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Stereoselective Syntheses of 1,2-Dialkyl-1-phenyl Cyclopentanes Involving Intramolecular Carbolithiation of α-Thioalkenes

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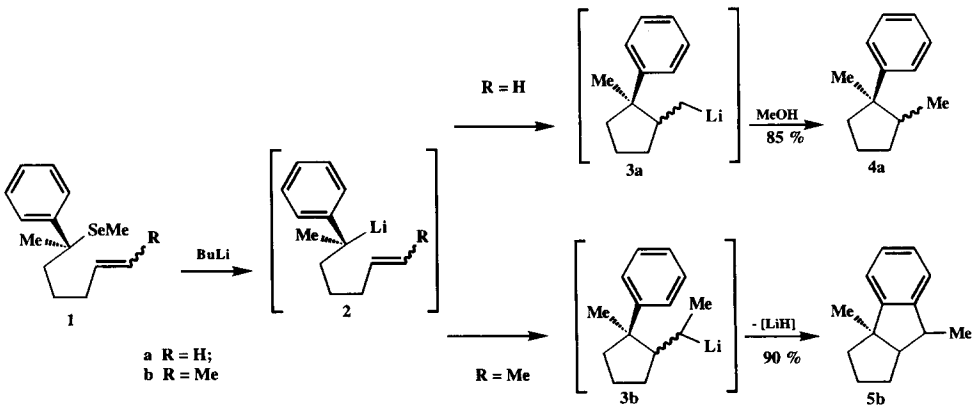
Abstract : 2-Ethyl-1-methyl-1-phenyl cyclopentane, unavailable by butyllithium-promoted carbocyclisation of the corresponding alkenyl selenide, has been synthesized from 6-methylseleno-6-phenyl-1-phenylthio-1-heptene and 7-methylseleno-7-phenyl-2-phenylthio-2-octene with high stereocontrol at all the three stereogenic centers. Depending upon the solvent used, the derivative in which the methyl- and the phenylthiomethyl groups are *cis* (in THF) or *trans* (in pentane) to each other are formed selectively. Copyright © 1996 Elsevier Science Ltd

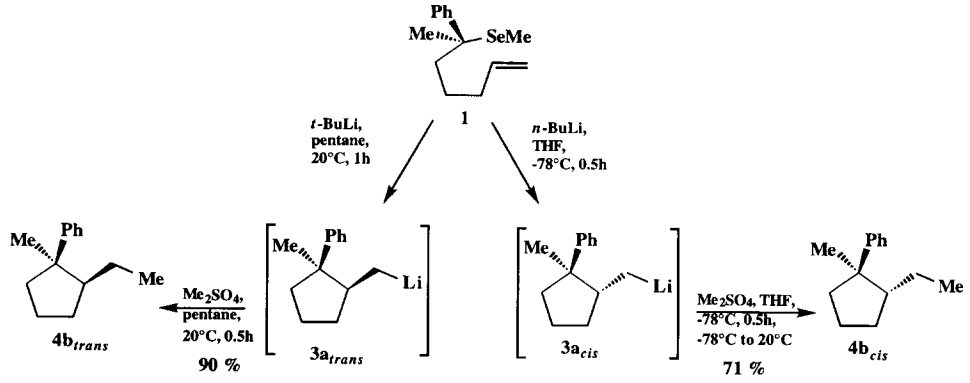
We have reported[1a] that the alkenyl benzylselenide **1a** (R= H) reacts with butyllithiums and produces, *via* the corresponding alkenyl benzyllithium **2a** and 2-lithiomethyl-1-methyl-1-phenyl cyclopentane **3a**, the 1,2-dimethyl-1-phenyl cyclopentane **4a** in very high yield and with almost complete stereocontrol [*cis*-methyl groups in THF (d.e. : 96%), *trans*-methyl groups in pentane (d.e. : 96%), Scheme 1)]. We also described[2] that this reaction cannot be extended to the synthesis of 2-ethyl-1-methyl-1-phenyl cyclopentane **4b** (R= Me), its higher homolog, owing to the high propensity of the 2-(1'-lithioethyl)-1-methyl-1-phenyl cyclopentane **3b** to further add across the C,C double bond of the aromatic ring, to produce the cyclopent[a]indenyl derivative **5b** (R= Me, 90% yield, Scheme 1).[2]

Scheme 1



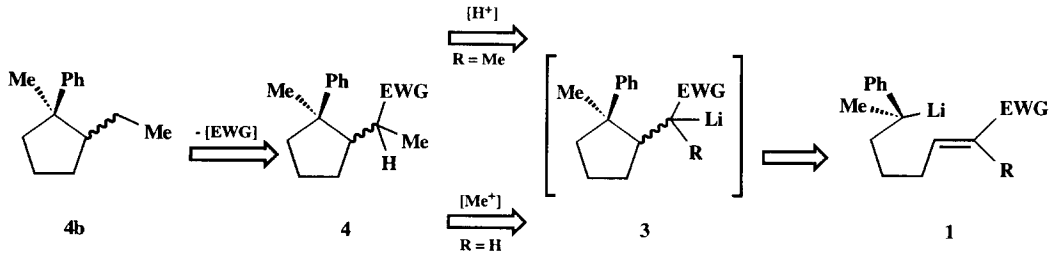
In the accompanying paper[1b] we have proposed three different solutions to this problem which all use 6-methylseleno-6-phenyl-1-methyl-1-heptene **1a** as the starting material and 2-lithiomethyl-1-methyl-1-phenyl cyclopentane **3a** as the common intermediate. The most efficient and direct route, shown in Scheme 2, involves the methylation of this intermediate with dimethyl sulfate.

Scheme 2



We present in this paper some alternative methods which use as the key step the carbocylisation of ω-alkenylbenzyllithiums suitably functionalized on their C,C double bonds (Scheme 3).

Scheme 3



These approaches to **4b** were expected to provide important information on the intimate mechanism of the carbocyclisation[3-6] reaction of organolithium compounds, especially benzyllithiums.[7,8] We decided to use the benzylselenides **1c** or **1d** bearing a phenylthio moiety to achieve the desired transformation[9] and presumed that this group would, by its aptitude to stabilize carbanions,[10-12] (i) favor the carbometallation[8,13-16] (ii) decrease the aptitude of the resulting organolithium to react further on the aromatic ring, and (iii) would be easily removed after cyclisation. Furthermore, we wanted access to both the *cis*- and the *trans*-series of carbocycles **4b** and expected that transposition of the results reported[1a] for the unsubstituted case **1a** would allow this (i.e. the *cis*-series when the reaction is performed in THF, and the *trans*-series if pentane or ether is used instead). Therefore, we allocated a pivotal role to the α-thioalkyllithium intermediate in the above transformation.

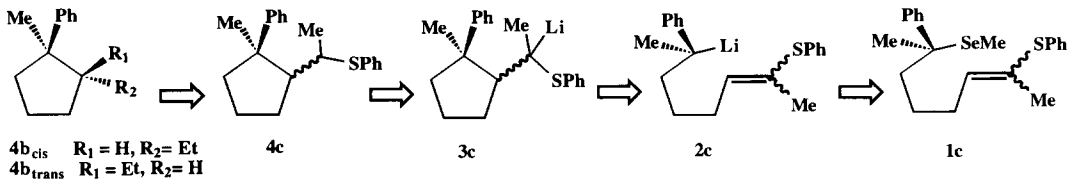
α-Thioalkyllithiums have been the subject, over the last thirty years, of intensive synthetic work[10-16] and physicochemical studies.[17-20] Recent studies have demonstrated that they are configurationally stable only at very low temperatures.[17,18,19,22]

Addition of organolithiums to vinyl sulfides allows the synthesis of α-thioalkyllithiums but only a few reports have been published on this subject.[10,13-16] The intermolecular carbolithiaton occurs efficiently on phenylthioethylene when carried out in ether,[13-15] is very poor with its alkylthio analogs,[13] and is solvent

dependent since competing metallation on the vinylic hydrogen can occur.[15] The intramolecular reaction has only very recently been reported.[16]

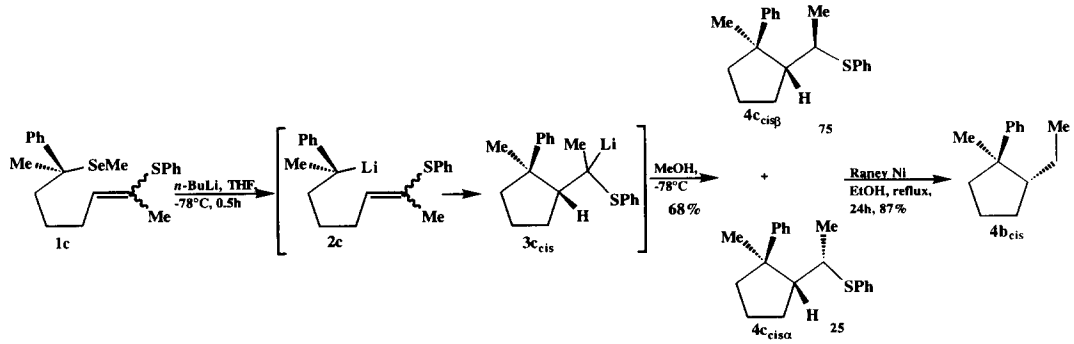
7-Methylseleno-7-phenyl-2-phenylthio-2-octene **1c** was chosen as the first obvious candidate (Scheme 4). Sequential (i) Se/Li, (ii) Li/H and (iii) SPh/H exchanges were expected to finally produce **4b** *via* **2c**, **3c**, and **4c**, whose stereochemistry would depend upon the nature of the solvent (THF : $\mathbf{4c}_{cis}$, pentane : $\mathbf{4c}_{trans}$) used in the cyclisation step (Scheme 5).[1]

Scheme 4



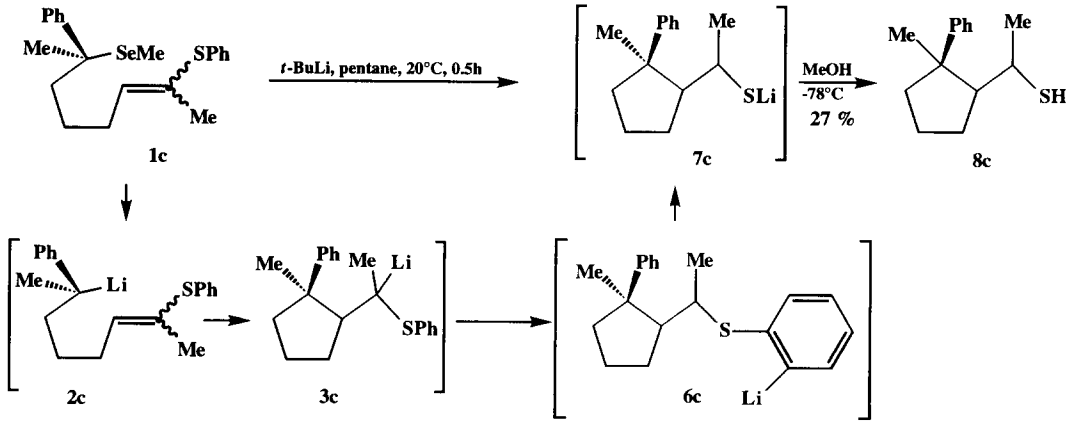
The reaction was first carried out on **1c** (*Z*/*E*= 27/73) in THF at -78°C (1 eq. *n*-BuLi, 0.5 h, Scheme 5) and leads, after quenching with methanol at that temperature, to the formation of **4c** in reasonable yield (68%) and with good control at the three stereogenic centers which have been constructed in one step. We observed, as expected, that the major stereoisomer belongs to the *cis*-series ($\mathbf{4c}_{cis}$ / $\mathbf{4c}_{trans}$= 95/5) and that one of the two epimers at the third stereogenic center $\mathbf{4c}_{cis\beta}$ predominates over the others ($\mathbf{4c}_{cis\beta}$ / $\mathbf{4c}_{cis\alpha}$= 75 / 25, Scheme 5).

Scheme 5



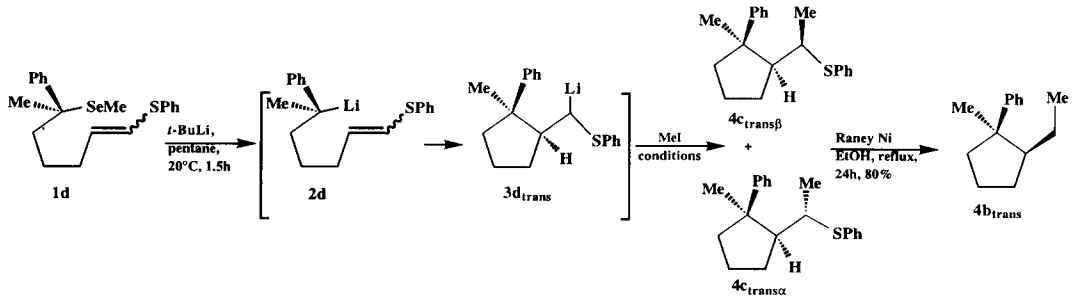
We subsequently tried to perform the same reaction in pentane in order to produce the *trans*-compound $\mathbf{4c}_{trans}$ (1 eq. *t*-BuLi, pentane, 20°C, 1 h) but the results were much more complex (Scheme 6). We have evidence the C-Se bond cleavage still takes place on the benzylselenide **1c** and that the desired cyclisation occurs. However, after the usual work-up, we obtained a mixture of compounds in which **4c** was missing. The major compound we isolated from the reaction performed in pentane proved to be the thiol **8c** whose basic structure was assessed by ^{1}H and ^{13}C NMR spectroscopy (Scheme 6). We do not have evidences about the mechanism which is taking place, but we suspect that the fully alkyl-substituted α-thioalkyllithium **3c** resulting from the carbocyclisation reaction is unstable under the conditions used and isomerises (*via* an inter- or intramolecular process) to the corresponding ortho-thioaryllithium **6c**. This, in turn, undergoes a β-elimination reaction leading to the thiolate **7c** and probably benzyne (Scheme 6).[21] The synthesis of the *trans*-stereoisomers $\mathbf{4c}_{trans}$ and of the desired 2-ethyl-1-methyl-1-phenyl cyclopentane $\mathbf{4b}_{trans}$ cannot, therefore, be achieved from **1c**.

Scheme 6



In order to circumvent this problem, we tried another, even more, connective route to **4b** starting from the 6-methylseleno-6-phenyl-1-phenylthio-1-heptene **1d** (Scheme 7). We hoped that the formation of a secondary α-thioalkyllithium **3d** (Scheme 7) instead of the fully substituted **3c** (Scheme 5) would allow, by increasing the stability of the carbanion, the use of pentane as solvent. This would consequently permit an entry to the *trans*-series of compounds leading finally to $\mathbf{4c}_{trans}$ after methylation and to $\mathbf{4b}_{trans}$ on further reduction (Scheme 7).

Scheme 7



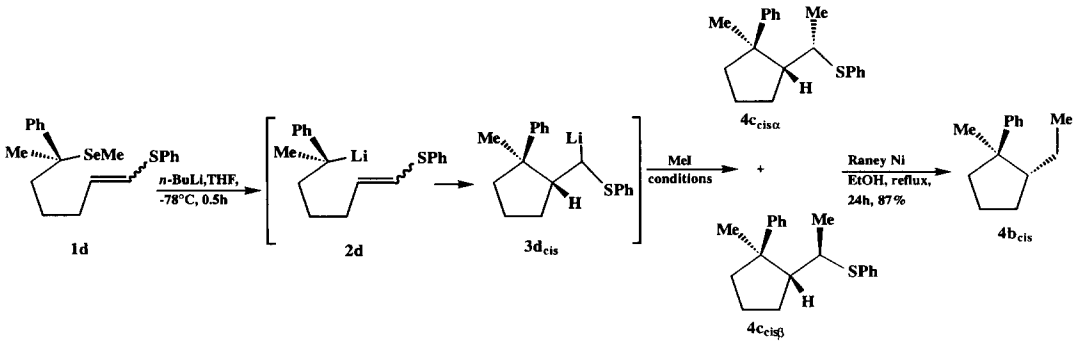
Entry	Conditions	4c [a] (%) [b]	$4c_{trans}$ / $4c_{cis}$	$4c_{trans}\beta$ /$4c_{trans}\alpha$
a	MeI, THF, -78°C	93 (54)	96/4	88/12
b	(i) CuI-DMS, THF, -110°C, 0.5 h (ii) MeI	50	96/4	92/8

(a) refers to the % of **4c** measured by GC[2] (b) refers to the yield in the major stereoisomer $\mathbf{4c}_{trans}\beta$ isolated as pure compound.

We found that 6-methylseleno-6-phenyl-1-phenylthio-1-heptene **1d** (*Z*/*E*= 50/50) delivers, on sequential reaction with *t*-butyllithium in pentane and methyl iodide in THF the desired *trans*-product $\mathbf{4c}_{trans}$ (Scheme 7, entry a). It was interesting to note that the alkylation does not take place when the reaction was carried out in pentane unless THF was used as a co-solvent.

The same reaction when carried out in THF ((i) *n*-BuLi, THF, - 78°C, 0.5 h (ii) MeI, THF, -78°C) gave the $\mathbf{4c}_{cis}$ stereoisomer (Scheme 8, entry a).

