3. Compounding Selectivity in Reactions of Diastereoisomeric Radical Intermediates

An Experimental Demonstration That the Yield of a Product from a Diastereotopic-Group-Selective Reaction Can Significantly Exceed the Level of Group Selectivity

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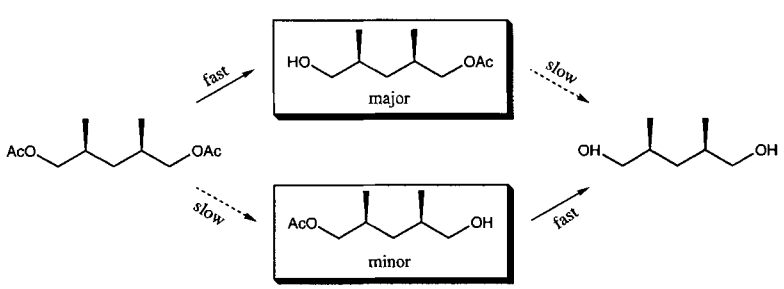
Reduction of a bis-radical precursor, 6-phenyl-1,1-bis[3-(phenylselanyl)propyl]-3a,4-dihydro-1*H*,3*H*-cyclopenta[*c*]furan-5-one (**6**), with 3 equiv. of Ph_3SnH provides mixtures of *cis,cis*- or *cis,trans*-angular triquinane products (3aα,5aβ,8β,8a*R**)- and (3aα,5aα,8β,8a*R**)-hexahydro-3a-propyl-8-phenyl-5*H*-dicyclopenta[*b*,*c*]furan-7(8*H*)-one (*cis,cis*-**12**/*cis,trans*-**12**), in yields that vary from 50%/50% to 91%/6% depending on the reaction concentration. A mechanistic model for this process is proposed that involves a non-selective phenylselenium-group abstraction step followed by successive kinetic resolutions of diastereoisomeric radical intermediates. This reaction shows how yields in group-selective reactions can be compounded to levels above that ostensibly permitted by the level of the group-selective step.

Introduction. – Enantiotopic- and diastereotopic-group-selective reactions are powerful tools in stereoselective synthesis. In such reactions, it is possible to reach high (sometimes exceedingly high) ratios of stereoisomeric products with only moderate-to-good levels of group selectivity [1–3]. This is done by selectively converting the minor stereoisomer of a given reaction to a non-isomeric product at a rate faster than that of the major stereoisomer. *Scheme 1* shows a typical example of this type of cooperative process, sometimes called the 'meso-trick' [4], as applied to an enzymatic hydrolysis of a diester.

Scheme 1

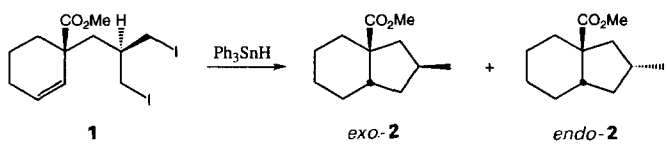


Very high ee values for the major enantiomer can be attained due to the selective destruction of the minor enantiomer.

The high levels of selectivity in such processes are obtained by selective destruction. An apparent corollary to this analysis then appears to logically follow: the yield of the major product in a group-selective process cannot exceed the level of selectivity in the group-selective step. For example, if a given group-selective step occurs in a 90:10 ratio, then the final ratio of products can far exceed 90:10, but the yield of the major product can never exceed 90%. Higher isomer ratios are achieved at the sacrifice of product yield.

We have recently suggested that this corollary is not universally true [5]. Specifically, transformations in which stereotopic functional groups react to form stereoisomeric reactive intermediates can theoretically provide not only ratios of isomeric products that are higher than the ratio of the group-selective step but also yields of the major product that are higher than the level of group selection. A conceptual framework for this process and a simplified kinetic model were supported by experiments with the diiodo ester **1** (*Scheme 2*) [5]. We demonstrated that the diastereotopic-group-selective reaction – I-atom abstraction from **1** by a triphenyltin radical – occurred without any selectivity, yet the ratio *exo*-**2**/*endo*-**2** varied from 1:1 to over 3:1, and the yield of the major product *exo*-**2** reached *ca.* 60%. Though the results with **1** clearly supported the proposed concepts and kinetic model, the demonstration that the yield of a product can be increased from 50 to 60% is of modest preparative significance. We, therefore, sought a more graphic demonstration of the proposed principles.

