(*p*-Toluenesulfonyl)[2.2]paracyclophane (19). Sulfoxide (−)-(R_P,S_S)-**17** (0.39 g, 1.1 mmol) was dissolved in 5 mL of CH_2Cl_2 and 20 mL of ether, and 0.264 g (1.3 mmol) of 85% *m*-CPBA was added at rt over 1 min. After stirring 1 h, a 10% $NaHSO_3$ solution was added until the excess oxidant had been reduced (potassium iodide/starch paper no longer turned purple). The organic layer was washed successively with 20-mL portions of 1.5 M NaOH solution (twice), water, and brine and dried (Na_2SO_4). Solvent removal provided 0.42 g of (−)-(R_P,S_S)-**19** as a white solid, which was used without further purification: mp 158–160 °C; $[\alpha]^{23}_D$ −74° (0.0015 g/mL in $CHCl_3$); NMR (270 MHz) δ 2.36 (s, 3 H), 2.83 (ddd, J = 13, 11, 6 Hz, 1 H), 2.95–3.32 (m, 5 H), 3.40 (ddd, J = 13, 11, 6 Hz, 1 H), 3.88 (≈td, J = 11.5, 1 Hz, 1 H), 6.42–6.6 (m, 4 H), 6.65 (dd, J = 7.5, 1 Hz, 1 H), 6.85 (d, J = 8 Hz, 1 H), 7.21 (d, J = 8 Hz, 2 H), 7.40 (d, J = 1 Hz, 1 H), 7.64 (d, J = 8 Hz, 2 H); IR (KBr) 2944, 2870, 1310, 1301, 1158 cm^{-1}; MS M^+ 362.1339 (calcd for $C_{23}H_{22}O_2S$, 362.13407), 362 (62), 194 (11), 193 (44), 179 (28), 105 (42), 104 (100).

(+)-4-Bromo-15-(*p*-toluenesulfonyl)[2.2]paracyclophane (20). A solution of bromine in CCl_4 (0.863 M, 1.45 mL, 1.25 mmol) was stirred with 6 mg of iron powder (0.10 g-atom) at rt for 30 min. After the addition of 0.40 g (1.1 mmol) of (−)-4-(*p*-toluenesulfonyl)[2.2]paracyclophane (**19**) in 8 mL of dry CH_2Cl_2, the mixture was refluxed for 1 h. The solution was washed successively with 5 mL of 10% $NaHSO_3$, 10 mL of saturated $NaHCO_3$, and then 10 mL of brine. Drying (Na_2SO_4), solvent removal, and recrystallization of the residue from methylene chloride–acetone gave 334 mg (0.76 mmol, 69%, second crop: 0.097 mg, 9%) of (+)-**20**: mp 264–265 °C; $[\alpha]^{23}_D$ +70.0° (0.0462 g/mL in $CHCl_3$); NMR (270 MHz) δ 2.29 (s, 3 H), 2.8–3.3 (m, 6 H), 3.83 (ddd, J = 13, 10, 5 Hz, 1 H), 4.47 (ddd, J = 13, 10, 2.5 Hz, 1 H), 6.50 (d, J = 8 Hz, 1 H), 6.58 (s, 2 H), 6.68 (s, 1 H), 6.74 (dd, J = 8, 1.5 Hz, 1 H), 7.12 (d, J = 8 Hz, 2 H), 7.37 (d, J = 1.5 Hz, 1 H), 7.52 (d, J = 8 Hz, 2 H); IR (KBr) 2934, 2858, 1608, 1595, 1404, 1316, 1159, 1103, 1046, 865, 722, 702, 675, 651 cm^{-1}; MS M^+ 442.0428 (calcd for $C_{23}H_{21}{}^{81}BrO_2S$, 442.04264), 442 (24), 440 (20), 195 (100), 193 (92), 184 (17), 182 (18), 179 (58).

Bis(15-(*p*-toluenesulfonyl)[2.2]paracyclophan-4-yl) Diselenide (22). A solution of 334 mg (0.76 mmol) of (+)-**20** in 25 mL of THF was placed under N_2 in a 50-mL 2-neck flask with a side arm. The side arm led to a 50-mL flask containing 258 mg (0.76 mmol) of dibenzyl diselenide in 15 mL of THF. Both solutions were cooled to −78 °C under N_2 and 0.44 mL of 1.74 M *n*-BuLi (0.77 mmol) was added to the bromo sulfone **20**. After being stirred for 5 min, the organolithium solution was poured