Scheme 8



Entry	Conditions	4c % [a] (%) [b]	$4c_{cis}$ / $4c_{trans}$	$4c_{cis}$ α / $4c_{cis}$ β
a	MeI, THF, -78°C, 0.5 h	95 (62)	95/5	72/28
b	MeI, THF, -110°C, 1 h	88 (67)	95/5	78/22
c	Me_2SO_4, THF, -78°C, 0.5 h	90 (45)	95/5	69/31
d	MeI, THF, 2 eq. HMPA, -78°C, 0.5 h	88	96/4	61/39
e	(i) 1.3 eq. *t*-BuOK, THF, -78°C (ii) MeI, -78°C, 0.5 h	92 (56)	95/5	85/15
f	(i) 0.5 eq. CuI-DMS, -110°C (ii) MeI, -110°C, 1 h	80 (60)	95/5	92/8
g	(i) 1 eq. CuI-DMS, -110°C (ii) MeI, -110°C, 1 h	75 (50)	95/5	92/08
h	(i) 0.5 eq. CuI-DMS, -78°C (ii) MeI, -78°C, 0.5 h	78 (53)	95/5	76/24

(a) refers to the % of **4c** measured by GC[2] (b) refers to the yield in the major stereoisomer $4c_{cis\alpha}$ isolated as pure compound.

In both cases, a small amount of product resulting from the protonation of the α-thioalkyllithium intermediate **3d** was also formed. Separation of **3d** from the methylated compound **4c** was not easy and was responsible for the relatively poor yields of pure **4c** reported (50-67%). Each of the $4c_{trans}$ and $4c_{cis}$ compound proved to be a mixture of stereoisomers, epimers at the methylated carbon, in which one predominates. Interestingly, the major stereoisomers ($4c_{cis\alpha}$, Scheme 5 and $4c_{cis}\beta$, Scheme 8), obtained in THF from **1d** and **1c** respectively, were epimers at the carbon bearing the phenylthio group.

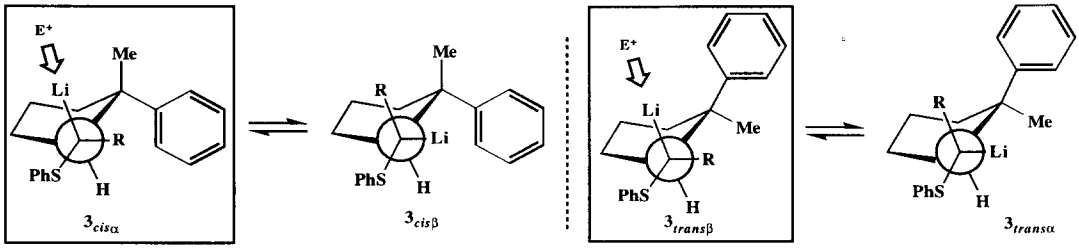
We wanted to obtained a better selectivity in the methylation reaction and have varied some of the parameters in order to achieve it.

Thus, we found that in THF the $4c_{cis\alpha}$ / $4c_{cis}\beta$ ratio, obtained from **1d**, was identical to that when the alkylation reaction was carried out at -78°C or at lower temperature (-110°C) and did not depend upon the methylating agent used (Scheme 8, entries a-c). The presence of HMPA, however, lowers the selectivity (Scheme 8, entry d). The nature of the counter ion greatly influences the stereochemistry of the methylation reaction. Thus, a much higher selectivity in favor of the stereoisomer $4c_{cis\alpha}$ was observed when the alkylation was carried out on the potassium instead of the lithium salt $3d_{cis}$ (Scheme 8, entry e). An even better stereoselectivity was obtained on the corresponding copper derivative (Scheme 8, entries f and g). The amount of copper salt did not affect the stereoisomeric ratio (Scheme 8, compare entries f and g) but the temperature at which the reaction was achieved (-78°C instead of -110°C, Scheme 8 compare entries f and h) was now important since lower diastereoselection was observed if the Li/Cu exchange and further methylation were carried out at a higher temperature.

The copper mediated methylation reaction also applies to the *trans*-series, but requires the use of a small amount of THF. This now allows the highly stereoselective synthesis of $\mathbf{4c}_{trans\beta}$ (Scheme 7, entry b). Only a few examples of stereoselective alkylation of α-thioalkylmetals have been reported[18,19,22,23] and none of them involve the connective synthesis of the organometallic by formation of a new C,C bond as reported here.
Since the reactions have been carried out on a Z/E mixture of stereoisomers **1d** and lead to the production of mainly one stereoisomer of **4c**, they imply stereochemical control at one or at several stages of the whole process : (i) addition (stereospecific or not) of the organolithium across the C,C double bond of the vinyl sulfide moiety (ii) conformational stability of the resulting α-thioalkyllithiums (iii) stereochemistry of the alkylation reaction (retention, inversion, face selective approach).

Whatever it is, it is known[17] that epimerisation occurs under the conditions (-78°C, 0.5 h) at which we conducted the reactions. Our results suggest that methylation, as well as protonation, takes place from the least hindered side of the α-thioalkyllithiums **3c** (R= Me) and **3d** (R= H) which adopt the preferred conformations tentatively shown in Scheme 9.

Scheme 9



We are currently repeating the reactions on pure *cis*- and *trans*- **1c** and **1d**, trying to trap each of the stereoisomers of **3**, by performing the reactions at the lowest temperature possible, eventually with the electrophile present in the medium. The electrophile must be properly chosen so as to react selectively with **3** and not with the first intermediate **2**.
The last step of the whole transformation involves the reduction of 2-(1'-phenylthioethyl)-1-methyl-1-phenylcyclopentanes $\mathbf{4c}_{trans}$ and $\mathbf{4c}_{cis}$ to 2-ethyl-1-methyl-1-phenyl cyclopentanes $\mathbf{4b}_{trans}$ and $\mathbf{4b}_{cis}$. We tried to cleave the carbon-sulfur bond using lithium di-*tert*-butylbiphenylide (LiDBB) in THF,[24-26] lithium in ethylamine[27] and Raney nickel.[28,29]

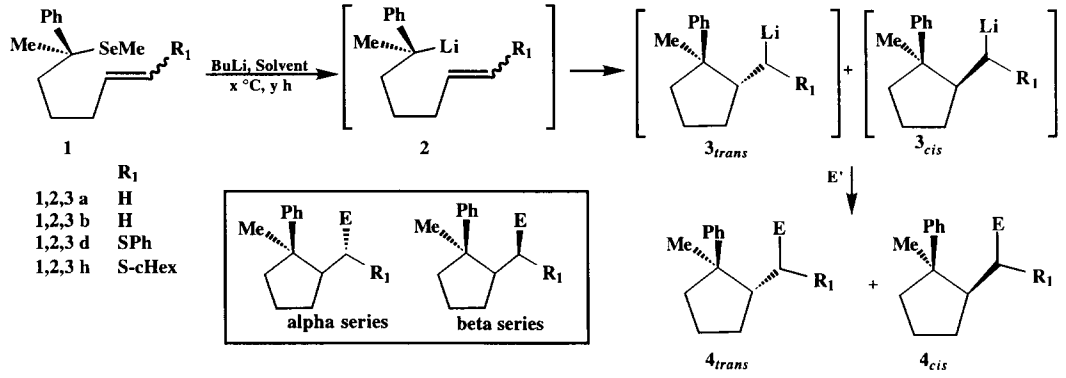
The first two reagents were expected to produce 2-(1'-lithioethyl)-1-methyl-1-phenylcyclopentane **3b** (Scheme 1). Ring opening of the five-membered ring (this is formally the "retro conversion" of the reaction described in Scheme 1) occurs with LiDBB,[30] whereas the reduction of the thio moiety seems to have taken place with lithium in ethylamine. We have not been able, however, on the small amount of **4c** used, to avoid concomitant reduction of the aromatic ring *via* a Birch reduction. Finally the reduction of $\mathbf{4c}_{trans}$ and $\mathbf{4c}_{cis}$ to $\mathbf{4b}_{trans}$ and $\mathbf{4b}_{cis}$ derivatives has been conveniently achieved with Raney nickel[28,29] (ethanol, reflux, 24 h, $\mathbf{4b}_{trans}$ or $\mathbf{4b}_{cis}$, >80 % yield, Schemes 5, 7 and 8).

During this work, we have extended the syntheses reported above. Thus, the organolithiums **3** react efficiently with a large variety of electrophiles (Scheme 10). Indeed, the reaction of 6-phenyl-6-methylseleno-1-heptene **1a**

sequentially with butyllithium and diphenyl disulfide in pentane or THF (Scheme 10, entries a,b) affords compounds identical to those resulting from sequential reaction of 6-phenyl-6-methylseleno-1-phenylthio-1-heptene **1d** with butyllithium and methanol under closely related conditions (Scheme 10, entries c and d, compare to entries a and b). These results allow the unambiguous determination of the structure and stereochemistry of compounds of different origins since the stereochemistry of related compounds resulting from the sequential reaction of 6-phenyl-6-methylseleno-1-heptene **1a** with butyllithium and methanol has been already assessed.[1] Reaction of [(2'-methyl-2'-phenyl)cyclopentyl]-1-phenylthiomethyllithium **3d** (R_1= SPh), produced from 6-phenyl-6-methylseleno-1-phenylthio-1-heptene **1c** and butyllithium, with carbon dioxide or allyl bromide provides the corresponding adducts in good yields, but as a mixture of stereoisomers (Scheme 10, entries g-k). Reasonably good stereochemical control has been achieved with carbon dioxide when the reaction was carried out at low temperature (-78°C; Scheme 10, entries h and i, compare entries h and g) but a much poorer one was observed with allyl bromide (Scheme 10, entries j and k). Performing the allylation in the presence of copper salts leads to much better stereocontrol (Scheme 10, entries l-o). These results parallel those already reported for the methylation of the same organometallics and increase the generality of the process in both *cis*- and *trans*-series of compounds.

The stereochemical control of the alkylation reaction was suspected to result from a π–π stacking between the aromatic rings of the phenyl groups attached to the cyclopentane ring and to the sulfur atom respectively which would have rigidified the molecule and favored a specific conformation around the reactive site. In order to have an insight on the intimate mechanism of such process, we have repeated most of the work presented above on the analogous thiocyclohexyl derivatives **1h** (Scheme 10).

Scheme 10



Entry	R1	Solvent	Conditions	E', Conditions	E	Product	4 % [a] (%) [b]	*trans*/*cis* [c]	α / β [d]
a	H	pentane	*t*-BuLi, 20°C, 3 h	PhSSPh, THF, -78°C, 0.5 h	SPh	**4d**	(73)	94/06	–
b	H	THF	*t*-BuLi, -78°C, 1.5 h	PhSSPh, THF, -78°C, 0.5 h	SPh	**4d**	(92)	05/95	–
c	SPh	pentane	*t*-BuLi, 20°C, 1.5 h	MeOH, 20°C	H	**4d**	(79)	96/04	–
d	SPh	THF	*n*-BuLi, -78°C, 0.5 h	MeOH, -78°C	H	**4d**	(89)	05/95	–
e	SPh	pentane	*t*-BuLi, 20°C, 1 h	CD_3OD, 20°C,	D	**4e**	(66)	90/10	23/77
f	SPh	THF	*n*-BuLi, -78°C, 0.5 h	CD_3OD, -78°C	D	**4e**	(90)	05/95	90/10
g	SPh	pentane	*t*-BuLi, 20°C, 1 h	CO_2, 20°C	CO_2H	**4f**	(58)	95/05	40/60
h	SPh	pentane	*t*-BuLi, 20°C, 1.5 h	CO_2, -78°C	CO_2H	**4f**	(63)	95/05	12/88
i	SPh	THF	*n*-BuLi, -78°C, 0.5 h	CO_2, -78°C	CO_2H	**4f**	(60)	05/95	85/15

Entry	R1	Solvent	Conditions	E', Conditions	E	Product	4 % [a] (%) [b]	*trans /cis* [c]	α / β [d]
j	SPh	pentane	*t*-BuLi, 20°C, 1 h	allyl-Br, 20°C	allyl	**4g**	78	96/04	40/60
k	SPh	THF	*n*-BuLi, -78°C, 0.5 h	allyl-Br, -78°C	allyl	**4g**	72	04/96	60/40
l	SPh	pentane	*t*-BuLi, 20°C, 1.5 h	(i) CuI-DMS, THF, -100°C (ii) allyl-Br	allyl	**4g**	87	96/04	20/80
m	SPh	THF	*n*-BuLi, -78°C, 0.5 h	(i) CuI-DMS, THF, -100°C (ii) allyl-Br	allyl	**4g**	87	05/95	90/10
n	SPh	pentane	*t*-BuLi, 20°C, 1 h	(i) CuSPh, THF, 20°C, 0.5 h (ii) allyl-Br	allyl	**4g**	84	96/04	12/88
o	SPh	THF	*n*-BuLi, -78°C, 1.5 h	(i) CuSPh, THF, -25°C, 0.25h (ii) allyl-Br	allyl	**4g**	88	04/96	87/13
p	S-*c*Hex	pentane	*t*-BuLi, 20°C, 1.5 h	MeOH, 20°C	H	**4h**	(80)	95/05	
q	S-*c*Hex	THF	*n*-BuLi, -78°C, 0.5 h	MeOH, -78°C	H	**4h**	(92)	04/96	
r	S-*c*Hex	pentane	*t*-BuLi, 20°C, 1 h	CD_3OD, 20°C,	D	**4i**	(60)	95/05	30/70
s	S-*c*Hex	THF	*n*-BuLi, -78°C, 0.5 h	CD_3OD, -78°C	D	**4i**	(60)	04/96	60/40
t	S-*c*Hex	pentane	*t*-BuLi, 20°C, 1 h	CO_2, 20°C	CO_2H	**4j**	(97)	95/05	40/60
u	S-*c*Hex	pentane	*t*-BuLi, 20°C, 1 h	CO_2, -78°C	CO_2H	**4j**	(87)	95/05	26/74
v	S-*c*Hex	THF	*n*-BuLi, -78°C, 0.5 h	CO_2, -78°C	CO_2H	**4j**	(60)	04/96	70/30
w	S-*c*Hex	pentane	*t*-BuLi, 20°C, 1 h	MeI, 20°C	Me	**4k**	(54)	95/05	18/82
x	S-*c*Hex	THF	*n*-BuLi, -78°C, 0.5 h	MeI, -78°C	Me	**4k**	69	04/96	61/39
y	S-*c*Hex	pentane	*t*-BuLi, 20°C, 1 h	allyl-Br, 20°C	allyl	**4l**	76	95/05	40/60
z	S-*c*Hex	THF	*n*-BuLi, -78°C, 0.5 h	allyl-Br, -78°C	allyl	**4l**	35	04/96	50/50
aa	S-*c*Hex	pentane	*t*-BuLi, 20°C, 1.5 h	(i) CuI-DMS, THF, -100°C (ii) MeI	Me	**4k**	55	95/05	45/55
ab	S-*c*Hex	THF	*n*-BuLi, -78°C, 0.5 h	(i) CuI-DMS, THF, -100°C (ii) MeI	Me	**4k**	70	04/96	60/40
ac	S-*c*Hex	pentane	*t*-BuLi, 20°C, 1 h	(i) CuSPh, THF, 20°C, 0.5 h (ii) MeI	Me	**4k**	73	95/05	16/84
ad	S-*c*Hex	THF	*n*-BuLi, -78°C, 1.5 h	(i) CuSPh, THF, -25°C, 0.25h (ii) MeI	Me	**4k**	79	04/96	75/25
ae	S-*c*Hex	pentane	*t*-BuLi, 20°C, 1.5 h	(i) CuI-DMS, THF, -78°C (ii) allyl-Br	allyl	**4l**		95/05	
af	S-*c*Hex	THF	*n*-BuLi, -78°C, 0.5 h	(i) CuI-DMS, THF, -78°C (ii) allyl-Br	allyl	**4l**	90	04/96	65/35
ai	S-*c*Hex	pentane	*t*-BuLi, 20°C, 1 h	(i) CuSPh, THF, 20°C, 0.5 h (ii) allyl-Br	allyl	**4l**	69	95/05	24/76
aj	S-*c*Hex	THF	*n*-BuLi, -78°C, 1.5 h	(i) CuSPh, THF, -25°C, 0.25 h (ii) allyl-Br	allyl	**4l**	92	04/96	82/18

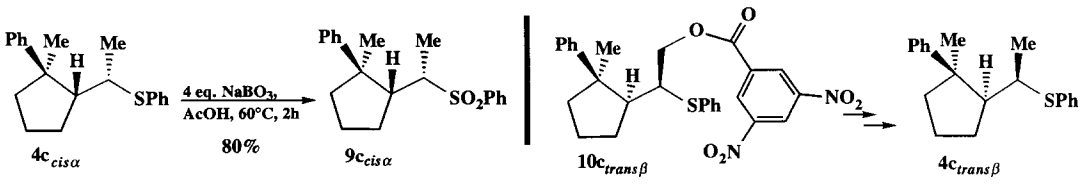
(a) refers to the % of **4c** measured by GC[2] (b) refers to the yield in the major stereoisomer **4** isolated as pure compound (c) refers to the $\mathbf{4}_{trans}$ / $\mathbf{4}_{cis}$ ratio (d) refers to the $\mathbf{4}_{\beta}$ /$\mathbf{4}_{\alpha}$ ratio of the major stereoisomer.