Scheme 2



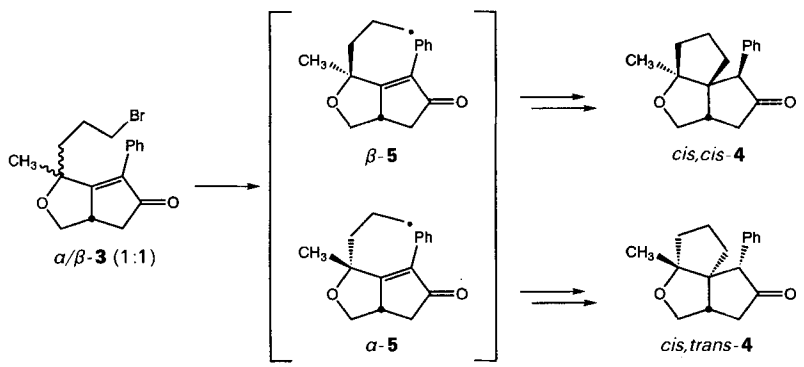
1 *exo*-**2** *endo*-**2**

The diastereotopic I-atoms in **1** are abstracted in a 50:50 ratio, yet the yield of *exo*-**2** can attain 60%.

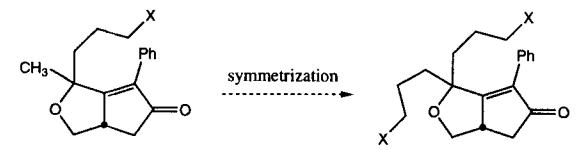
To attain dramatic increases in yield requires the generation of stereoisomeric reactive intermediates that progress to isomeric products at substantially different rates. In designing substrates meeting this requirement, we were drawn to a recent reaction of *Clive et al.* [6], which is summarized in *Scheme 3*. They observed that slow syringe pump addition of Bu_3SnH to a 1:1 mixture of diastereoisomers α-**3**/β-**3** provided tricycles **4** as a 1:1 mixture in 84% yield. In this reaction, each isomeric precursor provides its corresponding product: α-**3** gives radical α-**5**, which ultimately provides *cis,trans*-**4**, while β-**3** gives radical β-**5**, which ultimately provides *cis,cis*-**4**. Configurations of **4** were assigned by ^{1}H-decoupling and NOE studies, and an X-ray crystal-structure analysis established the structure of the unusual triquinane *cis,trans*-**4**.

Though it is not shown by the results, we felt confident that radical α-**5** must cyclize much more slowly than radical β-**5**. This is because α-**5** leads to a relatively strained [7] *cis,trans*-triquinane. 'Symmetrization' of **3** (*Scheme 4*) then provides a substrate **6** that has several attractive features: *1*) it should be readily prepared by straightforward modification of the route of *Clive et al.*, *2*) it is a precursor of diastereoisomeric radicals

Scheme 3



Scheme 4



3 two stereoisomeric precursors provide two stereoisomeric products

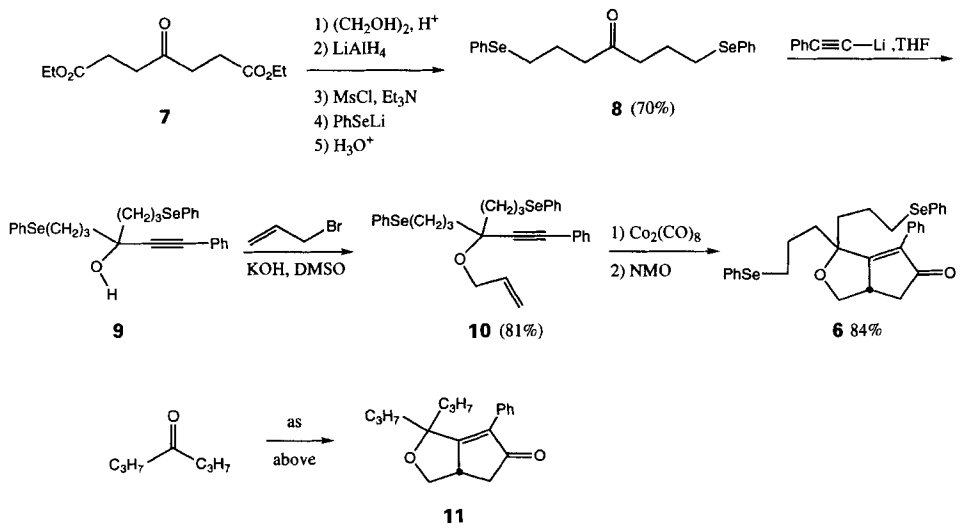
6 one precursor provides two stereoisomeric products

that are expected to cyclize at very different rates, and *3*) it provides products whose configurations can be assigned by direct analogy to the work of *Clive et al.*

