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COMPARISON BETWEEN ALKYLSELENO, ARYLSELENO AND ARYLTHIO SUBSTITUENTS STABILIZING ALKYLLITHIUM COMPOUNDS

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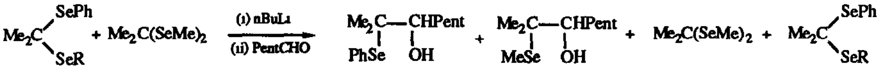
Abstract : This paper discloses the chemoselective cleavage of selenoacetals. Informations concerning the intimate mechanism of such process are produced as well as unambiguous experimental results concerning the relative stabilization of a carbanionic center by phenylthio, phenylseleno and methylseleno moieties.

In the preceding paper [1], we have shown that the cleavage by alkyllithiums of the C-Se bond of selenoacetals is a quite general reaction and that there is a clear cut difference of reactivity between selenoacetals (i) belonging to the phenylseleno and methylseleno series (ii) derived from aldehydes and ketones. In this paper, we disclose our results concerning chemoselective reactions between selenoacetals of different origin. These results are not only valuable for their synthetic applications but also in the theoretical field. We have at the same time devised experiments which unambiguously show that a carbanion substituted by a phenylseleno moiety is more stabilized than the one substituted by a methylseleno group. We have then extended this work to the phenylthio derivatives.

From the results disclosed in the preceding paper [1], some chemoselectivity was expected between selenoacetals belonging to the methylseleno and the phenylseleno series. We therefore decided to study in detail the reaction of n-butyllithium with a one to one mixture of 2,2-bis(phenylseleno)propane and its methylseleno analogue used as models. [2] The reaction has been carried out in a THF-hexane mixture at -78°C and has been quenched after 0.1 h with hexanal before hydrolysis (Scheme 1a). The ratio of each different set of compounds (selenoacetals, β-hydroxyalkyl selenides, butyl selenides) has been then analyzed.

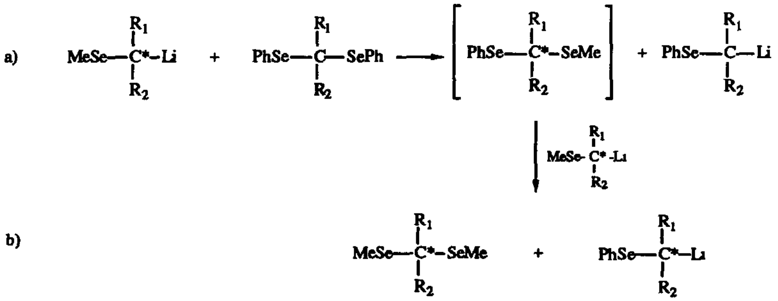
Scheme 1



a	R = Ph	THF-hexane, -78°C, 0.1h	62	10	65	10
b	R = Ph	THF-hexane, -78°C, 1h	75	08	85	15
c	R = Me	THF-hexane, -78°C, 0.1h	78	11	--	--

The ratios between the different β-hydroxyalkyl selenides (Ph/Me : 86/14) and the remaining selenoacetals (Ph/Me : 15/85), clearly show that the phenylselenoalkyllithium is mainly produced. However, these results do not tell if a kinetically controlled process has taken place [ie. n-butyllithium reacts faster with the phenylselenoacetal than with the methylselenoacetal] or if an equilibration between the 2-methylseleno-2-propyllithium and the phenylselenoacetal which finally leads to 2-phenylseleno-2-propyllithium has taken place. Such a process is tentatively disclosed in Scheme 2 and is commented below.

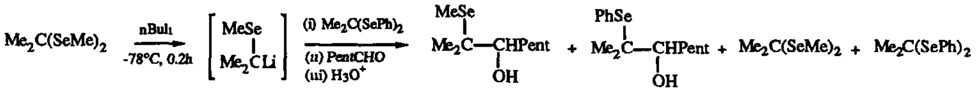
Scheme 2



The close relation between the ratios of the different β-hydroxyalkyl selenides (Ph/Me 86/14) and the butyl selenides (Ph/Me : 77/23) indicates that the first event (ie. kinetic control) mainly occurred but that the second one (ie. thermodynamic control) cannot be ruled out (Scheme 2) and even might have taken place to a very low extend (≈ 8 %).

We, in fact proved in a separate experiment shown in the Scheme 3 that this equilibration can occur. We have reacted for that purpose 2-methylseleno-2-propyllithium, independently prepared from 2,2-bis(methylseleno)propane and n-BuLi in THF-hexane with 2,2-bis(phenylseleno)propane and the resulting mixture was quenched with hexanal prior to hydrolysis.[2] The production of appreciable amounts of the β-hydroxyalkyl phenyl selenide and of 2,2-bis(methylseleno)propane unambiguously supports the intermediary formation of 2-phenylseleno-2-propyllithium.

Scheme 3

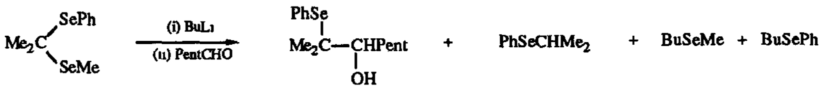


a	THF-hexane, -78°C, 0.1h	44	30	12	50
b	THF-hexane, -78°C, 0.3h	30	40	20	40

Surprisingly the reaction outlined in the scheme 3 does not produce significant amounts of the 2-methylseleno-2-phenylselenopropane, a compound which is expected to be primarily formed. Therefore it should react faster with 2-methylseleno-2-propyllithium than 2,2-bis-phenylselenopropane and should lead finally to 2,2-bis(methylseleno)propane and 2-phenylseleno-2-propyllithium (Scheme 2). It is interesting to point out that the hydrocarbon framework of the later intermediate should therefore originate in part from the phenylselenoacetal (Scheme 2 entry a) and in the other part from 2-methylseleno-2-propyllithium (Scheme 2 entry b).