The results gathered in Scheme 10 (entries p to aj) parallel those of the phenylthio series suggesting that, if such effect would have taken place, its is very limited. It is interesting to note the beneficial effect of the sulfur moiety on the cyclisation reaction although a thiocyclohexyl group is expected to stabilize a carbanion to a lower extent than the phenylthio one. We also note the reasonably high chemical yields obtained in the thiocyclohexyl series, although it has been stated that intermolecular carbocyclisation is very poor on vinyl alkyl sulfides.[13]

Last, but not least, we have unambiguously ascertained the stereochemistry, at each of the stereogenic centers, of some of the leading compounds by X-ray crystallography of (i) the sulfone $\mathbf{9c}_{cis\alpha}$ derived from $\mathbf{4c}_{cis\alpha}$ and of

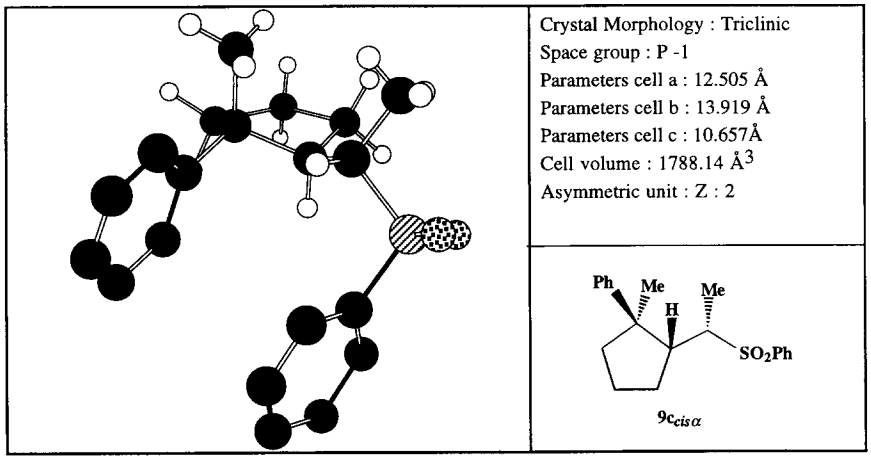
(ii) the m,m'-dinitrobenzoic ester **10c**$_{trans\beta}$ whose corresponding alcohol has been transformed in a few steps to **4c**$_{trans\beta}$ (Scheme 11).

Scheme 11



The first transformation (**4c**$_{cis\alpha}$ -> **9c**$_{cis\alpha}$) has been efficiently achieved with sodium perborate, under the conditions described by McKillop (4 eq. $NaBO_3$, AcOH, 60°C, 2 h, m.p. 94°C, 80%).[31] The X-Ray crystallography data is presented in Scheme 12.

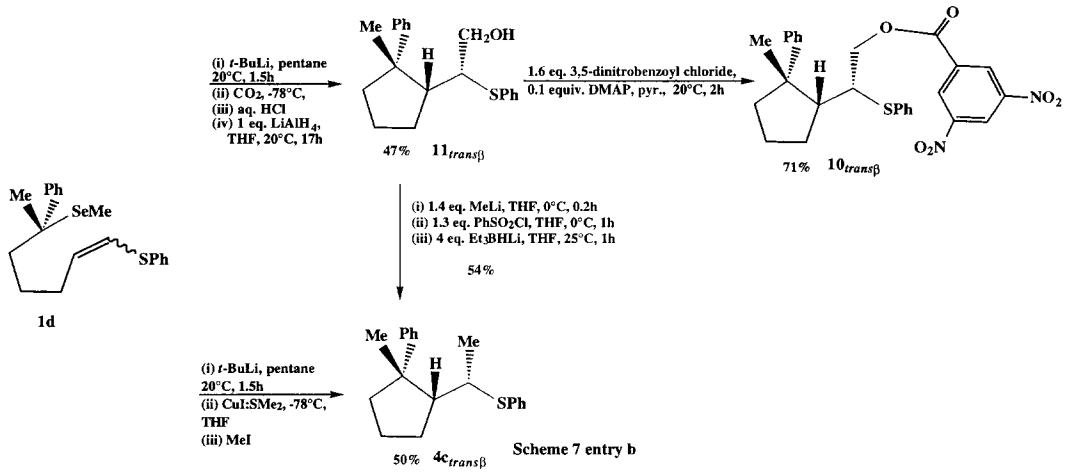
Scheme 12



The other structure determination required more steps since the crystals of the corresponding sulfone **9c**$_{trans\beta}$ derived from **4c**$_{trans\beta}$, using the same protocol as described above, were not good enough to allow a DRX analysis.

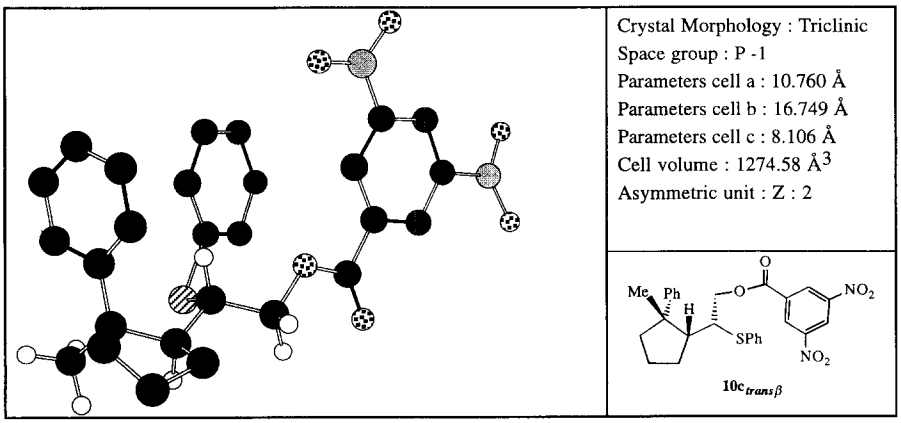
In order to achieve the desired structure elucidation, we have reduced with lithium aluminum hydride (1 eq. $LiAlH_4$, THF, 20°C, 17 h, 50%) the carboxylic acid **4f** obtained by sequantial reaction of the benzylic selenide **1d** with *t*-BuLi in pentane, carbon dioxide, and aqueous hydrochloric acid ((i) *t*-BuLi, pentane, 20°C, 1.5 h, (ii) CO_2, pentane, -78°C (iii) aq. HCl, 63%, **4f**$_{trans\beta}$ / **4f**$_{trans\alpha}$: 88/12, Scheme 10 entry h and Scheme 13). The major stereoisomer **11**$_{trans\beta}$ was freed from the other one at that stage by chromatography on silicagel and transformed to its crystalline 3,5-dinitro-benzoate **10**$_{trans\beta}$ on further reaction with 3,4-dinitrobenzoyl chloride (1.6 eq., 0.1 eq. DMAP, pyridine, 20°C, 2 h, m.p. 92°C, 71%). We have furthermore confirmed, by the chemical correlation shown in Scheme 13, that alkylation (Scheme 7 entry b, Scheme 13) and carbonation (Scheme 10 entry h and Scheme 13) of **3d**$_{trans}$ occur from the same side. For that purpose the alcohol **11**$_{trans\beta}$ has been transformed to its benzenesulfonate ((i) 1.4 eq. MeLi, THF, 0°C, 0.2h, (ii) 1.3 eq. $PhSO_2Cl$, THF, 0°C, 1 h) which has been reduced to **4c**$_{trans\beta}$ on further reduction with super hydride (4 eq. Et_3BHLi, THF, 25°C, 1 h, 54% overall).

Scheme 13



Those crystals were suitable for DRX analysis which shows the *cis*-relationship between the two groups linked to the cyclopentane ring and the stereochemistry at the carbon bearing the phenylthio moiety (Scheme 14).

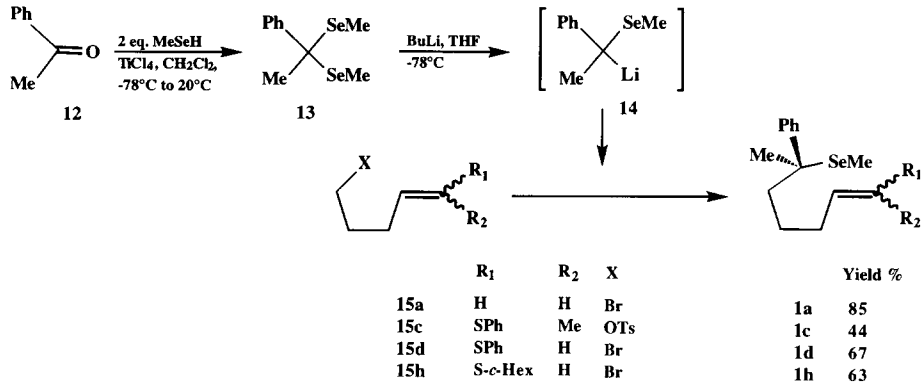
Scheme 14



The synthesis of the unsaturated benzylselenides required for this study was achieved [2,32-34] from 1-methylseleno-1-phenyl-ethyllithium **14** and alkenyl bromides **15a**, **15d** and **15h** or tosylate **15c** as shown in Scheme 15. The synthesis of the α-selenobenzyllithium **14** started from acetophenone **12** by sequential reaction with methaneselenol and titanium tetrachloride[35] and *n*-butyllithium in THF.[10,11,33,36,37] The alkylation of **14** with 5-bromo-1-pentene **15a**, 5-bromo-1-phenylthio-1-pentene **15d** or with 5-bromo-1-cyclohexylthio-1-pentene **15h** proceeds efficiently ((i) 1,1-bis(methylseleno)-1-phenyl-ethane **13**, 1 eq. *n*-BuLi, THF, -78°C, 0.5 h, (ii) 1.1 eq. alkenyl halide **15**, -78°C, 0.5 h, 20°C, 0.5 h; for **1d** : R_1= PhS, R_2= H : 67%, E/Z 55/45; for **1h** : R_1= *c*-HexS, R_2= H : 63%, E/Z 75/25). Lower yields were obtained from 2-phenylthio-6-tosyloxy-2-hexene **15c** but the reaction was carried out on the crude tosylate ((i) 1,1-bis(methylseleno)-1-phenylethane **13**, 1 eq. *n*-

BuLi, THF, -78°C, 0.5 h, (ii) 1 eq. alkenyl tosylate **15c**, 78°C, 0.5 h then 20°C, 0.5 h, R_1= SPh, R_2=Me : 44%, stereoisomeric ratio 71/29).

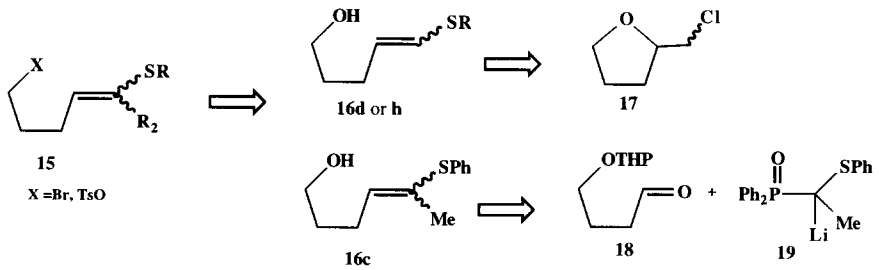
Scheme 15



	R_1	R_2	X		Yield %
15a	H	H	Br	1a	85
15c	SPh	Me	OTs	1c	44
15d	SPh	H	Br	1d	67
15h	S-*c*-Hex	H	Br	1h	63

The alkenyl bromides **15d** and **15h** have been synthesized from the corresponding alcohol and triphenylphosphine-carbon tetrabromide [36] (1.1 eq. CBr_4, 1.1 eq. PPh_3, CH_2Cl_2, 20°C, 1 h; : 31% (Z/E 45/55) for **15d** ; 13% (Z/E 45/55) for **15e**. These bromides were quite unstable and very sensitive to polymerization, especially the crude products. This reaction cannot be extended to **15c** which possesses an even higher propensity to polymerize. In such cases, the tosylate was prepared instead (1 eq. BuLi, 1 eq. TsCl, THF, 0°C, 0.5 h) and used without purification in the further step (Scheme 16).

Scheme 16

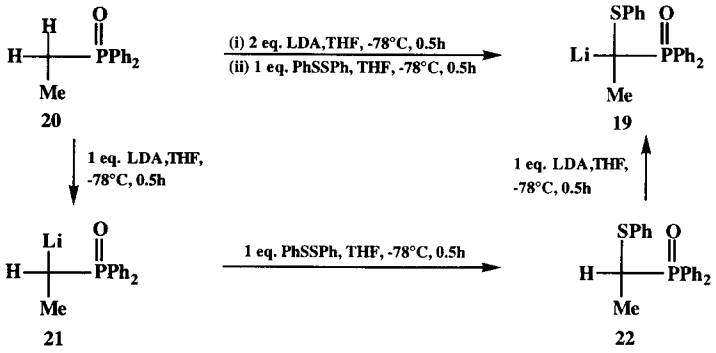


The alcohols **16** were in turn prepared depending upon their nature (i) from the furfuryl chloride in the case of terminal vinyl sulfides **15d** and **15h** (Scheme 16) or (ii) from tetrahydropyranyloxy butanal **18**[38] and 1-diphenylphosphino-1-phenylthioethyllithium **19**[39] for the trisubstituted vinyl sulfide **15c** (Scheme 16).

Reaction of 1-diphenylphosphinoethane with *n*-BuLi-TMEDA and diphenyl disulfide according to a published procedure [39] leads, in our hands, to the desired 1-diphenylphosphino-1-phenylthioethane (17%) along with substantial amounts of 1-diphenylphosphino-1,1-bis(phenylthio)ethane (41%) and recovered starting material (25%). We have nevertheless been able to produce 1-diphenylphosphino-1-phenylthioethyllithium by S/Li exchange by reaction of 1-diphenylphosphino-1,1-di(phenylthio)ethane with *s*-BuLi (THF, -78°C, 0.5 h; 76% of 1-diphenylphosphino-1-phenylthioethane on further reaction with methanol).[40] A better result was achieved on reaction of 1-diphenylphosphinoethane with LDA (2 eq.) and diphenyldisulfide (1 eq., THF, -78°C, 0.5 h,

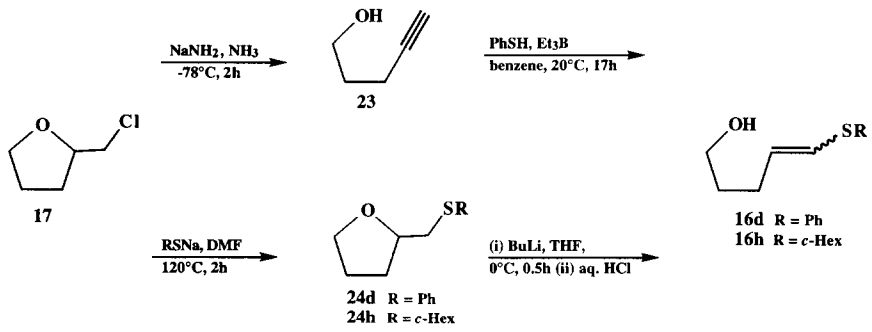
Scheme 17). Further reaction with tetrahydropyranyloxybutanal **18** (0.65 eq., THF, -78°C, 0.5 h then 20°C, 0.3 h) and acid methanolysis leads to 5-methyl-5-phenylthio-4-hexen-1-ol **16c** (0.6 eq. p-TsOH, MeOH, 20°C, 3 h, 93% from **18**).

Scheme 17



The terminal vinyl sulfides **16d** and **16h** were prepared (Scheme 18) from furfuryl chloride in a series of reactions, which involve (i) the transformation to 4-pentyn-1-ol **23** on reaction with a base ($NaNH_2$)[38] and addition of a thiol in the presence of triethylborane[41] (1.05 eq. PhSH, 1.05 eq. BEt_3, benzene, 20°C, 17h, 86%; Z/E= 45/55) or (ii) its substitution with a thiolate which leads to the furfuryl sulfides **24** (**24d** : R= Ph; 1 equiv. PhSH, NaOH, DMF, 120°C, 2 h, 71%; **24h** : R= *c*-Hex; 1 eq. *c*-Hex-SH, NaH, DMF, 120°C, 2 h,75%) and further reaction with butyllithium in THF (R= Ph : 1 eq. *n*-BuLi, THF, 0°C, 78%; R= *c*-Hex : 1 eq. *s*-BuLi, Et_2O, 0°C, 90%).

Scheme 18



In conclusion, we have described efficient syntheses of α-thioalkyllithiums **3c,d,h**, bearing one or two alkyl groups on their carbanionic center, which involve the addition of benzyllithiums to vinylsulfides. We have been able to synthesize, for the first time, such species in pentane. The synthesis of α-thioalkylmetals is not an easy task, and although the synthesis of the parent compound was easily achieved by metallation of dimethyl- or methyl phenyl thioethers by (i) butyllithium in THF-DABCO[42-44] or THF-TMEDA,[43] (ii) potassium *t*-butoxide-*n*-butyllithium (THF, -78°C),[45] the reaction proved to be much more difficult with higher homologs.[44] For example, metallation of *sec*-alkyl phenyl sulfides requires the concomitant use of *sec*-butyllithium and HMPA to

produce the corresponding α-thioalkyllithiums otherwise ring metallation takes place,[44] and unfortunately this procedure cannot be extended, with the exception of cyclopropyl phenylsulfide,[46] to higher homologs.
Heteroatom/lithium exchange was more successful. α-Halogeno-, α-thio-[46-48] and α-selenoalkylsulfides[10,19,33,49] have been used for that purpose.