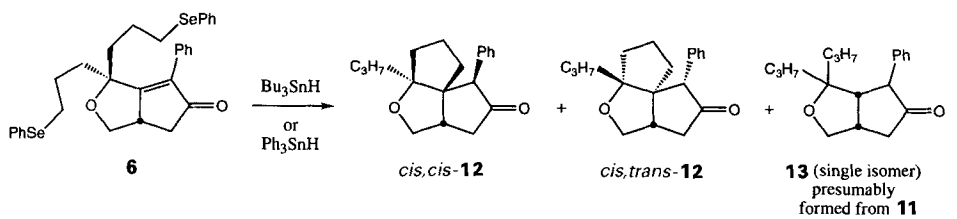
Results. – The preparation of **6** was straightforward, as summarized in *Scheme 5*. A series of five standard steps served to convert diethyl 4-oxopimelate (**7**) to bis[3-(phenylseleno)propyl] ketone (**8**) in 70% overall yield. Addition of lithium phenylacetylide provided the tertiary alcohol **9** (90%), which was then allylated with allyl bromide to give **10** (81%). *Pauson-Khand* cyclization of **10** according to *Clive et al.* [6] produced the requisite racemic enone **6** in 84% yield after purification by flash chromatography. The overall yield of this eight-step synthesis was 51%. Likewise, an authentic sample of the expected reduced, uncyclized product **11** was prepared from heptan-4-one by acetylide addition, allylation, and *Pauson-Khand* cyclization. As it turned out, this product was not detected in the radical experiments, but it was useful nonetheless (see below).

A preparative cyclization of **6** was conducted under standard conditions at 0.02M Bu_3SnH concentration (2.2 equiv.) in benzene. This reaction provided *cis,cis*-**12** and *cis,trans*-**12** in a ratio of 2.5:1 in 95% combined yield (*Scheme 6*). Since diastereoselective PhSe-group abstraction is inconceivable in this substrate, the preparative result already shows that the yield of the major product (68%) can exceed the level of group selection (50%). The two products were partially separable by flash chromatography, and individual pure samples of each were obtained. Configurations were assigned by comparison of

Scheme 5



Scheme 6



the spectra of these pure samples (^{1}H-NMR spectra are especially diagnostic) to the spectra reported by *Clive et al.* [6].

As stated above, the non-cyclized product **11** was not detected in any of the kinetic experiments. However, there was a third product formed in reactions conducted at high concentrations (see below), and this proved to be triply reduced product **13**. Hydrostannanation of enones is a known reaction [8] [9], and the supposition that enone **11** is an intermediate in the formation of **13** was supported by a control experiment; reduction of **11** with 1 equiv. of Bu_3SnH provides **13** as the only product. Ketone **13** must have a *cis*-ring fusion, but the relative configuration at the Ph-bearing C-atom was not assigned.

For the kinetic analysis, eight radical cyclizations of **6** were conducted with 3.0 equiv. of Ph_3SnH and 0.1 equiv. of AIBN at varying concentrations in benzene at 80°. Benzophenone dimethyl ketal was added as a standard, and products were quantified by integration of the ^{1}H-NMR spectra against the standard. Combined yields of the products *cis,cis*-**12**, *cis,trans*-**12**, and **13** were 100 ± 5%. In the data reported in the *Table*, the

combined yields are normalized to 100%. Good separation of the three products was observed by GC. This analytical method was superior, especially for assessing the small amounts of **13**, so it was used to determine the ratios reported in the *Table*.

Table. *Radical Cyclization of Compound* **6** *at Varying* Ph_3SnH *Concentrations*

Entry	[Ph_3SnH] [M]	*cis,cis*-**12** [%]	*cis,trans*-**12** [%]	**13** [%]
1	0.005	50.0	50.0	0
2	0.010	55.0	45.0	0
3	0.025	67.0	33.0	0
4	0.05	81.0	19.0	0
5	0.10	86.1	12.1	1.7
6	0.25	91.3	5.6	3.1
7	0.5	91.0	3.3	5.7
8	1.0	85.9	2.0	12.1