In order to have experimental support for the proposals presented above, we have prepared 2-methylseleno-2-phenylselenopropane from acetone, benzeneselenol and methaneselenol (1:1:1.ratio, 0.5 equiv. $ZnCl_2$, 20°C, 3 h, 45% yield) and we have studied its behaviour under different circumstances.[2] We found that on reaction with n-BuLi in THF-hexane or with s-BuLi in ether-hexane it leads, after quenching the reaction mixture with hexanal, to a β-hydroxyalkyl phenyl selenide and to butyl methyl selenide which both arise from the exclusive cleavage of its C-SeMe bond (Scheme 4).

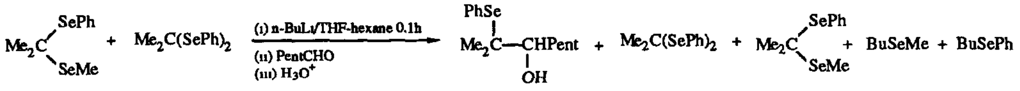
Scheme 4



a	n-BuLi/THF-hexane, -78°C, 0 2h	90	10	100	0
b	s-BuLi/ether-hexane, -78°C, 0 2h	80	15	100	0

Otherwise, when the above reaction is performed in the presence of equimolar amounts of 2,2-bis-methylselenopropane (Scheme 1c) or its phenylseleno analogue (Scheme 5), the mixed selenoacetal proved in all the cases more reactive towards n-BuLi than its other partners.

Scheme 5



90	59	21	70	30

The experiment presented in scheme 5 is particularly interesting since it unambiguously shows that the cleavage of the C-SeMe bond in the mixed selenoacetal is preferred over the C-SePh bond cleavage in the phenylselenoacetal although each of the two cleavages leads to the same 2-phenylseleno-2-propyllithium. This is confirmed not only from the ratio of unreacted selenoacetals recovered but also from the relative amount of butyl selenides recovered from the cleavage process (Scheme 5). These results can be tentatively explained by a precoordination of the most nucleophilic methylseleno moiety with the electrophilic lithium counter ion which might enhance the electrophilicity of this center.

The experiments just presented led to the following conclusions :

(i) The selenoalkyllithium which possesses the more stabilized carbanionic center is all the time preferentially produced whether a C-SePh or a C-SeMe bond has to be cleaved (compare the results described in schemes 1, 4 and 5).

(ii) Within the limits of rule (i) the C-SeMe bond cleavage is preferred over the C-SePh bond if it produces the same organometallic compound (Scheme 5).

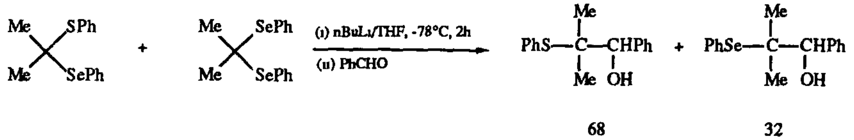
The strategy we have developed in order to compare the relative stabilization of a carbanionic center by a phenylseleno or a methylseleno moiety has been extended to the case of α-phenylthioalkyllithiums. It is well established that the heteroatomic moiety in α-heterosubstituted organometallics has a marked effect on the stabilization of a carbanionic center.[3] For example, third row elements stabilize to a larger extent a carbanionic center than second row elements do. [3] However ,the reasons of such stabilizing effects are not yet firmly understood although intense and controversial work has been carried out over the last two decades, especially in the chalcogen series of compounds. [2,8] The d orbital theory [3-9] and the polarization theory [3,6-9] both tend to explain the observed difference of acidity between ethers and sulfides. However, whereas the d orbital theory predicts that the seleno moiety will not stabilize a carbanionic center to the same extent the analogous thio moiety does [(carbanion) 2p - (Se) 4dxy π overlap is expected to be less efficient than (carbanion) 2p - (S) 3dxy π overlap] , the more polarisable selenium atom is expected in the polarization theory, to stabilize a carbanionic center to a larger extent than sulfur. Calculations from Lehn's group predicted the second alternative for sulfur [8] and selenium [9] derivatives.

In order to get some insight in this field (i) we have prepared mixed S,Se selenoacetals which are valuable precursors of α-thioalkyllithiums [9-14] in a reaction which parallels the one described for their seleno analogues and (ii) we have performed the competitive experiments described below.

2-Phenylthio-2-phenylselenopropane proved to be the candidate of choice since it is readily prepared [15] by slow addition of 2-phenylseleno-2-propyllithium to an excess of diphenyl disulfide and since it avoids the problem of competitive metallation which occurs when mixed S,Se acetals derived from aldehydes are instead used.

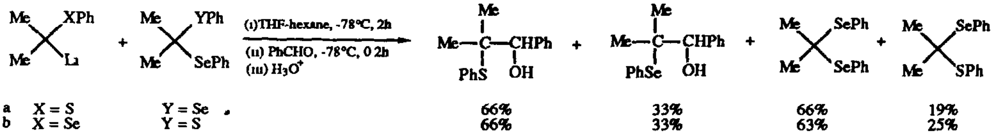
In a first experiment, we have reacted at -78°C n-butyllithium in THF with a one to one mixture of the (S,Se) and (Se,Se) acetals in THF-hexane and the resulting organometallics have been trapped with benzaldehyde to produce after hydrolysis a 68/32 mixture of the corresponding β-hydroxyalkyl sulfide and selenide shown in the scheme 6.