The sulfur/lithium[46,50,51] and selenium/lithium[33,49] exchange allows the synthesis of a whole series of thioalkyllithiums. However, the sulfur/metal exchange requires the use of lithium arenides in THF and leads to the concomitant formation of phenylthiolate.[46,50,51] Unfortunately, this side product competes with the α-thioalkyllithium in further reactions.[50,51] The selenium/lithium exchange avoids these complications, since it can be efficiently achieved with butyllithiums in ether or THF and produces, besides the α-thioalkyllithium, a butyl selenide which do not interfere with all further reactions so far tested.[10,33,49]

Finally the tin/metal exchange[22] on α-stannylalkylsulfides as well as the fluoride induced desilylation[23] of α-silylalkylsulfides are also described in the literature.

Experimental Section

General : ^{1}H-NMR spectra were performed on JEOL JNM EX 400 (400 MHz for ^{1}H or 100.4 MHz for ^{13}C), PMX 60 Si (60 MHz) and FX 90 Q (90 MHz) spectrometers. The spectra were measured in CCl_4 or $CDCl_3$ with TMS as an internal standard (δ : 0.00 ppm). IR data reported in cm^{-1} were obtained using a Perkin-Elmer model 337 spectrophotometer. The spectra were performed on neat liquids unless differently stated. Mass spectra were obtained on an HP 5995 A GC/MS spectrometer. In the discussion $M^{\bullet}$ refers to $M^{+\bullet}$ and only a few characteristics were reported. Microanalyses were performed in the Microanalysis Laboratory of the Paris VI University (Paris, France). Layer chromatography : Analytical thin-layer chromatography (TLC) were performed on pre-made, glass-backed plates SiO_2, $60PF_{254}$, 250 μ (Merck 5719). Compounds were visualized by UV illumination and by heating to 150°C after spraying phosphomolybdic acid in ethanol. Preparative layer chromatography (PLC) was performed on SiO_2 plates prepared as previously described.[1b] Preparative HPLC was performed on Prochrom LC 50 stainless steel column (Diam. : 50 mm, Length : 350 mm filled with 400 g of SiO_2, Merck 15.111 (15-40 μm)) using a flow rate of 100 ml/min. and the detection was performed using UV detector (λ=254 nm). All the reactions were performed in two necked round bottomed flasks equipped with a septum stopper, a stirring bar and an argon filled balloon or in sealed tubes *(vide infra)*. All glassware were flame dried prior use under 0.1 mmHg. Transfer of all reagents were performed *via* syringes. Reactions performed at -25, -78, or -110°C have been carried out in a flask immersed in a Dewar filled with dry-ice-CCl_4, dry-ice acetone or ether-liquid nitrogen respectively.
Reagents and solvents. Unless otherwise noted, the reagents and solvents used in this work have been purchased from Acros and were distilled under standard literature procedures. Anhydrous THF and ether were distilled from sodium benzophenone ketyl prior to use. Anhydrous dichloromethane was distilled from phosphorous pentoxide. *n*-BuLi (1.6 M in hexane, Aldrich), *s*-BuLi (1.3 M in cyclohexane, Acros) and *t*-BuLi (1.7 M in cyclopentane, Aldrich) were titrated prior to use using the procedure of Gilman.[52]

Synthesis of 5-phenylthio-4-penten-1-ol 16d.[41] Triethylborane (Acros, 1 M in hexanes, 52 ml, 52 mmol.) was added to a stirred solution of 4-pentyn-1-ol[53] **23** (4.2 g, 50 mmol.) and thiophenol (Aldrich, 5.7 g, 52 mmol.) in 100 ml of benzene, under argon, at room temperature. The reaction mixture was stirred for 17 h,

then quenched carefully with a saturated solution of ammonium chloride. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude alcohol was purified by preparative HPLC (eluent : AcOEt/pentane : 30/70 (v/v)) to afford 8.3 g of alcohol **16d** (86%) as a 55/45 mixture of two stereoisomers. TLC : R_f= 0.34 and 0.42 (eluent : AcOEt/pentane : 30/70 (v/v)); GC[2] (SE30; 100°C to 220°C, 10°C/min.)) : rt= 9.8 (isomer Z : 45%) and 10.8 (isomer E : 55%); IR (film) cm^{-1} : 3673 (O-H), 3328, 3070, 2857, 3057, 3005, 1944, 1869, 1793 (aromatic overtones), 1653, 1646, 1608 (C=C aromatic), 1583, 1478, 1373, 1349, 1304, 1243, 1156, 1089, 1057, 1024, 951 (H-CCSR), 913, 868, 690; ^1H NMR ($CDCl_3$, 90 MHz) δ (ppm) : 1.40-2.38 (m, 5 H, HO-CH_2-CH_2-CH_2-CC-SPh), 3.58 (t, J= 8.2 Hz, 2 H, -CH_2OH), 5.60 -6.05 (m, 1 H, -CH=CH-SPh), 6.10 -6.25 (m, 1 H, -CH=CH-SPh), 7.10-7.42 (m, 5 H, -C_6H_5); MS (m/e) : 194 ($M^{+\bullet}$, 24), 166 ([M-CH_2-CH_2]$^{+\bullet}$, 6), 149 ([M-$(CH_2)_2$OH]$^+$, 100), 134 (17), 110 ([PhSH]$^{+\bullet}$, 100), 91 (17), 77 (25).

Synthesis of 5-bromo-1-phenylthio-1-pentene 15d. Triphenylphosphine (9.9 g, 38 mmol., 1 M) in dichloromethane was added to a solution of carbon tetrabromide (12.4 g, 30 mmol.) and alcohol **16d** (7.06 g, 36 mmol., 0.5 M) in anhydrous dichloromethane cooled, under argon to 0°C. The reaction mixture was stirred for 0.5 h, then filtered through a pad of silicagel (Merck 7734) in order to eliminate the triphenylphosphine oxide. The silicagel was washed with pentane and the filtrate was concentrated *in vacuo* (20 mmHg) to give approximatively 50 ml of residue (Lower yields were obtained when the solvent was completely removed due to degradation of the bromide). The crude bromide was purify by silicagel column chromatography (eluent: pentane) to afford 3.1 g of the bromide **15d** (31%) as a 45/55 mixture of two stereoisomers. TLC : R_f= 0.30 and 0.34 (eluent : pentane); GC[2] (OV17; 120°C to 220°C, 10°C/min.) : rt= 11.6 (45%) and 11.7 (55%); IR (film) cm^{-1} : 3056, 3006, 2958, 2933, 1944, 1870, 1793 (aromatic overtones), 1609 (C=C aromatic), 1582 (C=CSR), 1478, 1438, 1338, 1304, 1297, 1269, 1251, 1231, 1201, 1089, 1069, 1024, 999, 948 (H-CCSR), 739, 690; ^1H NMR ($CDCl_3$, 90 MHz) δ (ppm) : 1.77-2.49 (m, 4 H, Br-CH_2-CH_2-CH_2-), 3.42 (t, J= 6.37 Hz, 2 H, CH_2Br), 5.58-6.07 (m, 1 H, -CH=CH-SPh), 6.10-6.25 (m, 1 H, -CH=CH-SPh), 7.10-7.42 (m, 5 H, -C_6H_5); MS (m/e) : 256 and 258 ([M]$^{+\bullet}$, 22 and 23),177 ([M-Br]$^+$, 14), 149 ([PhSCHCHCH$_2$]$^+$, 100), 116 (83), 77 (46), 91 (17), 77 (25); $C_{11}H_{13}BrS$: Calc. : C, 51.39%; H, 5.06%; Found : C, 51.90%; H, 5.32%.

Synthesis of 2-phenylthio-2-hexen-6-ol 16c. *n*-Butyllithium (1.6 M, 25 ml, 40 mmol.) was added to a slurry of diisopropylamine (4.5 g, 44 mmol.) and diphenylethylphosphine oxide[39] **20** (4.6 g, 19.5 mmol., 0.3 M) in anhydrous THF cooled, under argon to -78°C. The red solution was stirred for 0.5 h at this temperature and exactly one equivalent of diphenyl disulfide (4.36 g, 20 mmol., 2 M) dissolved in THF was added. The orange solution was stirred for 0.5 h and 4-[(tetrahydro-2H-pyran-2-yl)oxy]-butanal[38] **18** (2.2 g, 13 mmol., 1.3 M) dissolved in THF was added dropwise. The reaction mixture was stirred for 0.5 h at -78°C, for an additional 0.5 h at room temperature and quenched with water. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water, a saturated solution of sodium bicarbonate, water, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude olefin was used in the next reaction without purification. TLC : R_f= 0.7 (eluent : ether /pentane : 2/8 v/v)).

The crude olefin and PTSA (0.1 g, 0.65 mmol., 0.4 M) were stirred in methanol at room temperature. After 3 h, the reaction mixture was quenched with a saturated solution of sodium bicarbonate and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude alcohol was

purified by preparative HPLC (eluent : AcOEt/pentane : 7/3 (v/v)) to afford 2.35 g of alcohol **16c** (93% from the aldehyde **18**) as a 29/71 mixture of two stereoisomers. TLC : R_f= 0.28 (eluent : AcOEt/pentane : 30/70 (v/v)); GC[2] (OV17; 100°C to 220°C, 10°C/min) : rt= 9.5 (29%) and 10.0 (71%); IR (film) cm^{-1} : 3395 (O-H), 3057, 2933, 2869, 1946, 1871 and 1773 (aromatic overtone), 1734, 1700, 1647 (C=C), 1583, 1559, 1475, 1375, 1300, 1219, 1177, 1116, 1058, 1024, 742, 692; ^{1}H NMR ($CDCl_3$, 90 MHz) δ (ppm) : 1.48-2.57 (m, 8 H, HO-CH_2-CH_2-CH_2-C=C-CH_3 including -CH_3 (1.88 and 1.90, two s)), 3.62 (t, J= 6.37 Hz, 2 H, CH_2OH), 5.82 (m, 1 H, -CH=C-SPh), 7.09-7.38 (m, 5 H, -C_6H_5); MS (m/e) : 208 ($[M]^{+\bullet}$, 12), 163 ($[M-(CH_2)_2-OH]^+$, 8), 135 (22), 130 (15), 110 ($[PhSH]^{+\bullet}$, 100), 91 (12), 77 (10). The fragmentation was identical for the two stereoisomers (94% of correlation); $C_{12}H_{16}OS$: Calc. : C, 69.29%; H, 7.77%; Found : C, 69.06%; H, 7.99%.

Synthesis of the tosylate 15c. *n*-butyllithium (1.55 M, 3.2 ml, 4.6 mmol.) was added to a solution of alcohol **16c** (1.3 g, 4.5 mmol., 1 M) in anhydrous THF stirred, under argon at 0°C. After 0.1 h, tosyl chloride (0.96 g, 5 mmol., 0.5 M) in THF was added and the reaction mixture was stirred for an additional 0.5 h. This solution was directly used for the alkylation of the α-selenobenzyllithium **14**.

Synthesis of 2-methylcyclohexylthiotetrahydrofuran 24h. In a one liter flask, fitted with a magnetic stirrer and a condensor, containing a slurry of NaH (Acros, 80% w/w in oil, 3.6 g, 120 mmol.) in 40 ml of DMF was added cyclohexylmercaptan (Acros, 12.78 g, 110 mmol., 5 M in DMF). The grey reaction mixture was stirred for 0.5 h and 60 ml of DMF was added to facilitate the stirring. Tetrahydrofurfuryl chloride[53] **17** (12 g, 100 mmol.) was added dropwise at room temperature over a period of 0.6 h. The solution was warmed to 125°C and stirred for 1 h, cooled to room temperature and quenched with NaOH 1 M (80 ml). The organic layer was separated and washed with water, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude sulfide was distilled *in vacuo* (b.p. 105°C/0.5 mmHg) to afford 51.0 g of the sulfide **24h** (75%) as an oil. TLC : R_f= 0.68 (ether/pentane (2/8, v/v)); IR (film) : cm^{-1} : 2929, 2850, 2692, 2665, 1772, 1734, 1718, 1699, 1684, 1653, 1647, 1636, 1617, 1559, 1545, 1533, 1522, 1507, 1448, 1420, 1356, 1340, 1299, 1262, 1235, 1201, 1178, 1163, 1097, 1057, 1011, 949, 919, 886, 820, 743; ^{1}H NMR ($CDCl_3$/90 MHz) δ (ppm) : 0.90-2.20 (m, 14 H, -CH_2-CH_2-CH-O-, -S-CH(CH_2)$_5$), 2.40-2.90 (m, 3 H, CH_2-S-CH-), 3.50-4.20 (m, 3 H, -CH_2-O-CH-); ^{13}C NMR ($CDCl_3$, 22.4 MHz) δ (ppm) : 25.7, 25.8, 25.5, 25.6, 30.7, 33.4, 33.5, 34.9, 43.7, 67.9, 78.5; MS (m/e) : 200 $[M]^{+\bullet}$, 130, 114, 101, 83 $[C_6H_{11}]^+$, 71, 55; $C_{11}H_{20}SO$: Calc. : C, 65.95%; H, 10.05%; Found : C, 66.00%; H, 10.15%.

Synthesis of 1-cyclohexylthio-1-penten-5-ol 16h. *s*-BuLi (1.3 M, 50 ml, 65 mmol.) was added dropwise, under argon to a stirred solution of 2-methylcyclohexylthio tetrahydrofuran **24h** (10.02 g, 50 mmol., 0.3 M) in dry ether contained in a 250 ml flask and maintained at 0°C. The yellow reaction mixture was stirred for 0.5 h at this temperature and quenched with water. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude vinyl sulfide was purified by preparative HPLC (eluent : ether/pentane : 4/6 (v/v)) to afford 9.10 g of alcohol **16h** (90%). TLC : R_f= 0.28 and 0.36 (ether/pentane (4/6, v/v)); IR (film) : cm^{-1} : 3337, 2929, 2665, 1734, 1685, 1653, 1647, 1636, 1608, 1522, 1507, 1448, 1381, 1341, 1297, 1262, 1121, 1057, 998, 944, 741; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.00-2.00 (m, 13 H, HO-CH_2-CH_2-, -S-CH(CH_2)$_5$-), 2.10-2.20 (m, 2 H, -CH_2-CH=CH-), 2.90-2.70 (m, 1 H, S-CH(CH_2)$_5$), 3.60 (t, J= 6 Hz, 2 H, HO-CH_2-), 5.50-5.90 (m, 2 H, -CH=CH-); MS (m/e) : for the major isomer : 200 $[M]^{+\bullet}$, 117 $[HOC_4H_6S]^+$, 116, 115, 100, 99, 87, 86, 85 $[M-C_6H_{11}]^+$, 84, 83 $[C_6H_{11}]^+$, 82, 81, 73, 72, 71, 67, 66, 65,

59, 57, 55, 54, 53. The fragmentation of the minor isomer was identical; $C_{11}H_{20}SO$: Cal. : C, 65.95 %; H, 10.05 %; Found : C, 65.89 %; H, 10.08 %.

Synthesis of 5-bromo-1-cyclohexylthio-1-pentene 15h. Triphenylphosphine (9.9 g, 38 mmol., 1M) dissolved in dichloromethane was added, under argon, to a solution of carbon tetrabromide (16.40 g, 49.1 mmol.) and alcohol **16h** (7.58 g, 38 mmol., 0.5 M) in anhydrous dichloromethane cooled to 0°C. The reaction mixture was stirred for 0.5 h, then filtered through a pad of silicagel (Merck 7734) in order to eliminate the triphenylphosphine oxide. The silicagel was washed with pentane and the filtrate was concentrated *in vacuo* (20 mmHg). The crude bromide was purified by preparative HPLC (eluent : pentane) to afford 1.44 g of the bromide **15h** (13%) as a 75/25 mixture of two stereoisomers. TLC : R_f= 0.28 and 0.30 (pentane); ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.10-2.10 (m, 12 H, Br-CH_2-C$\underline{H}_2$- and -S-CH(C$\underline{H}_2$)$_5$-), 2.10-2.30 (m, 2 H, -C$\underline{H}_2$-CH=CH-), 2.60-2.80 (m, 1 H, S-C$\underline{H}$(CH_2)$_5$-), 3.40 (t, J=6 Hz, 2 H, Br-C$\underline{H}_2$-) and 5.50-5.90 (2 H, m, -C$\underline{H}$=C$\underline{H}$-); IR (film) : cm^{-1} : 3004, 2927, 2850, 1734, 1718, 1706, 1685, 1653, 1647, 1637, 1609, 1559, 1543, 1507, 1490, 1448, 1340, 1262, 1233, 1202, 942, 887, 855, 819, 740, 646; MS (m/e) : for the major isomer 262 $[M]^{+\bullet}$, 182 $[M\text{-}HBr]^+$, 179, 155, 100, 83 $[C_6H_{11}]^+$, 79, 55. The fragmentation of the minor isomer was identical.