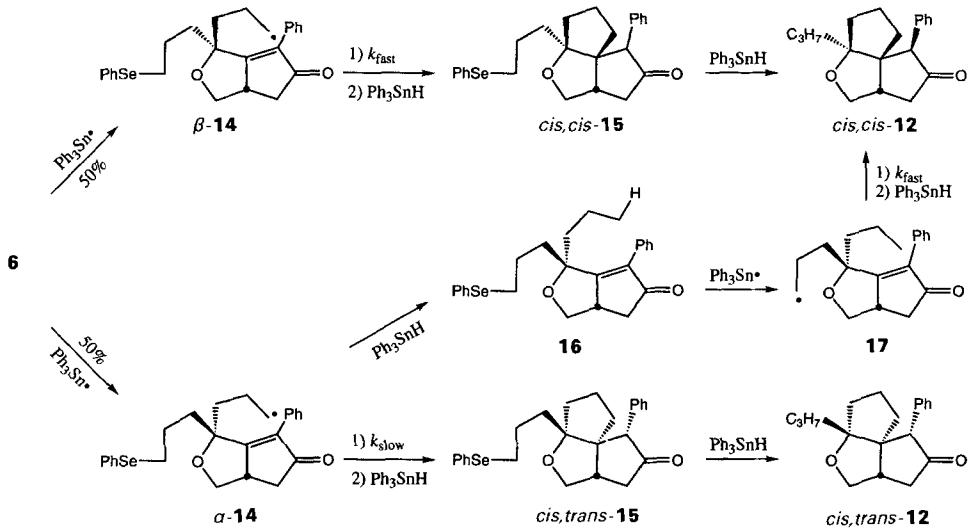
The results in the *Table* unambiguously confirm the premise for selecting this substrate. At the lowest Ph_3SnH concentration (0.005M), the direct reduction product **13** is not formed, and the ratio of *cis,cis*-**12** to *cis,trans*-**12** is 50:50. This experiment shows that there is no group selection in the PhSe-abstraction step. As the concentration of the reaction mixture (and hence, Ph_3SnH) increases, the yield of *cis,cis*-**12** increases, while that of *cis,trans*-**12** declines. At 0.1M, product **13** is formed in small but detectable quantities. The maximum yield of *cis,cis*-**12**, 91%, is reached in the range of 0.25–0.50M. In this range, the yield of *cis,trans*-**12** has decreased to 3–5%, while that of **13** has increased to 3–5%. The only difference between *Entries 1* and *7* is the volume of the benzene and, therefore, the concentration of the substrate and Ph_3SnH. *Exper. 7* uses 100 times less benzene, and provides a 41% higher yield of *cis,cis*-**12**.

As the reaction-mixture concentration is increased further, the yield of **13** increases at the expense of both isomers of **12**; however, the yield of *cis,trans*-**12** falls faster than that of *cis,cis*-**12**, so the stereoisomer ratio continues to climb. In *Entry 1*, the ratio *cis,cis*-**12**/*cis,trans*-**12** is 1:1, and the yield of *cis,cis*-**12** is 50%. By *Entry 8*, the ratio has climbed to 43:1, yet the yield of *cis,cis*-**12** (86%) is still significantly above 50%.

Discussion. – The data in the *Table* clearly show that the ratio *cis,cis*-**12**/*cis,trans*-**12** is altered by a simultaneous decrease in the yield of *cis,trans*-**12** along with an increase in the yield of *cis,cis*-**12**. This simultaneous change, exhibited to a smaller degree by the substrate in *Scheme 2*, is different from all the other group-selective processes that we are aware of; these other processes alter ratios by decreasing the yield of one of the isomeric products faster than that of the other.

Scheme 7 shows the mechanistic framework for the kinetic analysis of these results. All steps are assumed to be irreversible. The initial abstraction of the PhSe group from **6** by a $Ph_3Sn^{\cdot}$ radical is the only traditional diastereotopic-group-selective step, but this reaction occurs without selectivity to produce equal amounts of diastereoisomeric radicals β-**14** and α-**14**. At the lowest Ph_3SnH concentration, this group-selective step determines the product ratio. Both radicals β-**14** and α-**14** have sufficient time to cyclize, and a 1:1 ratio of products **15** results from the (stereoselective) hydrogen transfer from Ph_3SnH. Subsequent reductive deselenation of the remaining PhSe group gives the two isomers of **12** in equal amounts.

Scheme 7



However, as presaged by the results of *Clive et al.*, the cyclization of α-**14** to give *cis,trans*-**15** is considerably slower than cyclization of β-**14** to *cis,cis*-**15**. Thus, as the Ph_3SnH concentration is raised, the cyclization of β-**14** remains faster than bimolecular H transfer for some time, but the trapping of α-**14** to give **16** gradually becomes quite efficient. In effect, the product ratio is altered by setting the rate of a bimolecular reaction (H transfer) in between the rates of the two unimolecular cyclizations. After radical α-**14** abstracts H from Ph_3SnH to give **16**, abstraction of the second PhSe group provides a new radical **17**, which is again subject to partitioning between cyclization and reduction. However, radical **17** is very similar to β-**14**, so it can cyclize rapidly to *cis,cis*-**12** under the reaction conditions. Thus, raising the Ph_3SnH concentration opens a new pathway that increases the yield of *cis,cis*-**12** at the expense of the yield of *cis,trans*-**12**. Competitive reduction of radical **17** results in the formation of **11** (not shown), which is later reduced by a third equiv. of Ph_3SnH to give **13**. Reduction of β-**14** (not shown) also ultimately results mostly in formation of **11**, because the subsequent PhSe abstraction provides a radical that can only cyclize to the *cis,trans*-product.