Scheme 6



In a second set of experiments we have alternatively reacted at the same temperature (-78°C) 2-phenylthio-2-propyllithium with 2,2-bis(phenylseleno)propane and 2-phenylseleno-2-propyllithium with 2-phenylseleno-2-phenylthiopropane (scheme 7). In both cases the equilibrium is already reached after two hours at -78°C since the relative ratio of the β-hydroxyalkyl sulfide / selenide was found to be identical (66/33). Therefore although a phenylthio moiety stabilizes to a somewhat larger extend an α-carbanionic center than a phenylseleno moiety (66/33) the difference of stabilization energy is rather small (0.3 kcal/mol.) and by far different from the one predicted by calculation [9] (4 kcal/mol. in the inverse direction).

Scheme 7

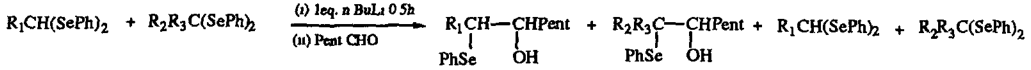


The scattered information available on the acidifying effect of arylthio / arylseleno moiety on methyl,[16,17a] allyl,[17b] propargyl, [18a] allenyl [18b] and phenacyl [19] sulfides / selenides and on bis(phenylthio) / phenylseleno methane [20] show that these sulfur derivatives are kinetically more acidic than their selenium analogues and therefore that sulfur stabilizes carbanions slightly more effectively than does selenium [17]. Our results compare well these data.

We finally studied the chemoselective cleavage of a selenoacetal derived from an aldehyde in the presence of a selenoacetal derived from a ketone and belonging to the same series (SePh or SeMe). In a standard procedure a one to one mixture of these selenoacetals has been reacted with equimolar amounts of butyllithium and the resulting mixture was quenched with hexanal or benzaldehyde prior hydrolysis.

We took advantage of the study presented in the preceding paper for the selection of the experimental conditions susceptible to give the best chemoselectivity. n-Butyllithium in THF-hexane or in ether-hexane has been selected for that purpose. Best results have been obtained in the phenylseleno series when the reactions are carried out at -42°C in ether-hexane. Under the last conditions, the difference of reactivity between the two selenoacetals is so high that the discrimination can be almost completely achieved (Scheme 8, compare entries b to d) probably under kinetically controlled conditions.

Scheme 8



$$R_1CH(SePh)_2 + R_2R_3C(SePh)_2 \xrightarrow[\text{(ii) Pent CHO}]{\text{(i) 1eq. n BuLi 0 5h}} R_1\underset{PhSe}{CH}-\underset{OH}{CH}Pent + R_2R_3\underset{PhSe}{C}-\underset{OH}{CH}Pent + R_1CH(SePh)_2 + R_2R_3C(SePh)_2$$

	R_1	R_2	R_3	Conditions	Yield in %	Yield in %	Recovery %	Recovery %
a	Me	Me	Me	ether, -42°C	89	--	--	94
b	Hex	Me	Me	ether, -42°C	82	--	5	93
c	Hex	$CH_2(CH_2)_3CH_2$		ether, -42°C	83	--	--	96
d	Hex	Me	Me	THF, -78°C	70	12	--	75

Unfortunately, the same chemoselectivity cannot be achieved under similar conditions in the methylseleno series since both selenoacetals are inert towards n-butyllithium in this solvent mixture (ether-hexane -42°C). Performing the reactions with s-BuLi in ether-cyclohexane (-78°C, 0.5h) or with n-butyllithium in THF-hexane (-110°C to -78°C) led to a rather poor chemoselectivity. The results gathered in the scheme 9 (entries a to d) suggest again that the reactions proceed under kinetic control.

Scheme 9

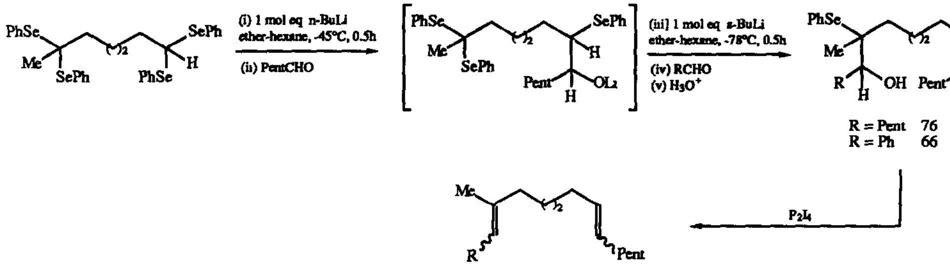
$$HexCH(SeMe)_2 + HexCMe(SeMe)_2 \xrightarrow[\substack{\text{(ii) PhCHO} \\ \text{(iii)}H_3O^+}]{\text{(i) RLi}} HexCH(SeMe)CHPh(OH) + HexCMe(SeMe)CHPh(OH)$$

		Yield	Yield	Chemoselectivity
a	s-BuLi - ether/hexane, -78°C, 0.5h	55%	25%	73%
b	*n*-BuLi - THF/hexane, -100°C, 0 5h	15%	05%	75%
c	n-BuLi - THF/hexane, -78°C, 0.05h	37%	11%	77%
d	n-BuLi - THF/hexane, -78°C, 1h	63%	23%	74%
e	n-BuLi - THF/hexane, -78°C, 0.1h then -40°C, 1h	78%	8%	90%

A somewhat better chemoselection was however achieved under thermodynamic control. Thus if the reaction is performed in THF-hexane at -78°C and then the medium is heated to -40°C for 1h prior quenching with benzaldehyde, the percentage of the α-selenoalkyllithium derived from the aldehyde increases up to 90 % (Scheme 9 entry e).