Synthesis of benzylselenides : General procedure I.[2] Exactly 1.0 molar equivalent of *n*-butyllithium in hexane was added dropwise, under argon, to a stirred 1.0 M solution of 1,1-bis(methylseleno)-1-phenyl ethane[35] **13** in anhydrous THF, cooled to -78°C. The dark red solution was stirred at this temperature for 0.5 h and a 1.0 M solution of the ω-alkenylhalide (1.1 eq.) in THF was added. The pale yellow solution was stirred for 0.5 h at -78°C, 0.5 h at room temperature then quenched with water (10 ml) and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water (10 ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The residual yellow liquid was purified by preparative HPLC to afford the benzylselenides as pale yellow liquids. Specific details as well as spectroscopical and analytical data are described below.

Synthesis of 6-methylseleno-6-phenyl-1-phenylthio-1-heptene 1d. Following general procedure I, 1,1-bis(methylseleno)-1-phenyl ethane[35] **13** (2.4 g, 8.3 mmol.) was sequentially reacted with *n*-butyllithium (1.6 M, 5.5 ml, 8.3 mmol.) and 5-bromo-1-phenylthio-1-pentene **15d** (E/Z= 55/45, 2.21 g, 8.7 mmol.) to afford, after purification by preparative HPLC (eluent : toluene/pentane : 20/80 (v/v)), 1.44 g of 6-methylseleno-6-phenyl-1-phenylthio-1-heptene **1d** (67%) as a 55/45 mixture of two stereoisomers. TLC : R_f= 0.58 (eluent : toluene/pentane : 30/70 (v/v)); IR (Film) cm^{-1} : 3054, 2924, 2861, 1944 (aromatic overtones), 1869, 1801, 1773, 1717, 1707, 1653, 1647, 1637, 1582 (C=C aromatic), 1494, 1478, 1459, 1438, 1375, 1089, 1068, 1025, 948 (CH=CHSPh), 925, 739, 697; ^1H NMR ($CDCl_3$, 90 MHz) δ (ppm) : 1.12-2.41 (m, 12 H, -(C$\underline{H}_2$)$_3$-, -SeC$\underline{H}_3$ (1.68, s) and CH_3Se-C-C$\underline{H}_3$ (1.83, s)), 5.66-6.24 (m, 2 H, -C$\underline{H}$=C$\underline{H}$-), 7.0-7.63 (m, 10 H, $C_6\underline{H}_5$- and $C_6\underline{H}_5$-S-); MS (m/e) : 376 ($[M]^{+\bullet}$, 2), 280 ($[M\text{-}MeSeH]^+$, 10), 171 ($[M\text{-}MeSeH\text{-}PhS^\bullet]^+$, 100), 131 ($[PhMeCCHCH_2]^+$, 25), 123 (70), 91 ([ion tropylium]$^+$, 93), 77 (44), 51 (33); $C_{20}H_{24}SSe$: Calc. : C, 63.98%; H, 6.44%; Found : C, 64.80%; H, 6.65%.

Synthesis of 7-methylseleno-7-phenyl-2-phenylthio-2-octene 1c. Following general procedure I, 1,1-bis(methylseleno)-1-phenyl ethane[35] **13** (1.3 g, 4.5 mmol.) was sequentially reacted with *n*-butyllithium (1.55 M, 2.9 ml, 4.5 mmol.) and with the solution of tosylate **15c** in THF, to afford, after purification by preparative HPLC (eluent : toluene/pentane : 20/80 (v/v)), 0.76 g of 2-methyl-7-methylseleno-7-phenyl-2-phenylthio-2-octene **1c** (44%) as a 29/71 mixture of two stereoisomers. TLC : R_f= 0.6 (eluent : toluene/pentane :

3/7 (v/v)); IR (Film) cm^{-1} : 2923, 2863, 1944, 1870, 1801, 1793 (aromatic overtones), 1734, 1718, 1598 (C=C aromatic), 1582, 1494, 1493, 1475, 1458, 1375, 1068, 899, 741; ^1H NMR ($CDCl_3$, 90 MHz) δ (ppm) : 1.04-2.36 (m, 15 H, -($C\underline{H}_2$)$_3$-CH=C-$C\underline{H}_3$, -Se$C\underline{H}_3$ (1.69, s) and $C\underline{H}_3$-C-Ph (1.84, s)), 5.75 (m, 1 H, -C$\underline{H}$=C-), 7.06-7.53 (m, 10 H, $C_6\underline{H}_5$- and $C_6\underline{H}_5$-S-); MS (m/e) : 390 ([M]$^{+\bullet}$, 4), 294 ([M-MeSeH]$^{+\bullet}$, 4), 185 ([M-MeSeH-PhS]$^{+\bullet}$, 76), 137 ([PhSCHCH$_2$]$^{+\bullet}$, 50), 129 (65), 105 ([PhCCH$_2$]$^+$, 83), 91 ([tropylium ion]$^+$, 100), 77 (45), 51 (30); $C_{21}H_{26}SSe$: Calc. : C, 64.77%; H, 6.68%; Found : C, 64.73%; H, 6.68%.

Synthesis of 6-methylseleno-6-phenyl-1-cyclohexylthio-1-heptene 1h. Following general procedure I, 1,1-bis(methylseleno)-1-phenyl ethane [35] **13** (8.78 g, 30.17 mmol.) was sequentially reacted with *n*-butyllithium (1.6 M, 19.9 ml, 30.17 mmol.) and 5-bromo-1-cyclohexylthio-1-pentene **15h** (E/Z= 75/25, 8.11 g, 10.5 mmol.) to afford, after purification by preparative HPLC (eluent : toluene/pentane : 10/90 (v/v)), 7.45 g of 6-methylseleno-6-phenyl-1-cyclohexylthio-1-heptene **1h** (63%) as a 50/50 mixture of two stereoisomers. TLC : R_f : 0.53 and 0.56 (pentane/toluene (90/10, v/v)). IR (film): cm^{-1} : 3084, 3054, 2928, 1942, 1869, 1801, 1734, 1717, 1599, 1445, 1375, 1066, 1029, 1012, 857, 819, 786, 653, 612; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.20-1.40 (m, 22 H, -($C\underline{H}_2$)$_3$-, -S-CH($C\underline{H}_2$)$_5$, $C\underline{H}_3$-C-Ph (1.67, s), -Se$C\underline{H}_3$ (1.86, s), 2.60-2.80 (m, 1 H, -S-C$\underline{H}$-(CH$_2$)$_5$), 5.40-6.00 (m, 2 H, -C$\underline{H}$=C$\underline{H}$-S-), 7.10-7.60 (m, 5 H,-$C_6\underline{H}_5$); MS (m/e) : 209, 171, 155, 93, 115 [S-C_6H_{11}]$^+$, 91 [tropylium ion]$^+$, 83 [C_6H_{11}]$^+$, 77, 55; $C_{20}H_{30}SeS$: Calc. : C, 62.97 %; H, 7.86 %; Found : C, 62.97 %; H, 7.90 %.

Synthesis of arylcycloalkanes by anionic cyclisation of benzylselenides : General procedure II. n-Butyllithium (1.0 M, exactly 1 eq.) was added dropwise into a two-necked flask fitted with a rubber septum, under argon and containing a stirred 0.5 M solution of the benzylselenide in an anhydrous solvent (THF, ether or pentane). The solution (yellow to dark red) was stirred at the temperature and for the time given for each example, before addition of the electrophile. The reaction mixture was stirred at the temperature and the time given for each example, then quenched with water. The organic layer was separated and the aqueous layer extracted with ether. The combined organic layers were washed with water (10 ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The residual liquid was purified by silicagel preparative thin layer chromatography. Specific details, as well as spectroscopical and analytical data, are described below for each cited cases. The composition was determined by GC[2] analysis using Se30 capillary column (F.I.D. detector, $T_{det.}$=$T_{inj.}$= 250°C, He d= 1 ml/min, 100 to 220°C, 10°C/min) and by GC/MS analysis.

Synthesis of *rel(1S,2R)*-1-methyl-2-methylthiophenyl-1-phenyl cyclopentane 4d$_{cis}$ using diphenyl disulfide. Following general procedure II, 6-methylseleno-6-phenyl-1-heptene **1a** (2.62 g, 10 mmol.) dissolved in dry THF was reacted with *t*-butyllithium (1.7 M, 5.9 ml, 10 mmol.) at -78°C for 0.5 h. Diphenyl disulfide (2.39 g, 11 mmol., 1 M) dissolved in THF was then added. The reaction mixture was stirred for 0.2 h at this temperature and then warmed to room temperature. The crude sulfide was purified (eluent : pentane) to afford 2.59 g of *rel(1S,2R)*-1-methyl-2-methylthiophenyl-1-phenyl cyclopentane **4d$_{cis}$** (92%, d.e. : 96%). TLC : R_f= 0.40 (eluent : pentane/toluene : 95/05 (v/v)); GC[2] (SE30; 220°C) : rt= 8.2 (isomer **4d$_{trans}$** : 5%) and 9.2 (isomer **4d$_{cis}$** : 95%); IR (Film) cm^{-1} : 3055, 3020, 2956 (-CH_2- cyclopentane), 2871, 1944 (aromatic overtones), 1875, 1801, 1599 (C=C Ar), 1582, 1496, 1479, 1436, 1377, 1089, 1025, 757, 737, 699; ^1H NMR ($CDCl_3$, 90 MHz) δ (ppm) : 1.21 (s, 3 H, $C\underline{H}_3$-C-Ph), 1.54-2.72 (m, 8 H, -($C\underline{H}_2$)$_3$-C$\underline{H}$-CH-SPh), 2.96 (dd, J= 2 and 9.4 Hz, 1 H, -C$\underline{H}$-SPh), 7.00-7.35 (m, 10 H, $C_6\underline{H}_5$- and $C_6\underline{H}_5$-S); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ (ppm) : 19.55, 21.72, 30.72, 34.62, 43.01, 48.43, 49.30, 125.31, 125.31, 125.86, 128.08, 128.60,

128.56, 136.90, 146.70; MS (m/e) : 282 ([M]$^{+\bullet}$, 3), 173 ([M-PhS$^{\bullet}$]$^{+}$, 4), 143 (3), 131 ([PhMeCCHCH$_2$]$^{+}$, 20), 109 ([PhS]$^{+}$, 40), 105 ([PhCHMe]$^{+}$, 60), 91 ([tropylium]$^{+}$, 100), 77 (26), 55 (18).

Synthesis of *rel(1S,2S)*-1-methyl-2-methylthiophenyl-1-phenyl cyclopentane 4d$_{trans}$ using diphenyl disulfide. Following general procedure II, 6-methylseleno-6-phenyl-1-heptene **1a** (2.62 g, 10 mmol.) dissolved in dry pentane was reacted with *t*-butyllithium (1.7 M, 5.9 ml, 10 mmol.) at 20°C for 3 h. Diphenyl disulfide (2.39 g, 11 mmol.) dissolved in THF was added and the reaction mixture was stirred for 0.2 h at this temperature. The crude sulfide was purified (eluent : pentane) to afford 2.0 g of *rel(1S,2S)*-1-methyl-2-methylthiophenyl-1-phenyl cyclopentane **4d$_{trans}$** (73%, d.e. : 90%). TLC : R$_f$= 0.61 (eluent : pentane/toluene : 80/20 (v/v)); GC[2] (SE30; 220°C) : rt= 8.2 (isomer **4d$_{trans}$** : 94%) and 9.2 (isomer **4d$_{cis}$** : 6%); IR (Film) cm^{-1} : 3056, 3020, 2957 (-CH$_2$- cyclopentane), 2871, 1944 (aromatic overtones), 1870, 1802, 1559 (C=C Ar), 1583, 1495, 1479, 1438, 1375, 1156, 1025, 765, 737, 702, 691; ^{1}H NMR ($CDCl_3$, 90 MHz) δ (ppm) : 1.32 (s, 3 H, C$\underline{H}_3$-C-Ph), 1.57-2.34 (m, 8 H, -(C$\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}$H-SPh), 2.56-3.00 (m, 1 H, -CH$\underline{H}$-SPh), 7.02-7.40 (m, 10 H, C$_6\underline{H}_5$- and C$_6\underline{H}_5$-S); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ (ppm) : 21.23, 29.09, 29.36, 36.13, 36.62, 49.14, 50.12, 125.43, 125.64, 126.83, 126.83, 127.87, 128.51, 128.51, 136.91, 146.12; MS (m/e) : 282 ([M]$^{+\bullet}$, 3), 173 ([M-PhS$^{\bullet}$]$^{+}$, 4), 143 (4), 131 ([PhMeCCHCH$_2$]$^{+}$, 21), 109 ([PhS]$^{+}$, 35), 105 ([PhCHMe]$^{+}$, 59), 91 ([tropylium]$^{+}$, 100), 77 (23), 55 (17); $C_{19}H_{22}S$: Calc. : C, 73.15%; H, 7.85%; Found : C, 73.57%; H, 7.97%.

Synthesis of *rel(1S,2R)*-1-methyl-2-methylthiophenyl-1-phenyl cyclopentane 4d$_{cis}$ by protonation of an α-thioalkyllithium. Following general procedure II, 6-methylseleno-6-phenyl-1-phenylthio-1-heptene **1d** (0.13 g, 0.4 mmol.) dissolved in dry THF was reacted with *n*-butyllithium (1.6 M, 0.24 ml, 0.4 mmol.) at -78°C. The reaction mixture was stirred for 0.5 h at this temperature, quenched with methanol at that temperature and then warmed to room temperature. The crude sulfide was purified (eluent : pentane) to afford 0.09 g of *rel(1S,2R)*-1-methyl-2-methylthiophenyl-1-phenyl cyclopentane **4d$_{cis}$** (89%; d.e. : 90%). This sample proved to be identical (IR, NMR, GC[2], TLC) to that described above and obtained by reaction of *rel(1S,2R)*-1-methyl-2-methyllithio-1-phenyl cyclopentane **3a$_{cis}$** with diphenyl disulfide.

Synthesis of *rel(1R,2R)*-1-methyl-2-methylthiophenyl-1-phenyl cyclopentane 4d$_{trans}$ by protonation of an α-thioalkyllithium. Following general procedure II, 6-methylseleno-6-phenyl-1-phenylthio-1-heptene **1d** (0.185 g, 0.5 mmol.) dissolved in dry pentane was reacted with *t*-butyllithium (1.7 M, 0.3 ml, 0.5 mmol.) at 20°C. The reaction mixture was stirred for 1.5 h at this temperature and then quenched with methanol. The crude sulfide was purified (eluent : pentane) to afford 0.11 g of *rel(1R,2R)*-1-methyl-2-methylthiophenyl-1-phenyl cyclopentane **4d$_{trans}$** (79%; d.e. : 88%). This sample proved to be identical (IR, NMR, GC[2], TLC) to that described above and to that obtained by the reaction of *rel(1R,2R)*-1-methyl-2-methyllithio-1-phenyl cyclopentane **3a$_{trans}$** with diphenyl disulfide.

Synthesis of *rel(1S,2R)*-1-methyl-2-methylthiocyclohexyl-1-phenyl cyclopentane 4h$_{cis}$ by protonation of an α-thioalkyllithium. Following general procedure II, 6-methylseleno-6-phenyl-1-cyclohexylthio-1-heptene **1h** (0.19 g, 0.5 mmol.) dissolved in dry THF was reacted with *n*-butyllithium (1.6 M, 0.32 ml, 0.5 mmol.) at -78°C. The reaction mixture was stirred for 0.5 h at this temperature, quenched with methanol at that temperature and then warmed to room temperature. The crude sulfide was purified (eluent : pentane/toluene : 90/10 (v/v)) to afford 0.03 g of *rel(1S,2R)*-1-methyl-2-methylthiocyclohexyl-1-phenyl cyclopentane **4h$_{cis}$** (92%; d.e. > 95%). TLC : R$_f$= 0.56 pentane-toluene (90/10 (v/v)); IR : (film) : cm^{-1} : 3083, 3055, 3021, 2923, 2666, 1944, 1870, 1801, 1599, 1543, 1533, 1522, 1508, 1495, 1458, 1096, 886, 764, 701;

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.00-2.60 (m, 23 H, -($C\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}_2$, -S-$C_6\underline{H}_{11}$, $C\underline{H}_3$-C-$C_6\underline{H}_5$ (1.2, s), 7.00-7.60 (m, 5 H; $C_6\underline{H}_5$); ^{13}C NMR ($CDCl_3$/100 MHz) δ (ppm) : 19.8, 21.7, 25.8, 26.0, 26.1, 30.3, 31.2, 33.5, 33.6, 43.0, 48.5, 50.0, 125.5, 125.8, 127.0, 128.0, 148.6.