This qualitative analysis can be augmented by a quantitative analysis based on the following assumptions: *1*) that all the steps are irreversible, *2*) that the initial partitioning to β/α-**14** occurs in a 50:50 ratio, and *3*) that radicals β-**14** and **17** (and also α-**14** and the epimer of **17**, not shown) cyclize with equal rate constants. The effective Ph_3SnH concentration was taken as the Ph_3SnH concentration at half-reaction time, without correction for consumption by initiation or by formation of the (minor) triply reduced product **13**. *Newcomb*'s recommended rate constant for Ph_3SnH was used [10], and the kinetic equations and data analysis are described in the preliminary communication [5]. We estimate that the rate constant $k_{fast} \approx 1 \times 10^8\ s^{-1}$ [5] and that the ratio $k_{fast}/k_{slow} \approx 180$. The lines in the *Figure* show the fit of the data points to the kinetic model for these values.

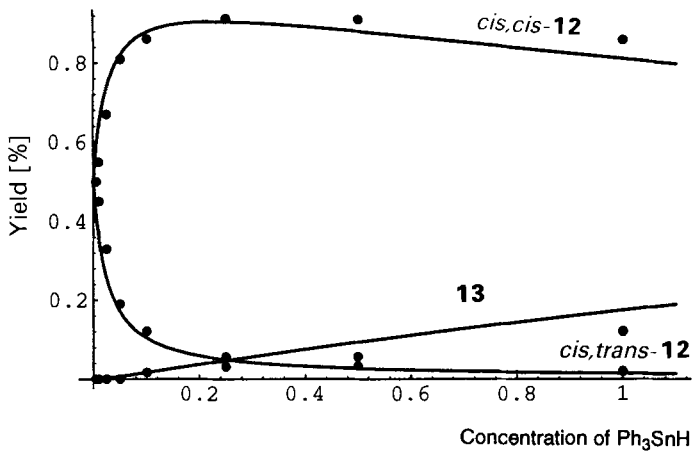


Figure. *Fit of data from the* Table *with theoretical linear for* $k_{fast} = 1 \times 10^8\ s^{-1}$ *and* k_{fast}/k_{slow}

These results verify the prediction that significant ratio and yield increases occur, when k_{fast}/k_{slow} ratios are $\geqslant 100$. The difference between this type of system and standard diastereotopic-group-selective reactions is that the diastereotopic functional groups are precursors of diastereoisomeric reactive intermediates. Differential partitioning of these intermediates by kinetic resolution then allows an added level of selectivity. That these diastereoisomeric intermediates are generated in a group-selective (as opposed to a face-selective [11]) reaction allows the yield of the major product to rise well above the level apparently permitted by the initial group-selective reaction. In effect, *partitioning compounds the yield.* Although many known rate constants of radical reactions facilitate design, the analysis that *Scheme 7* embodies is a general kinetic phenomenon that is not tied to radical intermediates. Nor is it unique to diastereoisomeric reactive intermediates. By using an enantioselective trap, it should be possible to resolve enantiomeric reactive intermediates. A publication detailing the conceptual and kinetic basis for all these types of reactions is planned.

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Experimental Part

Ethyl 3-{2-[-(Methoxycarbonyl)ethyl][1,3]dioxolan-2-yl}propionate. A mixture of diethyl 4-oxoheptanedioate (6.4 ml, 30 mmol; **7**), triethyl orthoformate (15 ml, 90 mmol), ethylene glycol (12 ml, 0.27 mol), and TsOH (0.57 g, 3 mmol) was heated at 55° for 10 h. The mixture was diluted with Et_2O, washed with H_2O, sat. $NaHCO_3$, H_2O, and brine. The ethereal soln. was dried ($MgSO_4$) and evaporated. The crude product was purified by flash chromatography (FC) (AcOEt/hexane 1:4) to give the acetal as a clear oil (7.1 g, 86%). IR: 2980, 2950, 1734, 1701, 1684, 1653, 1473, 1466, 1458, 1437, 1369, 1182, 1037. ^{1}H-NMR ($CDCl_3$): 4.03 (*q*, *J* = 7.2, 4 H); 3.85 (*s*, 4 H); 2.27 (*t*, *J* = 7.6, 4 H); 1.88 (*t*, *J* = 7, 4 H); 1.16 (*t*, *J* = 7.2, 6 H). ^{13}C-NMR: 173.3 (2 C); 109.8; 65.0 (2 C); 60.2 (2 C); 32.1 (2 C); 28.8 (2 C); 14.1 (2 C). LR-MS: 55, 99, 111, 132, 155, 173, 183, 201, 229. HR-MS: calc. for $C_{11}H_{17}O_5$ ($[M - C_2H_5O]^+$): 229.1076; found: 229.1075.