Using these observations, we have been able to chemoselectively and sequentially produce α-phenylselenoalkyllithiums derived from an aldehyde and a methyl ketone and which both belong to the same molecule (Scheme 10). The chemoselective cleavage of the selenoacetal derived from the aldehyde has been achieved under kinetic control with n-BuLi in ether-hexane using the conditions which already proved successful for these series of compounds. The resulting organometallic has been trapped with hexanal then the cleavage of the remaining acetal moiety has been successfully achieved using the more reactive s-butyllithium. Further reaction with benzaldehyde led to a bis β-hydroxyalkyl selenide which finally produced 2-methyl-1-phenyl 1,7-tridecadiene when reacted with P_2I_4.[16] This chemoselective reaction can be of some synthetic value since it allows the regioselective synthesis of such 1,6-diene in few steps (7 steps, 3 pots) and reasonable yield from 6-oxoheptanal without tedious protection deprotection procedures.

Scheme 10



In conclusion, it has been shown that the phenylthio, phenylseleno and methylseleno moieties exhibit decreasing ability to stabilize an α-carbanionic center. We also found that in reactions which produce the same α-selenoalkyllithium the C-SeMe bond is more readily cleaved than the C-SePh bond. Finally, selenoacetals derived from aldehydes are usually more reactive towards alkyllithiums than those derived from ketones. The best chemoselection has been achieved in the phenylseleno series under kinetically controlled conditions (n-BuLi, ether-hexane, -40°C) whereas in the methylseleno series, chemoselective reaction can be observed under thermodynamic control but with a lower selectivity. Work is now in progress to use these observations for the synthesis of more complex molecules.

Experimental

The procedures used and the precautions taken in this work are identical to those described in the preceding paper [1].

Competitive reaction of equimolar amounts of 2,2-bis (methylseleno)propane and 2,2-bis (phenylseleno)propane towards n-butyllithium. Typical experiment reported in scheme 1).

A mixture of 1.00 mmol of 2,2-bis(methylseleno)propane and 1.00 mmol (0.356 g) of 2,2-bis(phenylseleno)propane was dissolved in 5 ml of anhydrous THF at -78°C. Then, 1.00 mmol (0.63 ml) of n-butyllithium was slowly added and the mixture was allowed to react at -78°C for 0.1 h, then quenched by addition of 1.00 mmol (0.1 g) of hexanal in 1 ml of anhydrous THF. After methanolysis at -78°C and addition of water, the resulting mixture was extracted twice with ether. The combined organic layer was washed with water, dried over anhydrous $MgSO_4$ and the solvents were evaporated carefully under vacuum. The crude mixture was fractionated by preparative layer chromatography (SiO_2, pentane) to afford three main fractions. The most eluted ones(0.19 g) consisted mainly of a mixture of n butyl phenyl and n-butyl methyl selenide in the 77/23 ratio (based on lGC[2]). The medium one (0.22g) contained 2,2-bis(phenylseleno)propane and 2,2-bis(methylseleno)propane in the 15/85 ratio (based on NMR integration). The less eluted ones was again fractionated by preparative layer chromatography (SiO_2, benzene/EtOAc (9:1, v/v)) to give 2-methylseleno -2-methyl-octane-3-ol (0.024g,10%)and 2-phenylseleno-2-methyl-octane-3-ol(0.19g,62%).2-Methylseleno-2-methyl-octane-3-ol: Tlc Rf 0.5 eluent pentane-ether (85:15, v/v). ^1H NMR (CCl_4) δ 0.7-1.7 (m with s at 1.25 and 1.35, 17H,Me and CH_2), 1.9 (s, 3H,MeSe), 2.1-2.3 (m, 1H, OH), 3.05-3 45 (m, 1H, CHOH). IR (neat) 3467, 2956, 2929, 2859, 1462, 1424, 1386, 1296, 1272, 1197, 1166, 1130, 1112, 1058, 1001, 944,921, 897, 725 cm^{-1}. MS (m/e) 238 (M), 188, 167, 143 (M-MeSe). 2-phenylseleno-2-methyl-octane-3-ol:Tlc Rf 0 55 eluent pentane-ether(85:15,v/v). ^1H NMR (CCl_4) δ 0.7-1.7 (m with s at 1.30, 17H,Me and CH_2), 2.35 (s, 1H, OH), 3.1-3.35 (s, 1H, CHOH), 7.15-7.7 (2m, 10H, arom). IR (neat) 3475, 3070, 3056, 2956, 2927, 2558, 1950, 1879, 1727, 1579, 1475, 1460, 1436, 1385, 1366, 1301, 1260, 1126, 1111, 1065, 1022, 1000, 919, 741, 694 cm^{-1}. MS (m/e) 300 (M), 244, 199, 158 (PhSeH).

Synthesis of 2-methylseleno-2-phenylselenopropane.