Synthesis of *rel(1R,2R)*-1-methyl-2-methylthiocyclohexyl-1-phenyl cyclopentane $4h_{trans}$ by protonation of an α-thioalkyllithium. Following general procedure II, 6-methylseleno-6-phenyl-1-cyclohexylthio-1-heptene **1h** (0.210 g, 0.55 mmol.) dissolved in dry pentane was reacted with *t*-butyllithium (1.7 M, 0.35 ml, 0.55 mmol.) at 20°C. The reaction mixture was stirred for 0.5 h at this temperature and then quenched with methanol. The crude sulfide was purified (eluent : pentane/toluene : 90/10 (v/v)) to afford 0.13 g of *rel(1R,2R)*-1-methyl-2-methylthiocyclohexyl-1-phenyl cyclopentane $\mathbf{4h}_{trans}$ (80%; d.e. : 92%). TLC : Rf : 0.59 (pentane/toluene (90/10, v/v)); IR (film) : cm^{-1} : 3083, 3055, 3021, 2923, 2850, 2666, 1944, 1870, 1599, 1543, 1533, 1120, 1096, 1073, 787, 764, 701; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.00-2.60 (m, 23 H, ($C\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}_2$, -S-$C_6\underline{H}_{11}$, $C\underline{H}_3$-C-Ph (1.37, s), 7.00-7.60 (m, 5 H, $C_6\underline{H}_5$); ^{13}C NMR ($CDCl_3$/100 MHz) δ (ppm) : 21.3, 25.7, 25.8, 26.0, 26.1, 29.2, 29.6, 30.3, 31.2, 32.6, 33.4, 33.5, 33.8, 36.7, 43.6, 43.7, 50.2, 51.1, 125.5, 127.0, 127.2, 127.8, 127.9, 128.0, 128.1, 147.2; MS (m/e) : 288 $[M]^{+\bullet}$, 205 $[M\text{-}C_6H_{11}]^+$, 192, 131, 115 $[S\text{-}C_6H_{11}]^+$, 105, 91 [tropylium ion]$^+$, 83 $[C_6H_{11}]^+$, 77, 55.

Synthesis of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio ethane $4c_{cis\alpha}$ and $4c_{cis\beta}$ by protonation of an α-thioalkyllithium. Following general procedure II, 2-methyl-7-methylseleno-7-phenyl-2-phenylthio-2-octene **1c** (0.13 g, 0.3 mmol.) dissolved in dry THF was reacted with *n*-butyllithium (1.6 M, 0.21 ml, 0.35 mmol.) at -78°C. The reaction mixture was stirred for 0.5 h at that temperature, quenched with methanol and then warmed to room temperature. The crude sulfide was purified (eluent : pentane/toluene : 90/10 (v/v)) to afford 0.02 g of *rel(1S,1'R,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio ethane $\mathbf{4c}_{cis\alpha}$ (17%) and 0.05 g of *rel(1S,1'S,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio ethane $\mathbf{4c}_{cis\beta}$ (51%). ***Physical data for*** $\mathbf{4c}_{cis\alpha}$: TLC : R_f= 0.37 (eluent : pentane/toluene : 90/10 (v/v)); GC[2] (SE30; 220°C) : rt= 10.0; IR (Film) cm^{-1} : 3055, 3019, 2960 (-CH_2- cyclopentane), 2872, 1941 (aromatic overtones), 1872, 1794, 1599 (C=C aromatic), 1583, 1477, 1428, 1025, 753, 753, 698; ^{1}H NMR ($CDCl_3$, 90 MHz) δ (ppm) : 1.21 (d, J= 6.3 Hz, 3 H, $C\underline{H}_3$-CH-), 1.42 (s, 3 H, $C\underline{H}_3$-C-Ph), 1.57-2.51 (m, 7 H, -($C\underline{H}_2$)$_3$-C$\underline{H}$-), 3.18 (dd, J= 6.6 and 7.3 Hz, 1 H, CH_3-C$\underline{H}$-SPh), 7.00-7.57 (m, 10 H, $C_6\underline{H}_5$- and $C_6\underline{H}_5$-S); ^{13}C NMR ($CDCl_3$, 100.4 MHz) δ (ppm) : 19.83 and 20.41 (2x -$\underline{C}H_3$), 22.33 (-$\underline{C}H_2$), 28.70 (-$\underline{C}H_2$), 44.31 (-$\underline{C}$H), 45.58 (-$\underline{C}H_2$), 48.16 (Ph-$\underline{C}$-), 54.90 (-$\underline{C}$H-SPh), 125.30, 126.25, 127.71, 128.18, 131.64 (-$\underline{C}$H aromatic), 136.10 (-$\underline{C}$-S aromatic), 149.58 (ipso aromatic); MS (m/e) : 296 ($[M]^+$, 13), 186 ($[M\text{-}PhSH]^{+\bullet}$, 8), 171 ($[M\text{-}PhSH\text{-}CH_3{}^\bullet]^+$, 7), 131 ($[PhMeCCHCH_2]^+$, 19), 109 ($[PhS]^+$, 40), 105 ($[PhCHMe]^+$, 100), 91 ([tropylium]$^+$, 47), 77 (17), 55 (30); $C_{20}H_{24}S$: Calc. : C, 81.02%; H, 8.09%; Found : C, 81.02%; H, 8.18%. *Physical data for* $\mathbf{4c}_{cis\beta}$: TLC : R_f= 0.42 (eluent : pentane/toluene : 90/10 (v/v)); GC[2] (SE30; 220°C) : rt= 10.4; IR (Film) cm^{-1} : 3055, 3019, 2963 (-CH_2- cyclopentane), 2869, 1944 (aromatic overtones), 1872, 1801, 1599 (C=C aromatic), 1583, 1495, 1474, 1438, 1375, 1319, 1090, 1025, 755, 700; ^{1}H NMR ($CDCl_3$, 90 MHz) δ (ppm) : 0.77 (d, J= 6.4 Hz, 3 H, $C\underline{H}_3$-CH-), 1.39 (s, 3 H, $C\underline{H}_3$-C-Ph), 1.57-2.69 (m, 7 H, -($C\underline{H}_2$)$_3$-C$\underline{H}$-), 3.22 (dd, J= 7.5 and 6.4 Hz, 1 H, CH_3-C$\underline{H}$-SPh), 7.00-7.57 (m, 10 H, $C_6\underline{H}_5$- and $C_6\underline{H}_5$-S).

Synthesis of the [(2'-methyl-2'-phenyl)-cyclopentyl]-1-ethan-2-thiol 8c. Following general procedure II, 2-methyl-7-methylseleno-7-phenyl-2-phenylthio-2-octene **1c** (0.20 g, 0.5 mmol.) dissolved in dry pentane was reacted with *t*-butyllithium (1.7 M, 0.65 ml, 1 mmol.) at 20°C. The reaction mixture was stirred for 2

h at that temperature then quenched with hydrochloric acid. The crude compound was purified (eluent : pentane) to afford 0.03 g of *rel(1S,1'R,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-ethane-2-thiol **8c** (27%) and 0.02 g of unidentified products (18%). *Physical data for* **8c** : TLC : R_f= 0.38 (eluent : pentane/toluene : 90/10 (v/v)); GC^2 (SE30; 220°C) : rt= 9.74; IR (Film) cm^{-1} : 3084, 3055, 3021, 2976, 2857, 2869, 2842, 1950, 1863, 1734, 1717, 1685, 1599, 1496, 1473, 1458, 1443, 1400, 1375, 1253, 1155, 1221, 1031, 789, 755, 699; ^1H NMR ($CDCl_3$, 90 MHz) δ (ppm) : 0.9-2.6 (m, 14 H, -($C\underline{H}_2$)$_3$-C$\underline{H}$-, S$\underline{H}$, 1.35 (s, 3 H, $C\underline{H}_3$-C-Ph), 1.29 (d, 3 H, $C\underline{H}_3$-CH, J= 6.8 Hz)), 2.96 (dq, J= 6.8 and 3.9 Hz, 1 H, CH_3-C$\underline{H}$-), 7.01-7.42 (m, 5 H, $C_6\underline{H}_5$-); ^{13}C NMR ($CDCl_3$, 100.4 MHz) δ (ppm) : 18.97, 22.0, 25.7, 29.9, 36.5, 46.4, 47.9, 58.5, 127.9, 126.3, 125.5, 149.9; MS (m/e) : 220 ($[M]^{+\bullet}$, 12), 171 ($[M\text{-}SH_2\text{-}CH_3]^{+\bullet}$, 8), 143 (10), 131 ($[PhMeCCHCH_2]^+$, 35), 115 (40), 105 ($[PhCHMe]^+$, 100), 91 ([tropylium]$^+$, 70), 77 (31), 55 (34); $C_{14}H_{20}S$: Calc. : C, 76.34%; H, 9.08%; Found : C, 75.91%; H, 8.56%.

Reactions of the α-thioalkyllithiums 3d with electrophiles : General procedure III. Butyllithium was added to a flask containing a stirred 0.5 M solution of the unsaturated benzylselenide **1d** or **1h** under argon at the given temperature. The resulting solution was then stirred for an additional time (conditions as described in the Schemes), before being quenched with an excess of electrophile (deuterated methanol, MeI, Me_2SO_4, allyl-Br, CO_2). After 0.5 h, the solution was warmed-up to room temperature and hydrolysed with water. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The residual liquid was purified by SiO_2 preparative thin layer chromatography or preparative HPLC. Typically, the synthesis of the *trans*-series requires the use of *t*-butyllithium as the reagent and pentane as the solvent for the cyclisation step and was carried out at 20°C for 1.5 h; whereas the *cis*-series uses *n*-butyllithium, THF as the solvent and was carried out at -78°C for 0.5 h.

Those reactions carried out on the copper derivatives required the addition of : (i) CuI-DMS (0.5 eq.) to the precooled (-110°C) solution of **3** in THF or pentane or (ii) solid CuSPh (1 eq.) on the solution of **3** in THF maintained at -25°C or (iii) a 0.5 M THF solution of CuSPh (1 eq.) to a solution of **3** in pentane maintained at 20°C prior to the reaction of the electrophile (as described in the Schemes). Some reactions have been carrried out the potassium salt in THF (addition of 1.3 eq. *t*-BuOK on **3**) or with the addition of HMPA on **3** in THF prior to the addition of the electrophile. Specific details as well as spectroscopic and analytical data, are described below for each cited case. The composition was determined by GC analysis using Se30 capillary column (F.I.D detector, $T_{det.}$= $T_{inj.}$= 250°C, He : d= 1 ml/min, T_{oven} : 220°C) and by GC/MS analysis.

Synthesis of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio ethane $4c_{trans\alpha}$. Following general procedure III, the α-thioalkyllithium $3d_{trans}$ was prepared by reaction at 20°C of the selenide **1d** (0.63 g, 1.7 mmol.) and *t*-butyllithium (1.7 M, 1 ml, 1.7 mmol.) in pentane and added, under argon, to a pre-cooled (-78°C) solution of THF. The reaction mixture was stirred for 0.1 h and quenched with methyl iodide (0.78 g, 5 mmol.). The crude sulfide was purified by preparative HPLC (eluent : pentane/toluene : 90/10 (v/v)) to afford 0.26 g of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio ethane **4c** (54%) as a mixture of three diastereoisomers $4c_{trans\alpha}$, $4c_{trans\beta}$ and $4c_{cis\alpha}$: 80/15/5. TLC : R_f= 0.30 (eluent : pentane/toluene : 90/10 (v/v)); GC^2 (SE30; 220°C) : rt= 7.1 (isomer $4c_{trans\beta}$: 15%), 7.5 (isomer $4c_{trans\alpha}$: 80%) and 8.93 (isomer $4c_{cis\alpha}$: 5%); IR (Film) cm^{-1} : 3055, 3019, 2958, 2871, 1944 (aromatic overtones), 1871, 1801, 1734, 1599 (C=C aromatic), 1583, 1571, 1495, 1478, 1437, 1375, 1241, 1156, 1089, 1069, 1025, 985, 965, 944, 912, 842, 764, 740, 702; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 0.84 (d, 3 H, J= 6.9 Hz, $C\underline{H}_3$-CH-SPh of the

isomer **4c**$_{trans\alpha}$), 1.07 (d, J= 6.9 Hz, C$\underline{H}_3$-CH-SPh of the isomer **4c**$_{trans\beta}$), 1.30 (s, 3 H, C$\underline{H}_3$-C-Ph of the isomer **4c**$_{trans\beta}$), 1.39 (s, 3 H, C$\underline{H}_3$-C-Ph of the isomer **4c**$_{trans\alpha}$), 1.41-2.17 (m, 7 H, -(C$\underline{H}_2$)$_3$-C$\underline{H}$-), 2.99 (dq, J= 6.8 and 6.2 Hz, 1 H, CH$_3$-C$\underline{H}$-SPh), 7.01-7.42 (m, 10 H, C$_6\underline{H}_5$- and C$_6\underline{H}_5$-S); ^{13}C NMR of the major isomer ($CDCl_3$, 100.4 MHz) δ (ppm) : 18.02, 22.83, 27.82, 31.40, 45.41, 50.30, 54.10, 125.50, 126.61, 127.54, 127.89, 128.95, 132.19, 135.83, 147.15; MS (m/e) of the major isomer (by GC-MS) : 296 ([M]$^{+\bullet}$, 32), 131 ([PhMeCCHCH$_2$]$^+$, 34), 105 ([PhCHMe]$^+$, 100), 91 ([tropylium]$^+$, 53), 77, 55; $C_{20}H_{24}S$: Calc. : C, 81.02%; H, 8.09%; Found : C, 81.06%; H, 8.16%.

Synthesis of the deuterated [(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio-methanes 4e$_{cis\alpha}$ **and 4e**$_{cis\beta}$ **(90/10).** Following general procedure III, the α-thioalkyllithium **3d**$_{cis}$ was prepared by reaction at -78°C of the selenide **1d** (0.375 g, 0.1 mmol.) and *n*-butyllithium (1.6 M, 0.62 ml, 1 mmol.) in THF and the reaction mixture was quenched with d-4 methanol at this temperature. The crude sulfide was purified by preparative thin layer chromatography on SiO_2 (eluent : pentane/toluene : 90/10 (v/v)) to afford 0.257 g of *rel(1S,1'R,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio methane **4e**$_{cis}$ (90%) as a 90/10 mixture of **4e**$_{cis\alpha}$ **and 4e**$_{cis\beta}$ stereoisomers; TLC : Rf= 0.46 (eluent : pentane/toluene : 90/10 (v/v)); IR : (film) : cm^{-1} : 3054, 3019, 2957, 1942, 1868, 1792, 1772, 1684, 1670, 1598, 1582, 1559, 1533, 1522; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.24 and 1.32 (2s, 3 H, C$\underline{H}_3$-C-C$_6$H$_5$), 1.40-2.40 (m, 7 H, -(C$\underline{H}_2$)$_3$-C$\underline{H}$-), 3.00 (d, J= 3 Hz, 1 H, C$\underline{H}$D-S), 7.00-7.60 (m, 10 H,-S-C$_6\underline{H}_5$, C$_6\underline{H}_5$), ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) : 19.5, 21.7, 29.0, 29.4, 29.9, 30.0, 34.0, 34.2, 34.4, 34.5, 48.4, 49.0, 49.2, 49.3, 125.5, 125.6, 125.7, 125.9, 126.9, 128.1, 128.3, 128.5, 128.6, 128.7, 128.9, 136.9, 148.0; MS (m/e) : 283 [M]$^+$, 131 [PhMeCCHCH$_2$]$^+$, 110, 109, 105 [PhCHMe]$^+$, 92, 91 [tropylium]$^+$, 77, 65, 51; Anal. for $C_{19}H_{21}SD$: Calc. : C, 80.51%; H, 7.46%; Found : C, 79.69%; H, 7.83%. The diastereoisomeric excess was determined by ^{2}H NMR.

Synthesis of deuterated [(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio methanes 4e$_{trans\beta}$ **and 4e**$_{trans\alpha}$ **(77/23).** Following general procedure III, the α-thioalkyllithium **3d**$_{trans}$ was prepared by reaction at 20°C of the selenide **1d** (0.376 g, 0.1 mmol.) and *t*-butyllithium (1.5 M, 0.66 ml, 1 mmol.) in pentane and the reaction mixture was quenched with d-4 methanol at this temperature. The crude sulfide was purified by preparative thin layer chromatography on SiO_2 (eluent : pentane/toluene : 90/10 (v/v)) to afford 0.189 g of *rel(1S,1'S,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio methane **4e**$_{trans}$ (66%) as a 77/23 mixture of **4e**$_{trans\beta}$ and **4e**$_{trans\alpha}$ stereoisomers : TLC : Rf= 0.66 (eluent : pentane/toluene : 90/10 (v/v)); IR : (film) : cm^{-1} : 3055, 3021, 2956, 1944, 1868, 1801, 1684, 1598, 1583, 1559, 1494, 1479, 1375, 1299, 1261, 1155, 1089, 1072, 764, 702, 690; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.35 (2s, 3 H, C$\underline{H}_3$-C-C$_6$H$_5$), 1.40-2.40 (m, 7 H, -(C$\underline{H}_2$)$_3$-C$\underline{H}$-), 2.80 (d, J= 3 Hz, 1 H, C$\underline{H}$D-S), 7.00-7.60 (m, 10 H,-S-C$_6\underline{H}_5$, C$_6\underline{H}_5$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) : 21.3, 29.0, 29.1, 29.4, 35.6, 35.8, 36.0, 36.6, 43.0, 48.9, 49.1, 50.2, 125.3, 125.5, 125.7, 125.9, 126.9, 128.1, 128.3, 128.7, 128.8, 137.0, 146.9; MS (m/e) : 283 [M]$^+$, 186, 131 [PhMeCCHCH$_2$]$^+$, 129, 117, 110, 109, 105 [PhCHMe]$^+$, 92, 91 [tropylium]$^+$, 77, 65, 51. The diastereoisomeric excess was determined by ^{2}H NMR.