3-[2-(3-Hydroxypropyl)[1,3]dioxolan-2-yl]propan-1-ol. To a soln. of the above acetal (1.02 g, 7.4 mmol) in Et_2O (40 ml) at 0° was added $LiAlH_4$ (0.28 g, 7.4 mmol) in portions. The mixture was stirred for 2 h, and H_2O (0.28 ml), 15% NaOH (0.84 ml), and H_2O (0.28 ml) were added sequentially. The resulting yellow solid was filtered, and the filtrate was evaporated. The crude product was purified by FC (AcOEt) to give the diol as a glassy oil (0.637 g, 90%). IR: 3385, 2949, 2880, 1651, 1469, 1462, 1454, 1415, 1319, 1215, 1145, 1059. ^{1}H-NMR ($CDCl_3$): 3.92 (*s*, 4 H); 3.57 (*t*, *J* = 5.8, 4 H); 2.98 (br. *s*, 2 H); 1.72–1.65 (*m*, 4 H); 1.65–1.52 (*m*, 4 H). ^{13}C-NMR: 111.6; 64.9 (2 C); 62.7; 33.4 (2 C); 26.9 (2 C). LR-MS: 55, 69, 87, 97, 113, 131. HR-MS: calc. for $C_6H_{11}O_3$: ($[M - C_2H_3O_2]^+$): 131.0708; found: 131.0706.

3-{2-[3-(Methanesulfonyloxy)propyl][1,3]dioxolan-2-yl} Methanesulfonate. A soln. of the above diol (0.95 g, 5 mmol), MsCl (1.55 ml, 20 mmol), and Et_3N (3.6 ml, 26 mmol) in CH_2Cl_2 (50 ml) was stirred at 0° for 1 h. The mixture was diluted with Et_2O, washed with H_2O, sat. NH_4Cl, $NaHCO_3$, and brine. The solvents were evaporated and the residue purified by FC (AcOEt) to give the dimesylate as a glassy oil (1.38 g, 100%). ^{1}H-NMR ($CDCl_3$): 4.20 (*t*, *J* = 6.3, 4 H); 3.90 (*s*, 4 H); 2.97 (*s*, 6 H); 1.85–1.72 (*m*, 4 H); 1.72–1.62 (*m*, 4 H). ^{13}C-NMR: 110.4; 70.1 (2 C); 65.0 (2 C); 37.3 (2 C); 32.8 (2 C); 23.6 (2 C).

2,2-Bis[3-(phenylselanyl)propyl][1,3]dioxolane. A soln. of benzeneselenol (3.34 ml, 31.5 mmol) in Et_2O (130 ml) was cooled to 0°. MeLi (1.4M, 24 ml) was added to the above soln. dropwise. After 15 min, the dimesylate in Et_2O (5 ml) was added quickly to the soln. The mixture was maintained at 0° for 1 h and then quenched with sat. NH_4Cl. The ethereal soln. was washed with sat. $NaHCO_3$, H_2O, and brine, dried ($MgSO_4$) and evaporated. After FC (AcOEt/hexane 1:4), the diphenyl selenide (5.54 g, 92%) was obtained as a clear oil. IR: 2941, 2850, 1713, 1578, 1477, 1437, 1369, 1298, 1184, 1072, 1043, 1022, 999, 736, 690. ^{1}H-NMR ($CDCl_3$): 7.50–7.47 (*m*, 4 H); 7.26–7.23 (*m*, 4 H); 3.87 (*s*, 4 H); 2.89 (*t*, *J* = 7.1, 4 H); 1.82–1.62 (*m*, 8 H). ^{13}C-NMR: 132.6 (4 C); 130.4 (2 C); 129.0 (4 C); 126.8 (2 C); 111.1; 64.9 (2 C); 37.1 (2 C); 28.1 (2 C); 24.5 (2 C). LR-MS: 69, 91, 111, 131, 157, 185, 271, 313, 426, 470. HR-MS: calc. for $C_{21}H_{26}O_2Se_2$: 470.0263; found: 470.0277.

1,7-Bis(phenylselanyl)heptan-4-one (**8**). A soln. of the above acetal (2.29 g, 5 mmol) and TsOH (0.190 g, 1 mmol) in acetone (50 ml) was stirred for 12 h at 25°. The acetone was then evaporated and the residue dissolved in Et_2O and washed with H_2O, sat. $NaHCO_3$, H_2O, and brine. Evaporation of Et_2O gave **8** as a clear glassy oil (2.07 g, 100%). This was used in the synthesis of **9** without further purification. IR: 2936, 1713, 1578, 1477, 1437, 1408, 1371, 1300, 1186, 1072, 1022, 999, 736. ^{1}H-NMR ($CDCl_3$): 7.50–7.47 (*m*, 4 H); 7.27–7.22 (*m*, 6 H); 2.89 (*t*, *J* = 7.1, 4 H); 2.49 (*t*, *J* = 7.1, 4 H); 1.98–1.91 (*m*, 4 H). ^{13}C-NMR: 209.1; 132.5 (4 C); 130.0 (2 C); 129.1 (4 C); 126.8 (2 C); 42.0 (2 C); 27.2 (2 C); 23.9 (2 C). LR-MS: 69, 78, 91, 111, 157, 185, 269, 314, 426. HR-MS: calc. for $C_{12}H_{22}OSe_2$: 426.0001; found: 425.9997.