To a solution of 0.1 mol (15.6 g) of benzeneselenol, 0.1 mol (9.6 g) of methaneselenol and 0.1 mol (5.8 g) of acetone in 100 ml of CCl_4, was added, at 0°C, 0.05 mol (6.8 g) of anhydrous zinc dichloride. The mixture was vigorously stirred for 0.5 h at 0°C and 15 h at 20°C, then diluted with 300 ml of ether, washed three times with a 10 % aqueous solution of hydrochloric acid, three times with a saturated aqueous solution of sodium bicarbonate and finally with water. The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvents were removed under vacuum. Distillation of the crude mixture afforded 13,2 g of pure 2-methylseleno 2-phenylselenopropane (45 % yield) (bp 90-92/0.3 mmHg). Tlc Rf 0.2 eluent pentane. ^1HNMR (CCl_4) d 1.7 (s, 6H, MeC), 2.05 (s, 3H,MeSe), 7.05-7.60 (2m, 5H, arom.). IR (neat) 3060,3040,2940,2910,1570,1470, 1435,1360, 1140,1100,1070,1060,1020,1000,790,760,740,690cm^{-1}.Anal. Calcd. for $C_{10}H_{14}Se_2$: C 41.1, H 4.83. Found C 41.48, H 4.96.

Reaction of 2-methylseleno-2-phenylselenopropane with n-butyllithium in THF. (Typical experiment reported in scheme 4).

To 1.00 mmol (0.294 g) of 2-methylseleno-2-phenylselenopropane in 2 ml of anhydrous THF, was added, at -78°C, 1.00 mmol (0.63 ml) of n-butyllithium . After 0.2 h stirring at -78°C, 1.00 mmol (0.1 g) of heptanal in 1 ml of anhydrous THF was introduced. The mixture was allowed to react for 0.2 h at -78°C, then hydrolysed and extracted three times with ether. The combined organic layer was washed with water, dried over anhydrous $MgSO_4$, filtered and the solvents were evaporated under vacuum.The resulting mixture was fractionated by preparative layer chromatography (SiO_2, pentane/ether : 8/2) to give 0.27 g of 2-phenylseleno-2-methyl octane-3-ol (90 % yield). No significant amount of 2-methylseleno-2-methyloctane-3-ol could be detected. 2-phenylseleno-2-methyl-octane-3-ol : Tlc Rf 0.65 eluent pentane-ether(8:2,v/v).^{1}H NMR (CCl_4) δ 0.8-1.7(m with s at1.3,19H,Me and CH_2), 2.3-2.4 (m,1H,OH), 3.1-3.3 (m,1H,C$\underline{H}$OH), 7.2-7.6(m,5H,arom). IR (neat) 3450, 3080,3060, 2960, 2940, 2875, 1585, 1480, 1475, 1465, 1445, 1390, 1370, 1310,1130,1070,1030, 1010, 750, 700 cm^{-1}.Anal Calcd for $C_{16}H_{26}OSe$ C 58.35,H 7.96.Found C 58.05,H 7.73.

Competitive reaction of equimolar amounts of 2-methylseleno-2-phenylselenopropane and 2,2-bis (phenylseleno)propane towards n-butyllithium.

A mixture of 1.00 mmol (0.294g) of 2-methylseleno-2-phenylselenopropane and 1.00 mmol (0.356 g) of 2,2-bis(phenylseleno)propane was dissolved in 5 ml of anhydrous THF at -78°C. Then, 1.00 mmol (0.63 ml) of n-butyllithium was slowly added and the mixture was allowed to react at -78°C for 0.1 h, then quenched by addition of 1.00 mmol (0.1 g) of hexanal in 1 ml of anhydrous THF. After methanolysis at -78°C and addition of water, the resulting mixture was extracted twice with ether. The combined organic layer was washed with water, dried over anhydrous $MgSO_4$ and the solvents were evaporated carefully under vacuum. The crude mixture was fractionated by preparative layer chromatography (SiO_2, pentane) to afford three main fractions. The most eluted ones (0.18 g) consisted mainly of a mixture of n-butyl phenyl and n-butyl methyl selenide in the 30/70 ratio (based on lGCl^{2}). The medium one (0.28g) contained 2,2-bis(phenylseleno)propane (59% yield) and 2-methylseleno-2-phenylselenopropane (21% yield) (based on NMR integration). The less eluted ones(0.27g) was pure 2-phenylseleno-2-methyl-octane-3-ol(90%yield) whose analytical data are reported above.

Synthesis of 2-phenylthio-2-phenylselenopropane.

To a solution of 15 mmol (5.34 g) of 2,2-bis(phenylseleno)propane dissolved in 30 ml of anhydrous THF was added ,at -78°C, 15 mmol (9.4 ml) of n-butyllithium. After 0.5 h stirring, the mixture is syringed at -78°C and slowly added to a precooled (-78°C) and vigorously stirred solution of 20 mm (4.36 g) of diphenyl disulfide in 15 ml of anhydrous THF. The resulting mixture was stirred for 2 h at -78°C, then hydrolysed. The organic layer was separated and the aqueous layer was extracted twice with ether. The combined organic layer was washed with water and dried over anhydrous $MgSO_4$. After filtration and solvent removal under vacuum, the 2-phenylthio-2-phenylselenopropane is isolated by SiO_2 column chromatography (eluent pentane) and crystallized in pentane (3.3 g, 72 % yield, 52-53°C). Tlc Rf. 0.24 eluent pentane. ^{1}H NMR (CCl_4) δ 1.56 (s, 6H,Me_2C), 7.11-7.76 (m, 10H, arom). IR (neat) 3070, 3060, 2960, 2860, 1950, 1880, 1810, 1760, 1580, 1480, 1440, 1380, 1365, 1305, 1220, 1150, 1100, 1070, 1025, 1000, 750, 695 cm^{-1}. HRMS Calcd. for M 308.0137. Found 308.0124. MS (m/e) 308 (M), 158 (C_6H_5SeH), 151 (M-C_6H_5SeH). Anal. Calcd. for $C_{15}H_{16}SSe$: C 58.63, H 5.25. Found C 58.51, H 5.46.