Synthesis of the esters 4f'$_{cis\alpha}$ **and 4f'**$_{cis\beta}$ **(85/15).** Following general procedure III, the α-thioalkyllithium **3d**$_{cis}$ was prepared by reaction at -78°C of the selenide **1d** (1.87 g, 4.95 mmol.) and *n*-butyllithium (1.6 M, 3.5 ml, 4.95 mmol.) in THF and a small piece of dry-ice was introduced rapidly. The white slurry was warmed to room temperature, quenched with 1M KOH aqueous solution and diluted with ether and the organic layer was washed twice with 1M KOH aqueous solution. The combined aqueous layers were acidified

with 4M HCl and extracted with ether. These organic extracts were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude acid (0.99 g, 60%, 85/15 mixture of two epimers) was used in the following step without further purification. The acid was reacted then with an excess of diazomethane in ether. The crude ester was purified by preparative thin layer chromatography on SiO_2 (eluent : pentane/ether : 90/10 (v/v)) to afford 0.74 g of the methyl ester of *rel(1S,2'R,3'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio-1-acetic acid was obtained in 70%. TLC : R_f= 0.52 (eluent : pentane/ether : 90/10 (v/v)); IR : (film) : cm^{-1} : 3447, 3055, 3021, 2956, 1793, 1599, 1581, 1495, 1479; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.36 and 1.44 (2s, 3 H, C$\underline{H}_3$-C-), 1.5-3.0 (m, 7 H, -(C$\underline{H}_2$)$_3$-C$\underline{H}$-CH-S-), 3.40-3.60 (s, 3 H, -COOC$\underline{H}_3$) 3.60-3.80 (3.64, 1 H (d, J=12 Hz, -C$\underline{H}$-S- of the minor isomer), 3.70 (d, J=12 Hz, -C$\underline{H}$-S of the major isomer)), 7.00-7.30 (m, 10 H; -S-C$_6\underline{H}_5$, C$_6\underline{H}_5$); MS (m/e) : 340 $[M]^{+\bullet}$, 199, 171, 131 $[PhMeCCHCH_2]^+$, 115, 105 $[PhCHMe]^+$, 103, 91 [tropylium]$^+$, 84, 77, 59.

Synthesis of the acid $4f_{trans}$ as a 88/12 mixture of stereoisomers of $4f_{trans}\beta$ and $4f_{trans}\alpha$. Following general procedure III, the α-thioalkyllithium $3d_{trans}$ was prepared by reaction at 20°C of the selenide **1d** (0.18 g, 0.49 mmol.) and *t*-butyllithium (1.7 M, 0.29 ml, 0.49 mmol.) in pentane. The reaction medium was then cooled to -78°C and a small piece of dry-ice was introduced rapidly. The white slurry was warmed to room temperature, quenched with 1M KOH aqueous solution and diluted with ether. The organic layer was washed twice with 1M KOH aqueous solution. The combined aqueous layers were washed with ether, acidified with 4M HCl and extracted with ether. These organic extracts were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude acid (0.10 g, 88/12 mixture of two epimers, 63%) of *rel(1S,2'S,3'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio-1-acetic acid (70%). TLC : R_f= 0.25 and 0.40 (eluent : pentane/ether : 50/50 (v/v)); IR : (film) : cm^{-1} : 3058, 2956, 2873, 2671, 1945, 1878, 1801, 1706, 1647, 1599, 1582, 1559, 1540, 1534, 1522, 1496, 1480, 1439, 1412, 1377, 1349, 1288, 1194, 1086, 1068, 1025, 1001, 909, 841, 789, 763, 703; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.0-3.0 (m, 10 H, -(C$\underline{H}_2$)$_3$-C$\underline{H}$-, C$\underline{H}_3$-C (1s, 1.39 and 1.45), 3.10-3.50 (3.14, 1 H (d, J=13 Hz, -C$\underline{H}$-S- of the minor isomer), 3.26, 1 H (d, J=13 Hz, -C$\underline{H}$-S- of the major isomer), 7.10-7.60 (m, 10 H;-S-C$_6\underline{H}_5$, C$_6\underline{H}_5$), 10-10.6 (boad s, 1 H , COO$\underline{H}$); MS (m/e) : 340 $[M]^{+\bullet}$, 199, 171, 131 $[PhMeCCHCH_2]^+$, 115, 105 $[PhCHMe]^+$, 103, 91 [tropylium]$^+$, 84, 77, 59.

Synthesis of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio-3-butene as a 60/40 mixture of stereoisomers of $4g_{cis}\alpha$ and $4g_{cis}\beta$. Following general procedure III, the α-thioalkyllithium $3d_{cis}$ was prepared by reaction at -78°C of the selenide **1d** (0.37 g, 1 mmol.) and *n*-butyllithium (1.6 M, 0.62 ml, 1 mmol.) in THF. The reaction mixture was stirred for 0.5 h and quenched with allyl bromide. The crude sulfide was purified by preparative TLC (eluent : pentane/toluene : 90/10 (v/v)) to afford 0.23 g of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio-3-butene $4g_{cis}$ (54%) as a mixture of three compounds $4g_{cis}\alpha$, $4g_{cis}\beta$ and $4d_{cis}$: 55/20/24. TLC : R_f= 0.53 (eluent : pentane/toluene : 90/10 (v/v)); GC^2 (SE30; 220°C) : rt= 9.0 (isomer $4g_{cis}\alpha$: 55%), 9.1 (isomer $4g_{cis}\beta$: 20%) and 6.4 (compound **4d**: 20%); IR (Film) cm^{-1} : 3382, 3055, 3019, 2956, 2872, 1944, 1801, 1734, 1717, 1699, 1684, 1653, 1637, 1598, 1495, 1477, 1437, 1375, 1300, 1261, 1089; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.20-2.60 (m, 13 H, (C$\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}$-S-, -C$\underline{H}_2$-CH, C$\underline{H}_3$-C- (1.30 and 1.40, s)), 4.60-6.20 (m, 3 H, C$\underline{H}$=C$\underline{H}_2$), 7.00-7.60 (m, 10 H, S-C$_6\underline{H}_5$ and C$_6\underline{H}_5$).

Synthesis of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio-3-butenes $4g_{trans}\beta$ and $4g_{trans}\alpha$ (60/40). Following general procedure III, the α-thioalkyllithium $3d_{trans}$ was prepared by reaction at 20°C of the selenide **1d** (0.37 g, 1 mmol.) and *t*-butyllithium (1.7 M, 0.58 ml, 1 mmol.) in pentane. The reaction mixture

was stirred for 1 h and quenched with allyl bromide. The crude sulfide afforded 0.32 g of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio-3-butene **4g** (43%) as a 43/29/20 mixture of the three compounds $\mathbf{4g}_{trans\beta}$, $\mathbf{4g}_{trans\alpha}$ and $\mathbf{4d}_{trans}$. TLC : R_f= 0.50 (eluent : pentane/toluene : 90/10 (v/v)); GC^2 (SE30; 220°C) : rt= 8.1 (isomer $\mathbf{4g}_{trans\beta}$: 43%), 7.4 (isomer $\mathbf{4g}_{trans\alpha}$: 29%) and 6.4 (compound **4d** 20%); IR (Film) cm^{-1} : 3377, 3055, 3019, 2957, 2871, 1944, 1868, 1801, 1772, 1734, 1717, 1699, 1684, 1653, 1637, 1495, 1477, 1437, 1374, 1364, 1300, 1264, 1157, 1088, 1025, 741; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.20-2.60 (m, 13 H, -($C\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}$-S-, $C\underline{H}_2$-CH, $C\underline{H}_3$-C- (1.30 and 1.40, s) 4.80-6.20 (m, 3 H, C$\underline{H}$-C=C$\underline{H}_2$), 7.00-7.60 (m, 10 H, S-$C_6\underline{H}_5$ and $C_6\underline{H}_5$).

Synthesis of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio ethanes $\mathbf{4k}_{cis\alpha}$ and $\mathbf{4k}_{cis\beta}$ (61/39). Following general procedure III, the α-thioalkyllithium $\mathbf{3h}_{cis}$ was prepared by reaction at -78°C of the selenide **1h** (1.140 g, 3 mmol.) and *n*-butyllithium (1.6 M, 1.8 ml, 3 mmol.) and the reaction mixture was quenched with methyl iodide (0.70 g, 5 mmol.) at this temperature. The crude sulfide was purified by preparative HPLC (eluent : pentane) to afford 0.169 g of *rel(1S,1'R,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio ethane $\mathbf{4k}_{cis}$ (53%). Characteristic of $\mathbf{4k}_{cis}$: TLC : R_f= 0.30 (pentane); IR : (film) : cm^{-1} : 3054, 2929, 2850, 1935, 1869, 1617, 1559, 1444, 1201; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 0.80-3.00 (m, 25 H, -($C\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}$-$C\underline{H}_3$, -S-$C_6\underline{H}_{11}$, $C\underline{H}_3$-C-C_6H_5 (1.6, s), $C\underline{H}_3$-C-C_6H_5 (1.9, s)), 7.00-7.30 (m, 5 H; $C_6\underline{H}_5$); MS (m/e) : 302 $[M]^{+\bullet}$, 219, 192, 185, 171, 143, 131, 118, 105 $[PhCHMe]^+$, 91 [tropylium]$^+$, 77, 61, 55; $C_{20}H_{30}S$: Calc. : C, 79.40%; H, 9.99%; Found : C, 79.32%; H, 9.51%.

Synthesis of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio ethanes $\mathbf{4k}_{trans\beta}$ and $\mathbf{4k}_{trans\alpha}$ (82/18). Following general procedure III, the α-thioalkyllithium $\mathbf{3h}_{trans}$ was prepared by reaction at 20°C of the selenide **1h** (0.380 g, 1 mmol.) and *t*-butyllithium (1.7 M, 0.56 ml, 1 mmol.) and the reaction mixture was quenched with methyl iodide (0.70 g, 5 mmol.) at this temperature. The crude sulfide was purified by preparative HPLC (eluent : pentane) to afford 0.169 g of *rel(1S,1'S,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio ethane $\mathbf{4k}_{trans}$.Analysis of the crude sulfide by GC^2 showed a mixture of the rel*(1S,1'R,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio ethane $\mathbf{4k}_{trans\beta}$ (56%), the minor stereoisomer $\mathbf{4k}_{trans\alpha}$ (15%) and the thioether $\mathbf{4h}_{trans}$ resulting from the protonation reaction (7%). Characteristics of the mixture : TLC : R_f= 0.30 (pentane/toluene (v/v)); IR : (film) : cm^{-1} : 3083, 3054, 3019, 1942, 1870, 1717, 1653, 1599, 1577, 1559, 1507, 1494, 1445; ^1H NMR ($CDCl_3$/90 MHz) δ (ppm) : 0.80-3.00 (m, 25 H, -($C\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}$-$C\underline{H}_3$, -S-$C_6\underline{H}_{11}$, $C\underline{H}_3$-C-C_6H_5 (1.6, s)), 7.00-7.30 (m, 5 H; $C_6\underline{H}_5$); MS (m/e) : 302 $[M]^{+\bullet}$, 217, 183, 169, 143, 105 $[PhCHMe]^+$, 91 [tropylium]$^+$, 77, 67, 61, 55.

Synthesis of deuterated [(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio-methanes $\mathbf{4i}_{cis\alpha}$ and $\mathbf{4i}_{cis\beta}$ (60/40). Following general procedure III, the α-thioalkyllithium $\mathbf{3h}_{cis}$ was prepared by reaction at -78°C of the selenide **1h** (0.384 g, 1.01 mmol.) and *n*-butyllithium (1.5 M, 0.67 ml, 1.01 mmol.) and the reaction mixture was quenched with d-4 methanol at this temperature. The crude sulfide was purified by preparative thin layer chromatography on SiO_2 (eluent : pentane/toluene : 90/10 (v/v)) to afford 0.100 g of *rel(1S,1'R,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio-methane $\mathbf{4i}_{cis}$ (60%) : TLC : R_f= 0.54 (eluent : pentane/toluene : 90/10 (v/v)); IR : (film) : cm^{-1} : 3083, 3055, 3025, 1734, 1718, 1699, 1598, 1495, 1458, 1444; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.00-2.80 (m, 22 H, $C\underline{H}_3$-C-C_6H_5 (1.18, s), -($C\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}$-, -S$C_6\underline{H}_{11}$)), 7.00-7.60 (m, 5 H; $C_6\underline{H}_5$). The diastereomeric excess was determined by ^2H NMR.

Synthesis of deuterated [(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio methanes $4i_{trans}s\beta$ and $4i_{trans}s\alpha$ (70/30). Following general procedure III, the α-thioalkyllithium $3h_{trans}$is prepared by reaction at 20°C of the selenide **1h** (0.330 g, 0.86 mmol.) and *t*-butyllithium (1.5 M, 0.57 ml, 0.86 mmol.) and the reaction mixture was quenched with d-4 methanol at this temperature. The crude sulfide was purified by preparative thin layer chromatography on SiO_2 (eluent : pentane/toluene : 90/10 (v/v)) to afford 0.189 g of *rel(1S,1'R,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio methane $4i_{trans}$ (60%) : TLC : R_f= 0.60 (eluent : pentane/toluene : 90/10 (v/v)); IR : (film) : cm^{-1} : 3083, 3055, 3021, 1942, 1869, 1801, 1699, 1684, 1570, 1559, 1534, 1495, 999, 912, 886, 820, 764, 701, 640; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.00-2.80 (m, 22 H $C\underline{H}_3$-C-C_6H_5 (1.40, s) -($C\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}$-, -$SC_6\underline{H}_{11}$), 7.00-7.60 (m, 5 H; $C_6\underline{H}_5$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) : 21.2, 25.7, 25.8, 26.0, 29.0, 29.5, 31.7, 32.1, 32.3, 32.5, 33.4, 33.5, 36.5, 36.6, 43.4, 49.9, 50.8, 125.4, 125.7, 126.8, 127.8, 127.9, 147.3; MS (m/e) : 289 $[M]^+$, 192, 158, 131 $[PhMeCCHCH_2]^+$, 118, 117, 117, 115, 110, 92, 91 [tropylium]$^+$, 77, 51.The diastereomeric excess was determined by ^2H NMR.

Synthesis of the esters $4j'_{cis}\beta$ and $4j'_{cis}\alpha$ (70/30). Following general procedure III, the α-thioalkyllithium $3h_{cis}$ was prepared by reaction at -78°C of the selenide **1h** (0.19 g, 0.5 mmol.) and *n*-butyllithium (1.6 M, 0.32 ml, 0.5 mmol.) in THF and a small piece of dry-ice was then introduced rapidly. The resulting white slurry was warmed to room temperature, quenched with 1M KOH aqueous solution and diluted with ether. The organic layer was washed twice with 1M KOH aqueous solution. The combined aqueous layers were washed with ether, acidified with 4M HCl and extracted with ether. These organic extracts were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude acid **4j** (0.099 g, 60%, 70/30 mixture of two epimers) was used in the following step without further purification. It was reacted with an excess of diazomethane in ether and the resulting crude ester **4j'** was purified by preparative thin layer chromatography on SiO_2 (eluent : pentane/ether : 90/10 (v/v)) to afford 0.07 g of the methyl ester of *rel(1S,2'R,3'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio-1-acetic acid (70%). TLC : R_f= 0.46 and 0.52 (eluent : pentane/ether : 90/10 (v/v)); IR : (film) : cm^{-1} : 3085, 3055, 3022, 2929, 1944, 1879, 1727, 1684, 1599, 1579, 1559, 1495, 1473, 1445, 887, 857, 818, 757, 733, 699, 631; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 0.70-2.80 (m, 21 H, -($C\underline{H}_2$)$_3$-C$\underline{H}$,, -S-$C_6\underline{H}_{11}$, $C\underline{H}_3$-C-C_6H_5 (1.37, s)), 2.82-3.80 (m, 4 H, with at 3.27, d, -C$\underline{H}$-S-, J=7 Hz of the minor isomer, at 3.30, d, -C$\underline{H}$-S-, J=7 Hz of the major isomer, at 2.82, s, $COOC\underline{H}_3$ of the minor isomer and at 3.68, s, $COOC\underline{H}_3$ of the major isomer), 7.00-7.30 (m, 5 H; $C_6\underline{H}_5$); MS (m/e) : 346 $[M]^{+\bullet}$, 232 $[M\text{-}SC_6H_{11}]^+$, 171, 131 $[PhMeCCHCH_2]^+$, 115 $[SC_6H_{11}]^+$, 91 [tropylium]$^+$, 83 $[C_6H_{11}]^+$, 77, 59, 55; $C_{21}H_{30}SO_2$: Calc. : C, 72.27%; H, 8.65%; Found : C, 71.56%; H, 8.59%.