into the cold dibenzyl diselenide solution and stirred for 2 min at −78 °C. The mixture was allowed to warm to about 0 °C over 10 min. Chloroacetic acid (0.1 g, 1.0 mmol) was added in 1 mL of 1.5 M NaOH, and the mixture was poured into 50 mL of 1.5 M NaOH solution 15 min later and extracted with 50 mL of ether (the chloroacetic acid was added to permit easy removal of phenylmethaneselenoate as (benzylseleno)acetic acid). The organic layer was washed with water and brine. Drying over Na_2SO_4 and removing solvent provided 0.51 g of white solid (crude mixture of **21** and *n*-butyl benzyl selenide). This white solid was dissolved in 20 mL of CH_2Cl_2 and 2.7 mL of bromine in CCl_4 (0.863 M, 2.33 mmol) was added dropwise over 90 s. After 10 min at rt the mixture was shaken with 30 mL of 10% $NaHSO_3$ solution in a separatory funnel. The CH_2Cl_2 layer and suspended solids were drained off, and the aqueous layer was extracted with several small portions of CH_2Cl_2 until most of the suspended solids were removed. The combined brown CH_2Cl_2 layers (with solids) were stirred with 0.160 g (0.160 mL, 5.0 mmol) of anhydrous hydrazine at rt for 40 min. The solution was washed successively with 1.2 N HCl, saturated $NaHCO_3$, and brine. After filtering through a Na_2SO_4 cone, the orange solid was purified by column chromatography (26 × 2.8 cm column, 50 g of silica gel) to provide 0.272 g (0.31 mmol, 81%) of the orange diselenide (+)-**22**: mp 280 °C dec; $[\alpha]^{24}_D$ +250° (0.0038 g/mL in $CHCl_3$); NMR (270 MHz) δ 2.28 (s, 3 H), 2.63–2.80 (m, 2 H), 2.90–3.20 (m, 4 H), 3.44 (apparent t, J = 10 Hz, 1 H), 3.98 (apparent t, J = 10 Hz, 1 H), 6.36–6.55 (m, 3 H), 6.68 (dd, J = 8, 1.7 Hz, 1 H), 6.80 (d, J = 0.8 Hz, 1 H), 7.08 (d, J = 8 Hz, 2 H), 7.17 (d, J = 1.7 Hz, 1 H), 7.47 (d, J = 8 Hz, 2 H); IR (KBr) 2940, 2867, 1325, 1311, 1300, 1160, 1100 cm^{-1}.

Racemic diselenide (±)-**22** was prepared from (±)-4-(*p*-tolylthio)[2.2]paracyclophane by using a minor modification of the procedures above. The racemic diselenide was a 1:1 mixture of *dl* and *meso* diastereomers. The most noticeable difference between the NMR spectrum of the *meso* diastereomer and the one listed above is a clearly resolved signal at δ 3.58 signal (ddd, J = 13.5, 10.5, 5.5 Hz, 1 H).

4-(Methylseleno)-15-(*p*-toluenesulfonyl)[2.2]paracyclophane (23). A solution of 70 mg (0.080 mmol) of diselenide **22** in 6 mL of *N,N*-dimethylacetamide was stirred under N_2 while 9.1 mg (0.24 mmol) of $NaBH_4$ was added. The mixture was heated (85 to 95 °C over 30 min) and became red-orange. It was slowly cooled to 50 °C over 25 min, the heating bath was removed, and the solution was allowed to attain rt. Upon the addition of 0.11 g (0.050 mL, 0.80 mmol) of CH_3I the solution faded to a light yellow color. After 10 min the solution was poured into 10 mL of ether and washed with 1.2 N HCl (H_2 evolution), saturated $NaHCO_3$, water, and brine. Drying (Na_2SO_4), solvent removal, and purification by preparative TLC (CH_2Cl_2) gave 35.3 mg (0.0792 mmol, 50%) of **23** as a white solid: mp 159–161 °C; NMR (200 MHz) δ 2.18 (J_{Se-H} = 11.8 Hz, 3 H), 2.27 (s, 3 H), 2.8–3.3 (m, 6 H), 3.72 (ddd, J = 13, 10, 4.6 Hz, 1 H), 4.41 (ddd, J = 12.5, 10.5, 2 Hz, 1 H), 6.42 (s, 1 H), 6.50 (m, 3 H), 6.72 (dd, J = 7.5, 1.5 Hz, 1 H), 7.08 (d, J = 8 Hz, 2 H), 7.23 (d, J = 1.5 Hz, 1 H), 7.50 (d, J = 8.5 Hz, 2 H); IR (KBr) 2950, 2875, 1610, 1591, 1328, 1316, 1306, 1164, 1104, 725, 704, 676 cm^{-1}; MS M^+ 456.0662 (calcd for $C_{24}H_{24}O_2S^{80}Se$, 456.0662) 456 (36), 198 (85, $C_9H_{10}{}^{80}Se^+$), 193 (100).