1-Phenyl-6-(phenylselanyl)-3-[3-(phenylselanyl)propyl]hex-1-yn-3-ol (**9**). BuLi (1.6M, 2.3 ml, 3.69 mmol) was added to a stirred and cooled (−78°) soln. of phenylacetylene (0.43 ml, 3.93 mmol) in THF (20 ml). After 10 min, a soln. of **8** (1.02 g, 2.46 mmol) in THF (2 ml) was added over 10 min. Stirring at −78° was continued for 1 h, and the mixture was then quenched with H_2O and extracted with Et_2O. The combined org. extracts were dried ($MgSO_4$) and evaporated to afford crude **9**, which was purified by FC (AcOEt/hexane 1:4): 1.19 g (94%). IR: 3450, 3070, 2938, 2860, 1651, 1574, 1504, 1487, 1477, 1462, 1435, 1415, 1288, 1068, 1022. ^{1}H-NMR ($CDCl_3$): 7.52–7.48 (*m*, 4 H); 7.30–7.20 (*m*, 11 H); 3.01–2.92 (*m*, 4 H); 2.07–1.92 (*m*, 4 H); 1.90–1.79 (*m*, 5 H). ^{13}C-NMR: 132.7, 131.7, 130.2, 129.1, 128.4, 128.3, 126.8, 122.4 (total 18 C); 91.2; 85.1; 71.1; 42.1 (2 C); 27.9 (2 C); 25.1 (2 C). LR-MS: 77, 91, 111, 157, 171, 185, 195, 213, 227, 269, 371, 426, 511, 528.

1-Phenyl-6-(phenylselanyl)-3-[3-(phenylselanyl)propyl]-3-[(prop-2-en-1-yl)oxy]hex-1-yne (**10**). 3-Bromopropene (3.18 ml, 36.8 mmol) and KOH (2.7 g, 67 mmol, freshly crushed) were added to a soln. of **9** (6.34 g, 12.28 mmol) in DMSO (100 ml). The mixture was stirred at 55° for 10 h and then cooled and diluted with Et_2O. The soln. was washed with sat. aq. $NaHCO_3$ and H_2O, dried ($MgSO_4$), and evaporated. FC of the residue (AcOEt/hexane 1:9) gave **10** as a clear oil (5.62 g, 81%). IR: 2939, 2866, 1578, 1489, 1477, 1437, 1280, 1051, 1022, 999, 920. ^{1}H-NMR ($CDCl_3$): 7.52–7.44 (*m*, 4 H); 7.37–7.20 (*m*, 11 H); 5.98–5.83 (*m*, 1 H); 5.28–5.10 (*m*, 2 H); 4.12–4.10 (*m*, 2 H); 3.02–2.90 (*m*, 4 H); 2.00–1.82 (*m*, 8 H). ^{13}C-NMR: 135.3; 132.6; 131.8; 129.1; 128.4; 128.3; 126.8; 122.6; 116.3; 89.4; 76.3; 65.3; 38.8; 28.1; 24.8. LR-MS: 57, 67, 77, 97, 117, 129, 143, 152, 171, 183, 213, 261, 283, 309, 369.

6-Phenyl-1,1-bis[3-(phenylselanyl)propyl]-3a,4-Dihydro-1H,3H-cyclopenta[c]furan-5-one (**6**). $Co_2(CO)_8$ (3.7 g, 10.82 mmol) was added in portions to a soln. of **10** (5.28 g, 9.94 mmol) in CH_2Cl_2 (200 ml). The resulting brown soln. was stirred for 2 h at 25°, then cooled to 0°, and 4-methylmorpholine *N*-oxide (NMO, 6.89 g, 58.6 mmol) was added. The mixture was stirred at 25° for 12 h and then filtered through a short silica-gel plug. The filtrate was evaporated and the residue was purified by FC (AcOEt/hexane 1:2) to give **6** as a glassy oil (4.98 g, 84%). IR: 2941, 2850, 1716, 1655, 1578, 1477, 1458, 1437, 1290, 1126, 1072, 1022, 910, 735, 694, 669. ^{1}H-NMR ($CDCl_3$): 7.52–7.06 (*m*, 15 H); 3.35–3.20 (*m*, 2 H); 3.10–2.89 (*m*, 2 H); 2.74 (*dd*, *J* = 12.2, 5.2, 1 H); 2.60–2.40 (*m*, 2 H); 2.20 (*dd*, *J* = 17.9, 2.9, 1 H); 2.10–1.88 (*m*, 3 H); 1.82–1.70 (*m*, 1 H); 1.67–1.50 (*m*, 2 H); 1.45–1.30 (*m*, 2 H).