Competitive reaction of equimolar amounts of 2-phenylthio-2-phenylselenopropane and 2,2-bis (phenylseleno)propane towards n-butyllithium.

A mixture of 1.00 mmol (0.308g) of 2-phenylthio-2-phenylselenopropane and 1.00 mmol (0.356 g) of 2,2-bis(phenylseleno)propane was dissolved in 5 ml of anhydrous THF at -78°C. Then, 1.00 mmol (0.63 ml) of n-butyllithium was slowly added and the mixture was allowed to react at -78°C for 2h, then quenched by addition of 1.00 mmol (0.106 g) of benzaldehyde in 1 ml of anhydrous THF. After methanolysis at -78°C and addition of water, the resulting mixture was extracted twice with ether. The combined organic layer was washed with water, dried over anhydrous $MgSO_4$ and the solvents were evaporated under vacuum. The crude mixture was fractionated by preparative layer chromatography (SiO_2, pentane-ether(9:1, v/v)) to give a mixture of the corresponding β-hydroxyalkyl sulfide and β-hydroxyalkyl selenide in the 68/32 ratio (based on NMR integration (0.3g). This ratio was determined by ^{1}H (NMR (CCl_4) integration of the signals respectively attributed to Me_2CSe (2s at 1.18 and 1.20) and to Me_2CS (2 s at 1.05 and 1.1). The analytical data of pure 1-phenyl-2-methyl-2-phenylseleno-ethane-1-ol are given above whereas those of 1-phenyl-2-methyl-2-phenylthio-ethane-1-ol are given in the literature [11].

Reaction of 2-lithio-2-phenylthiopropane on 2,2-bis(phenylseleno)propane.

To a solution of 1.00 mmol (0.308 g) of phenylthio-2-phenylselenopropane dissolved in 4 ml of anhydrous THF was added, at -78°C ,1.00 mmol (0.625 mol) of n-butyllithium . After 0.5 h stirring at -78°C, was added a solution of 1.00 mmol (0.356 g) of 2,2-bis(phenylseleno)propane in 3 ml of anhydrous THF.The mixture was allowed to react for 2h at -78°C, then quenched with 1.00 mmol (0.106 g) of benzaldehyde dissolved in 2 ml of anhydrous THF. After 0.2 h at -78°C,1 ml of methanol was added followed by water . The organic layer was separated and the aqueous layer was extracted twice with ether. The combined organic layer was washed with water and dried over anhydrous $MgSO_4$. After filtration and solvent removal under vacuum, the resulting crude mixture (0.83 g) was fractionated by preparative layer chromatography (SiO_2, pentane) affording a mixture (0.3 g) of 2-phenylthio-2-phenylselenopropane and 2,2-bis(phenylseleno)propane in the ratio 78/22 (based on NMR integration) and a mixture (0.305 g) of products which were not eluted . This last mixture was purified by preparative layer chromatography (SiO_2, pentane-ether(9:1,v/v) to give the corresponding β-hydroxyalkyl sulfide and β-hydroxyalkyl selenide in the 66/33 ratio (based on NMR integration , see above)(0.29g).

Reaction of 2-lithio-2-phenylselenopropane on 2-phenylthio-2-phenylselenopropane.

To a solution of 1.00 mmol (0.356 g) of 2,2-bis(phenylseleno)propane dissolved in 4 ml of anhydrous THF was added, at -78°C ,1.00 mmol (0.625 ml) of n-butyllithium . After 0.5 h stirring at -78°C, was added a solution of 2-phenylthio-2-phenylselenopropane in 3 ml of anhydrous THF. The mixture was allowed to react for 2 h at -78°C, then quenched with 1 00 mmol (0.106 g) of benzaldehyde dissolved in 2 ml of anhydrous THF. Addition of methanol and water and usual work-up gave 0.9 g of crude mixture. After the two purifications as described above, the following results were obtained : a mixture (0.29 g) of 2-phenylthio-2-phenylselenopropane and 2,2-bis(phenylseleno) propane in the 72/28 ratio and a mixture (0.29 g) of the corresponding β-hydroxyalkyl sulfide and β-hydroxyalkyl selenide in the 66/33 ratio (based on ^{1}H NMR integration, see above).

Competitive reaction of equimolar amounts of 2,2-bis(phenylseleno)propane and 1,1-bis(phenylseleno)heptane towards n-butyllithium in ether.