Synthesis of the esters $4j'_{trans}\beta$ and $4j'_{trans}\alpha$ (74/26). Following general procedure III, the α-thioalkyllithium $3h_{trans}$ was prepared by reaction at 20°C of the selenide **1h** (0.37 g, 0,97 mmol.) and *t*-butyllithium (1.7 M, 0.57 ml, 0,9 mmol.). The reaction mixture was then cooled to -78°C and a small piece of dry-ice was introduced rapidly. The resulting white slurry was warmed to room temperature, quenched with 1M KOH aqueous solution and diluted with ether. The organic layer was washed twice with 1M KOH aqueous solution. The combined aqueous layers were washed with ether, acidified with 4M HCl and extracted with ether. These organic extracts were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude acid $4j_{trans}$ (0.09 g, 87%, 74/26 mixture of two epimers) was used in the following step without further purification. The acid reacted then with excess of diazomethane in ether. The crude ester was purified by preparative thin layer chromatography on SiO_2 (eluent : pentane/ether : 90/10 (v/v)) to afford 0.19 g of the methyl ester *rel(1S,2'S,3'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio-1-acetic acid $4j'_{trans}$ (57%). TLC :

R_f= 0.73 (eluent : pentane/ether : 90/10 (v/v)); IR : (film) : cm^{-1} : 3085, 3054, 3021, 2929, 1754, 1685, 1599, 1578, 1559, 1496, 999, 911, 886, 856, 788, 733, 702; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 0.80-2.40 (m, 21 H, -($C\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}$-S-$C_6\underline{H}_{11}$, C$\underline{H}_2$-CH=CH_2 and C$\underline{H}_3$-C-C_6H_5 (2s at 1.62 and 1.42), 2.80-3.00 (2d, J=7 Hz, 1 H, -C$\underline{H}$-S-), 3.40-3.6 0 (2s, 3 H), 3.42(3 H, s, $CO_2C\underline{H}_3$ of the minor isomer), 3.60 (3 H, s, $CO_2C\underline{H}_3$ of the major isomer), 7.00-7.30 (m, 5 H; $C_6\underline{H}_5$); MS (m/e) : 346 $[M]^{+\bullet}$, 288, 232 $[M\text{-}SC_6H_{11}]^+$, 171, 131 $[PhMeCCHCH_2]^+$, 115 $[SC_6H_{11}]^+$, 91 [tropylium]$^+$, 83 $[C_6H_{11}]^+$, 77, 59, 55.

Synthesis of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio-3-butenes $4l_{cis}$ (50/50). Following general procedure III, the α-thioalkyllithium $\mathbf{3h}_{cis}$ was prepared by reaction at -78°C of the selenide **1h** (0.37 g, 1 mmol.) with *n*-butyllithium (1.6 M, 0.62 ml, 1 mmol.) in THF and the reaction mixture was quenched with allyl bromide at this temperature. The composition of the crude sulfide as determined by GC[2], was rel*(1S,1'R,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio-3-butene $\mathbf{4l}_{cis\alpha}$ (17.5%), and equimolar amount of its stereoisomer $\mathbf{4l}_{cis\beta}$ (17.5%) and the thioether $\mathbf{4h}_{cis}$ resulting from the protonation reaction (9%). Characteristic of the mixture $\mathbf{4l}_{cis}$: TLC : R_f= 0.41 (pentane/toluene 90/10 (v/v)); IR : (film) : cm^{-1} : 3056, 3021, 1942, 1801, 1734, 1700, 1599, 1495, 1444, 755, 699, 629; ^1H NMR ($CDCl_3$/90 MHz) δ (ppm) : 0.80-2.80 (m, 24 H, ($C\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}$-S-$C_6\underline{H}_{11}$, C$\underline{H}_2$-CH=CH_2 and C$\underline{H}_3$-C-C_6H_5 (1.40, s)), 4.60-5.20 (m, 2 H, CH=C$\underline{H}_2$), 5.50-6.10 (m, 1 H, C$\underline{H}$=CH_2), 7.00-7.50 (m, 5 H, $C_6\underline{H}_5$).

Synthesis of [(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio-3-butenes $\mathbf{4l}_{trans\beta}$ and $\mathbf{4l}_{trans\alpha}$ (60/40). Following general procedure III, the α-thioalkyllithium $\mathbf{3h}_{trans}$ was prepared by reaction, at -20°C, of the selenide **1h** (0.38 g, 1 mmol.) and *t*-butyllithium (1.7 M, 0.56 ml, 1 mmol.) in pentane and the reaction mixture was quenched with allyl bromide at this temperature. The crude sulfide was purified by preparative HPLC (eluent : pentane/toluene (v/v)) to afford 0.43 g of *rel(1S,1'S,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-cyclohexylthio-3-butene $\mathbf{4l}_{trans}$.The crude sulfide was composed, by GC[2], of the rel*(1S,1'R,2'S)*-[(2'-methyl-2'-phenyl)-cyclopentyl]-1-phenylthio-3-butene $\mathbf{4l}_{trans\beta}$ (42%), the minor stereoisomer $\mathbf{4l}_{trans\alpha}$ (28%) and the thioether $\mathbf{4h}_{trans}$ resulting from the protonation reaction (22%). Characteristic of of the mixture $\mathbf{4l}_{trans}$: TLC : R_f= 0.43 (pentane/toluene 90/10 (v/v)); IR : (film) : cm^{-1} : 3055, 3021, 2925, 1944, 1870, 1801, 1700, 1599, 1577, 1559, 1494, 1445, 887, 819, 763, 702, 628; ^1H NMR ($CDCl_3$/90 MHz) δ (ppm) : 0.40-3.80 (m, **24** faux 25 H, ($C\underline{H}_2$)$_3$-C$\underline{H}$-C$\underline{H}$-C$\underline{H}_2$-CH, -S-$C_6\underline{H}_{11}$, C$\underline{H}_3$-C-C_6H_5 (1.40, s)), 4.60-6.20 (m, 3 H, C$\underline{H}$=C$\underline{H}_2$), 7.00-7.50 (m, 5 H, $C_6\underline{H}_5$).

Synthesis of *rel(1S,1'R,2'S)*-1-[(2'-methyl-2'-phenyl)cyclopentyl]-1-phenylsulfonyl ethane $\mathbf{9c}_{cis\alpha}$. A solution of thioether $\mathbf{4c}_{cis\alpha}$ (0.08 g, 0.25 mmol.) and sodium perborate (0.15 g, 1 mmol.) in glacial acetic acid was heated at 50°C for 2 h (formation of a white precipitate). The slurry was cooled to room temperature and concentrated *in vacuo* (20 mmHg). The white solid was dissolved in ethyl acetate. The organic layer was washed in turn with water, a saturated solution of sodium bicarbonate, water, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude sulfone was purified by preparative thin layer chromatography on SiO_2 (eluent : ether/pentane : 50/50 (v/v)) to afford 0.07 g of *rel(1S,1'R,2'S)*-1-[(2'-methyl-2'-phenyl)cyclopentyl]-1-phenylsulfonyl ethane $\mathbf{9c}_{cis\alpha}$ (80%) as a white solid, M.P. : 94°C; TLC : R_f= 0.64 (eluent : pentane/ether : 50/50 (v/v)); IR (KBr) cm^{-1} : 3085, 3057, 3020, 2956, 1959 (aromatic overtones), 1899, 1813, 1799, 1599 (C=C aromatic), 1445, 1358, 1363, 1324, 1299, 1235, 1179, 1135, 1085, 1069, 798, 769, 697, 687; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.19 (s, 3 H, C$\underline{H}_3$-C-Ph), 1.36 (d, J= 6.9 Hz, 3 H, C$\underline{H}_3$-CH-SO_2Ph), 1.66-2.40 (m, 6 H, -($C\underline{H}_2$)$_3$-CH-), 2.53-3.19 (m, 2 H, -C$\underline{H}$-C$\underline{H}$-SO_2Ph), 7.15-7.82 (m, 10 H, $C_6\underline{H}_5$-

and $C_6\underline{H}_5$-SO_2-); MS (m/e) : 187 ([M-$PhSO_2^{\bullet}$]$^+$, 5), 141 ([$PhSO_2$]$^+$, 4), 131 ([PhMeCCHCH_2]$^+$, 17), 105 ([PhCHMe]$^+$, 100), 91 ([tropylium]$^+$, 40), 77 (50), 55 (20); $C_{20}H_{24}SO_2$: Calc. : C, 73.13%; H, 7.36%; Found : C, 73.01%; H, 7.42%.

Synthesis of *rel(1'R,2S,2'S)*-2-[(2'-methyl-2'-phenyl)cyclopentyl]-2-phenylthio-1-ethanol $\mathbf{11}_{trans\beta}$. Following general procedure II, 6-methylseleno-6-phenyl-1-phenylthio-1-heptene **1d** (1.12 g, 3 mmol., 0.25 M) dissolved in dry pentane was reacted with *t*-butyllithium (1.7 M, 1.73 ml, 3 mmol.) at 20°C. The reaction mixture was stirred for 1.5 h at this temperature, cooled to -78°C and a small piece of dry-ice was introduced rapidly. The white slurry was warmed to room temperature, quenched with 1M KOH aqueous solution and diluted with ether. The organic layer was washed twice with 1M KOH aqueous solution. The combined aqueous layers were washed with ether, acidified with 4M HCl and extracted with ether. These organic extracts were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude acid (0.73 g, 88/12 mixture of two epimers) was used in the following step without further purification. The crude acid (0.73 g, 2.4 mmol.) was added dropwise to a slurry of $LiAlH_4$ (0.12 g, 3 mmol.) in THF (1 M), cooled to 0°C. The mixture was stirred for 17 h at 20°C, quenched carefully with 4 M HCl and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed in turn with water, a saturated solution of sodium bicarbonate, water, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude alcohol was purified by preparative thin layer chromatography on SiO_2 (eluent : ether/pentane : 10/90 (v/v)) to afford 0.44 g of *rel(1'R,2S,2'S)*-2-[(2'-methyl-2'-phenyl)cyclopentyl]-2-phenylthio-1-ethanol $\mathbf{11}_{trans\beta}$ (47% from the selenide **1d**). TLC : R_f= 0.41 (eluent : pentane/ether : 90/10 (v/v)); IR (Film) cm^{-1} : 3441 (OH), 3055, 3019, 2953, 2874, 1946 (aromatic overtones), 1879, 1803, 1598 (C=C aromatic), 1582, 1495, 1478, 1376, 1263, 1234, 1204, 1155, 1087, 1025, 973, 940, 920, 763, 748, 703; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.40-1.65 (m, 4 H, -O$\underline{H}$; C$\underline{H}_3$-C-Ph (1.63, s)), 1.70-2.30 (m, 7 H, -(C$\underline{H}_2$)$_3$-C$\underline{H}$-), 2.72 (m, 1 H, -C$\underline{H}$-SPh), 3.23 (dd, J= 8.2 and 1.0 Hz, 1 H, -C$\underline{H}$HOH), 3.37 (dd, J= 8.2 and 2.5 Hz, 1 H, -CH$\underline{H}$OH), 6.80-7.50 (m, 10 H, $C_6\underline{H}_5$- and $C_6\underline{H}_5$-S); ^{13}C NMR ($CDCl_3$, 100.4 MHz) δ (ppm) : 23.92 (-$\underline{C}H_2$), 31.19 (-$\underline{C}H_3$), 32.18 (-$\underline{C}H_2$), 44.25 (-$\underline{C}H_2$), 49.04 (Ph-C-$\underline{C}H_3$), 52.70 (-$\underline{C}$H-CH-SPh), 55.46 (-$\underline{C}$H-SPh), 62.56 (-$\underline{C}H_2$OH), 125.35, 127.68, 128.27, 128.47, 129.38, 132.73 (-$\underline{C}$H aromatic), 134.61 (-S-C-ipso aromatic), 147.71 (ipso aromatic); MS (m/e) : 312 ([M]$^{+\bullet}$, 21), 186 ([M-PhSOH]$^{+\bullet}$, 15), 171 (36), 131 ([PhMeCCHCH_2]$^+$, 48), 109 ([PhS]$^+$, 50), 105 ([PhCHMe]$^+$, 92), 91 ([tropylium]$^+$, 100), 77 (40), 55 (33).

Synthesis of the dinitrobenzoate $\mathbf{10}_{trans\beta}$. The alcohol $\mathbf{11}_{trans\beta}$ (0.08 g, 0.25 mmol.) was added dropwise to a solution of 3,5-dinitrobenzoyl chloride (Merck, 0.09 g, 0.4 mmol.) and 4-dimethylamino pyridine (0.005 g, 0.04 mmol.) in pyridine (2 ml). The reaction was stirred for 2 h, quenched with HCl (4 M) and diluted with ethyl acetate. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with water, HCl (4M), water, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude ester was purified by preparative thin layer chromatography on SiO_2 (eluent : ether/pentane : 20/80 (v/v)) to afford 0.09 g of the benzoate $\mathbf{10}_{trans\beta}$ (71%) as a yellow solid, M.P. : 92°C; TLC : R_f= 0.35 (eluent : pentane/ether : 80/20 (v/v)); IR (KBr) cm^{-1} : 3098, 2957, 2871, 1946 (aromatic overtones), 1879, 1803, 1734 (C=O), 1598 (C=C aromatic), 1544, 1458, 1437, 1343, 1276, 1163, 1074, 730 (C-SPh), 720, 703; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 1.66 (s, 3 H, C$\underline{H}_3$-C-Ph), 1.70-2.30 (m, 7 H, -(C$\underline{H}_2$)$_3$-C$\underline{H}$-), 3.22 (ddd similar to dt, J= 4.4 and 7.9 Hz, 1 H, -C$\underline{H}$-SPh), 4.34 (dd, J= 11.2 and 7.8 Hz, 1 H, -CH$\underline{H}$O-), 4.39 (dd, J= 11.2 and 4.4 Hz, 1 H, -C$\underline{H}$HO-), 6.70-7.47 (m, 10 H, $C_6\underline{H}_5$- and $C_6\underline{H}_5$-S), 8.76 (d, J= 1.9 Hz, 2 H, -C$\underline{H}_{ortho}$ and -C$\underline{H}_{ortho}$), 9.10 (d, J=1.9 Hz, 1 H, -CH_4); ^{13}C NMR ($CDCl_3$, 100.4 MHz) δ (ppm) : 23.58 (-

$\underline{C}H_2$), 30.72 (-$\underline{C}H_3$), 31.46 (-$\underline{C}H_2$), 43.18 (-$\underline{C}H_2$), 48.94 (Ph-C-$\underline{C}H_3$), 49.11 (-$\underline{C}$H-CH-SPh), 52.97 (-$\underline{C}$H-SPh), 68.75 (-$\underline{C}H_2O$-), 126.03, 126.41, 127.86, 127.98, 128.68, 129.12, 129.17, 129.23, 131.00 (-$\underline{C}$H aromatic), 131.26 (-O=C-$\underline{C}$- ipso aromatic), 134.04 (-S-$\underline{C}$- ipso aromatic), 146.71 (ipso aromatic), 148.34 (-$\underline{C}$-NO_2) and 162.02 (-$\underline{C}$=O); MS (m/e) : 185 ([M-DNBOH-SPh•]$^+$, 4), 143 (3), 131 ([PhMeCCH]$^+$, 49), 129 (60), 105 ([PhCHMe]$^+$, 71), 91 ([tropylium]$^+$, 100); $C_{27}H_{26}N_2O_6S$: Calc. : C, 64.02%; H, 5.20%; N, 5.53%; Found : C, 64.15%; H, 5.20%; N, 5.65%.

Synthesis of *rel(1S,1'S,2'S)*-1-[(2'-methyl-2'-phenyl)cyclopentyl]-1-thiophenyl-ethane $4c_{trans\alpha}$ by the reduction of the alcohol $11_{trans\beta}$. Methyllithium (1.5 M, 0.26 ml, 0.35 mmol.) was added under argon to a solution of alcohol $11_{trans\beta}$ (0.08 g, 0.25 mmol., 0.1 M) in anhydrous THF cooled to 0°C. The reaction mixture was stirred for 0.1 h, then benzenesulfonyl chloride (0.07 g, 0.25 mmol.) dissolved in THF was added dropwise. The yellow solution was stirred for an additional hour and $LiHBEt_3$ (1.0 M in hexane, 1.4 ml, 1.4 mmol.) was added dropwise at 0°C. The yellow colour faded up rapidly. After 2 h at 20°C, the reaction mixture was quenched with a saturated solution of ammonium chloride. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water, dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mmHg). The crude sulfide was purified by preparative thin layer chromatography on SiO_2 (eluent : toluene/pentane : 10/90 (v/v)) to afford 0.06 g of the thioether $4c_{trans\alpha}$ (54%). This sample proved to be identical (IR, NMR, GC^2, TLC) with that prepared by the alkylation of an α-thioalkyllithium with methyl iodide.

Synthesis of $4d_{cis}$ by reduction with Raney nickel. Raney nickel in ethanol (8g, 8 ml) was introduced in a 25 ml flask, fitted with a condensor and filled with argon. The nickel was washed 5 times with fresh ethanol. The thioether $4c_{cis}$ or $4c_{trans}$ (0.29 g, 1 mmol.) in ethanol was then added. The reaction mixture was refluxed for 24h, filtered through a pad of celite and concentrated in vacuo (20 mmHg). The alkane was then purified (eluent : pentane) to afford 0.19 g of *rel(1R,2R)*-2-ethyl-1-methyl-1-phenyl cyclopentane $4d_{cis}$ (87%) or 0.15 g of *rel(1R,2S)*-2-ethyl-1-methyl-1-phenyl cyclopentane $4d_{trans}$ (80%). These samples are identical to the ones described in the following paper.[1b]

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