4-(Geranylseleno)-15-(*p*-toluenesulfonyl)[2.2]paracyclophane (26). A suspension of diselenide (+)-**22** (0.2419 g, 0.275 mmol) in 40 mL of THF and 10 mL of absolute ethanol was stirred under N_2, and 32.9 mg (0.87 mmol) of $NaBH_4$ was added (slow evolution of H_2). After 105 min, 94.9 mg (0.55 mmol) of geranyl chloride was added and the mixture was stirred for 1 h at rt. The mixture was worked up as described for **23** above, and the residue was purified by preparative TLC (CH_2Cl_2) to afford 0.1485 g (0.257 mmol, 47%) of selenide **26** plus 58.9 mg (0.0669 mmol, 24%) of diselenide **22** (racemic selenide (±)-**26** was similarly prepared in an 88% yield from racemic diselenide **22**, mp 114–115.5 °C): NMR (270 MHz) δ 1.32 (s, 3 H), 1.57 (s, 3 H), 1.66 (s, 3 H), 1.80–2.05 (m, 4 H), 2.27 (s, 3 H), 2.80–3.35 (m, 8 H), 3.81 (ddd, J = 13, 10, 5 Hz, 1 H), 4.30 (br t, J = 8 Hz, 1 H), 5.03 (m, 1 H), 5.28 (br t, J = 8 Hz, 1 H), 6.52 (m, 3 H), 6.72 (overlapping s and d, J = 8 Hz, 2 H), 7.10 (d, J = 8 Hz, 2 H), 7.28 (d, J = 1 Hz, 1 H), 7.51 (d, J = 8 Hz, 2 H); ^{13}C NMR (50 MHz, 29 of 31 signals resolved, >95% one isomer) δ 15.5, 17.6, 21.3, 25.6, 26.4, 26.6, 33.9, 34.5, 34.8, 36.2, 39.6, 120.5, 124.3, 126.7, 129.4, 131.2, 131.6, 133.1, 135.0, 137.3, 137.8, 137.9, 138.2, 138.9, 139.0, 140.6, 141.2, 141.8, 142.8; IR (KBr) 2950, 2875, 1610, 1594, 1329, 1319, 1309, 1141, 678 cm^{-1}; MS M^+ 578.1756 (calcd for $C_{33}H_{38}O_2S^{80}Se$, 578.17577).

Optically Active Linalool. A solution of 0.1485 g (0.257 mmol) of the geranyl selenide **26** in 5 mL of CH_2Cl_2 was cooled to −66 °C, and 63 mg (0.31 mmol) of 85% *m*-CPBA was added dropwise over 1 min. The cloudy solution was warmed to −40 °C over 10 min, and 78 mg (0.110 mL, 1.07 mmol) of diethylamine was added (solution clears). The mixture was warmed to −25 °C over 10 min, the cold bath was removed, and 40 mg (0.040 mL, 1.25 mmol) of anhydrous hydrazine was added. After 30 min of stirring at rt, the solution was washed twice with 1.5 M NaOH, the CH_2Cl_2 layer was concentrated, and 10 mL of pentane was added to the residue. The yellow solid was filtered and rinsed with pentane to give 99.2 mg (0.113 mmol, 88%) of diselenide (+)-**22**. The pentane filtrate was washed with 1.2 N HCl, saturated $NaHCO_3$, and brine and filtered through a Na_2SO_4 cone. Solvent was removed and the residue was bulb-to-bulb distilled (rt/0.006 mm, liquid nitrogen cooled receiver) to give 19.1 mg (0.124 mmol, 48%) of linalool. The addition of 22 mg of $Eu(facam)_3$ to a 0.45 M solution of the product in $CDCl_3$ showed a 5:1 ratio of enantiomers by NMR analysis. The doublet (J = 18 Hz) originally at δ 5.23 moved to δ ≈5.73 with the two enantiomers conveniently resolved. It is the most useful signal for analysis although other signals help to verify the ratio.

The $CDCl_3$ was removed by rotary evaporation and the linalool was separated from the shift reagent by bulb-to-bulb distillation and its rotation was measured: $[\alpha]^{23}_D$ +10° (0.0036 g/mL in $CDCl_3$) (lit.[44a] $[\alpha]^{20}_D$ +19.3°) demonstrating that the major enantiomer was (*S*)-linalool.[44b] The sign of rotation of linalool does not change in chloroform.[44c]

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Supplementary Material Available: Proton NMR spectra of compounds **11** + **12**, **16**, **17**, **19**, **20**, **22**, **23**, **26**, and **28** and experimental procedures for determination of the absolute configuration of **17** and the enantiomeric purity of **22** (preparation of **28** and **29**) (14 pages). Ordering information is given on any current masthead page.

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