To a mixture of 1.00 mmol (0.356 g) of 2,2-bis(phenylseleno)propane and 1.00 mmol (0.412 g) of 1,1-bis(phenylseleno)heptane in 8 ml of anhydrous ether, was added, at -45°C, 1.00 mmol (0.63 ml) of n-butyllithium. The mixture was stirred for 0.75 h at -45°C and 1mmol (0.1g) of hexanal in 1 ml of anhydrous ether was introduced.The mixture was allowed to react for 0.2 h at -45°C then hydrolysed and extracted three times with ether. The combined organic layer was washed with water, dried over anhydrous $MgSO_4$, filtered and the solvents were removed under vacuum. The residue was fractionated by preparative layer chromatography (SiO_2, pentane-ether (8:2, v/v)) to give 0.29 g of 7-phenylseleno-tridecane-6-ol (82% yield). The most eluted fraction was again purified by preparative layer chromatography (SiO_2, pentane) to afford 0.31 g of 2,2-bis(phenylseleno)propane (93 % recovered).7-phenylseleno-tridecane-6-ol: Tlc Rf. 0.66 and 0.74 (mixture of diastereoisomers) eluent pentane-ether(8:2,v/v). ^{1}H NMR (CCl_4) δ 0.75-1 (t, 6H, Me), 1.1-1.9 (m, 18H, CH_2), 2.9-3.3 (2m, diastereoisomeric mixture), 1H C$\underline{H}$Se), 3.3-3.6 (m, 1H, C$\underline{H}$OH) 7.1-7.6 (2m, 5H, arom.). IR (neat) 3450 , 3080, 3060, 2960, 2930, 2880, 2860, 1580, 1485, 1475, 1460, 1440, 1390, 1310, 1270, 1125, 1075, 1030, 1010, 800, 750, 700 cm^{-1}.

Competitive reaction of equimolar amounts of 1,1-bis(phenylseleno)cyclohexane and 1,1-bis(phenylseleno)heptane towards n-butyllithium in ether.

To a mixture of 1.00 mmol (0.406 g) of 1,1-bis(phenylseleno)cyclohexane and 1.00 mmol (0.412 g) of 1,1-bis(phenylseleno)heptane in 8 ml of anhydrous ether, was added, at -45°C, 1.00 mmol (0.63 ml) of n-butyllithium The mixture was stirred for 0.75 h at -45°C and 1mmol (0.1g) of hexanal in 1 ml of anhydrous ether was introduced.The mixture was allowed to react for 0.2 h at -45°C then hydrolysed and extracted three times with ether. The combined organic layer was washed with water, dried over anhydrous $MgSO_4$, filtered and the solvents were removed under vacuum. The residue was fractionated by preparative layer chromatography (SiO_2, pentane-ether (8:2, v/v)) to give 0.295 g of 7-phenylseleno-tridecane-6-ol (83% yield) whose analytical data are given above. The most eluted fraction was again purified by preparative layer chromatography (SiO_2, pentane) to afford 0.39 g of 1,1-bis(phenylseleno)cyclohexane (96 % recovered).

Competition between equimolar amounts of 1,1-bis(methylselenoheptane and 2,2-bis(methylseleno) octane towards n-butyllithium in THF. Thermodynamic control.

To a solution of 1.00 mmol (0.288 g) of 1,1-bis(methylseleno)heptane and 1.00 mmol (0.302 g) of 2,2-bis(methylseleno)octane in 3 ml of anhydrous THF, was added, at -78°C, 1.00 mmol (0.63 ml) of n-butyllithium. The mixture was allowed to react for 0.1 h at -78°C and for 1 h at -40°C. Then, 1.00 mmol (0.106 g) of benzaldehyde in 1 ml of THF was added. After 0.2 h at -40°C, water was added and the mixture extracted three times with ether. The combined organic layer was washed with water, dried over anhydrous $MgSO_4$, filtered and the solvents were removed under vacuum. Fractionation of the residue by preparative layer chromatography(SiO_2 eluent pentane-ether(8:2 , v/v)) gave 0.035 g of 1-phenyl -2-methyl- 2-methylseleno-octane-1-ol (8 % yield) and 0.235 g of 1-phenyl- 2-methylseleno- octane-1-ol (78 % yield).1-phenyl-2-methyl-2-methylseleno-octane-1-ol: Tlc Rf 0.65 eluent pentane-ether(8:2 ,v/v). ^{1}H NMR (CCl_4) for a mixture of diastereoisomers. δ 0.7-1.6 (m, 13H,Me and CH_2), 1.75 and 1.8 (2s, 3H,MeSe), 2.4-3.0(2m, 2H, OH and CHSe), 4.2-4.4 and 4.6-4.7 (2m, 1H, C$\underline{H}$OH), 7-7.3 (m, 5H, arom). IR (neat) 3450 3060, 3020, 2960, 2930, 2875, 2860, 1500, 1470, 1450, 1380, 1190, 1060, 1030, 910, 765, 700 cm^{-1} Anal. Calcd. for $C_{15}H_{24}OSe$: C 60.19, H 8.08. Found C 60.21, H 8.23.

1-phenyl-2-methylseleno-octane-1-ol: Tlc Rf 0.6 eluent pentane:ether (8·2, v/v). ^{1}H NMR for a mixture of diastereoisomers (CCl_4) δ 0.6-1.8 (m with s at 1 1 and 2 s at 1.65 and 1.7 (MeSe), 19H, Me, CH_2 and MeSe), 2.8-3.2 (m, 1H, OH), 4.35 and 4.4 (2s, 1H, C$\underline{H}$OH), 7-7.3 (m, 5H, arom.). IR (neat) 3450 , 3080, 3060, 3030, 2960, 2930, 2880, 1495, 1470, 1455, 1425, 1380, 1330, 1245, 1190, 1125, 1085, 1060, 1030, 920, 900, 760, 710 cm^{-1}. Anal. Calcd. for $C_{16}H_{26}OSe$: C 61.33, H 8.36. Found C 61.89, H 8.09

Synthesis of 1,1,6,6-tetrakis(phenylseleno)heptane

25 mmol (2.4 g) of 1-methyl -cyclohexene were dissolved in 50 ml of CCl_4 and ozone was bubbled in the solution at 0°C for 4h. Then 10 ml of dimethyl disulfide were added and the mixture was stirred overnight at 20°C. Ether was then added and the resulting solution was washed with a saturated aqueous solution of sodium bicarbonate, water and dried over anhydrous $MgSO_4$, filtered and concentrated under vacuum to give 2.62 g of crude dicarbonyl compound which was used without further purification.The crude dicarbonyl compound (2.6g) was dissolved in 60 ml of dichloromethane and 80 mmol (12.7 g) of benzeneselenol was added. This solution was slowly added to a cooled (-25°C) solution of 14 mmol (2.7 g) of titanium tetrachloride in 50 ml of dichloromethane. The mixture was stirred for 2h at -28°C and then for 2 h at 20°C, then diluted with ether and washed three times with an 10 % aqueous solution of hydrochloric acid then with an saturated aqueous solution of sodium bicarbonate and finally with water. The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvents were removed under vacuum. Fractionation of the crude mixture by column chromatography gave 4.7 g of 1,1,6,6-tetrakis(phenylseleno)heptane (26 % overall yield from 1-methyl cyclohexene). Tlc Rf. 0.2 eluent pentane:ether,(95:5 , v/v). ^{1}H NMR(CCl_4) δ 1.1-2 (m, 11H, Me and CH_2), 4 2-4.44 (t, 1H, CH), 7-7.65 (2m, 20H, arom.). IR (neat) 3080, 3060, 2950, 2940, 2870, 1585, 1480, 1445 cm^{-1}. Anal. Calcd. for $C_{31}H_{32}Se_4$: C 51.68, H 4.48 Found C 50.62, H 4.20.

Reaction of 1,1,6,6-tetrakis(phenylseleno)heptane with organolithiums

To 1.00 mmol (0.712 g) of the 1,1,6,6-tetrakis(phenylseleno)heptane dissolved in 8 ml of anhydrous ether, was added, at -45°C, 1.00 mmol (0.63 ml) of n-butyllithium . After 0.75 h stirring at -45°C, 1.00 mmol (0.1 g) of hexanal in 1ml of anhydrous ether was added. The mixture was allowed to react for 0.25 h at -45°C, cooled at -78°C and 1mmol (1 ml) of s butyllithium was introduced. After 0.5 h stirring at -78°C, 1.00 mmol (0.10 g) of benzaldehyde in 1 ml of anhydrous ether was added. The mixture was then stirred for 0.3 h at -78°C, hydrolysed and extracted three times with ether. The combined organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under vacuum. The residue was fractionated by preparative layer chromatography (SiO_2 pentane:ether (1:2 ,v/v) to give 0.4 g of the bis β-hydroxyalkyl selenide (yield 66 %). Tlc Rf 0.35-0.45 (several spots) eluent pentane-ether(1:2 v/v). ^1H NMR (CCl_4) d 0.7-1.8 (m, 22H, Me and CH_2), 2-2.3 (m, 2H, OH), 2.8-3.6 (2m, 2H, HCSe and HC(OH)pent), 4.2 and 4.3 (2s, 1H, HC(OH)Ph), mixture of stereoisomers). 7-7.6 (2m, 15H, arom.). IR (neat), 3450 , 3060, 2980, 2930, 2860,1580, 1500, 1480, 1460, 1440, 1380, 1330, 1305, 1240, 1190, 1030, 920, 750, 710, 700 cm^{-1}. Anal. Calcd. for $C_{32}H_{42}O_2Se_2$: C 62.33, H 6.87. Found C 61.85, H 6.46.

In a second experiment and following the procedure given above, both organometallics were quenched with 1.00 mmol (0 1 g) of hexanal to afford after treatment and purification 0.46 g the bis β-hydroxyalkyl selenide (yield 76 %). Tlc Rf. 0.4-0.55 (several spots) eluent pentane:ether(1:1,v/v). ^1H NMR (CCl_4) δ 0 7-2.2 (m, 35H,Me, CH_2 and OH) 3-3.6 (2m, 3H, HCOH and HCSe), 7.1-7.6 (2m, 10H, arom). IR (neat) 3450 , 3080, 3060, 2960, 2940, 2880, 2860, 1580, 1480, 1470, 1460, 1440, 1380, 1310, 1265, 1120, 1070, 1030, 1005, 750, 700 cm^{-1}.

Typical procedure for the syntheses of diolefins from bis β-hydroxyalkyl selenides.

To a suspension of 0.26 mmol. (0.15g) of diphosphorus tetraiodide in 2 ml. of anhydrous dichloromethane, was added at 20°C 0.26 mmol. of the bis β-hydroxyalkyl selenide in 3ml. of anhydrous dichloromethane. After 0.25h. at 20°C, ether (50ml.) was added followed by a saturated aqueous solution of sodium bicarbonate (10ml.). The organic layer was separated,washed with water and dried over anhydrous $MgSO_4$. The crude mixture was fractionated by preparative layer chromatography (SiO_2, pentane) to afford the diolefin as the most eluted fraction. For instance, starting from 0.26mmol. (0.16g) of the last bis β-hydroxyalkyl selenide described above, 7-methyl-octadeca-6,12-diene is obtained (0.53g, 76% yield) Tlc Rf. 0.9 eluent pentane. ^1H NMR (CCl_4) δ 0.75-1.0(t, 6H, CH_2CH_3), 1.1-1.45(m, 16H, non allylic CH_2), 1.55(d, 3H, CH_3-C=C), 1.7-2.1(m,8H allylic CH_2), 4.9-5.4 (2m, 3H C=C-H). IR(neat) 3020, 2965, 2940, 2880, 2860, 1475, 1465, 1445, 1385, 970 cm^{-1}.

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