^{13}C-NMR: 207.0, 181.5, 137.3, 132.8, 132.7, 130.6, 130.1, 129.1, 128.9, 128.8, 128.6, 128.5, 126.9 (total 18 C); 83.8; 71.2; 45.0; 41.3; 39.9; 37.0; 28.1; 27.6; 25.3; 24.9. LR-MS: 69, 91, 115, 129, 141, 157, 185, 239, 263, 281, 421, 439, 578, 596. HR-MS: calc. for $C_{31}H_{32}O_2Se_2$: 596.0739; found: 596.0706.

*(3aα,5aβ,8β,8a*R*)- and (3aα,5aα,8β,8a*R*)-Hexahydro-3a-propyl-8-phenyl-5*H*-dicyclopenta[*b,c*]furan-7(8*H*)-one* (*cis,cis*-**12** and *cis,trans*-**12**, resp.). A mixture of **6** (55 mg, 0.0925 mmol), AIBN (3.6 mg, 0.022 mmol), and Bu_3SnH (0.059 ml, 0.222 mmol) in benzene (11 ml, 0.02M of Bu_3SnH) was refluxed (80°) for 10 h. Workup of the reaction mixture by a standard procedure [12] followed by FC (AcOEt/hexane 1:4) of the crude products gave *cis,cis*-**12** *cis,trans*-**12** as a 2.5:1 mixture (GC; 25 mg total, 95%). Partial separation was performed by using AcOEt/hexane 1:9 for FC.

cis,trans-**12** (less polar). IR: 3568, 2959, 2874, 1740, 1686, 1653, 1560, 1496, 1456, 1406, 1147, 1088, 1035, 700. ^{1}H-NMR ($CDCl_3$): 7.37–7.25 (*m*, 3 H); 7.15–7.12 (*m*, 2 H); 4.05 (*dd*, *J* = 7.2, 7.2, 1 H); 3.64 (*dd*, *J* = 11.2, 7.7, 1 H); 3.60 (*s*, 1 H); 2.79–2.65 (*m*, 1 H); 2.52 (*dd*, *J* = 17.3, 6.9, 1 H); 2.31 (*dd*, *J* = 17.2, 14.3, 1 H); 2.02–1.95 (*m*, 1 H); 1.75–1.40 (*m*, 7 H); 1.20–1.08 (*m*, 2 H); 1.03 (*t*, *J* = 6.6, 3 H). ^{13}C-NMR: 216.7; 135.5; 130.5 (2 C); 128.5 (2 C); 127.3; 91.3; 67.2; 65.0; 62.6; 47.1; 38.4; 38.1; 38.0; 26.4; 22.5; 18.0; 15.1. LR-MS: 79, 91, 105, 119, 148, 155, 167, 195, 213, 214, 254, 266, 284. HR-MS: calc. for $C_{19}H_{24}O_2$: 284.1776; found: 284.1775.

cis,cis-**12**. IR: 2957, 2872, 1741, 1707, 1655, 1560, 1508, 1496, 1475, 1458, 1124, 1059. ^{1}H-NMR ($CDCl_3$): 7.35–7.23 (*m*, 3 H); 7.04–7.01 (*m*, 2 H); 4.08 (*dd*, *J* = 9.1, 6.4, 1 H); 3.77 (*s*, 1 H); 3.51 (*dd*, *J* = 9.1, 7.4, 1 H); 2.73–2.62 (*m*, 2 H); 2.42–2.30 (*m*, 1 H); 1.95–1.88 (*m*, 1 H); 1.70–1.50 (*m*, 5 H); 1.50–1.22 (*m*, 4 H); 0.98 (*t*, *J* = 7.2, 3 H). ^{13}C-NMR: 218.4; 137.2; 130.7; 130.4; 129.0; 128.5; 127.1; 95.4; 71.1; 63.9; 60.0; 47.4; 40.2 (2 C); 38.5; 36.2; 22.8; 8.4; 15.0. LR-MS: 71, 91, 115, 151, 171, 193, 214, 241, 269, 284. HR-MS: calc. for $C_{19}H_{24}O_2$: 284.1776; found: 284.1784.

1-Phenyl-3-propylhex-1-yn-3-ol. The procedure for the synthesis of **9** was followed, using BuLi (1.6M, 1.56 ml, 2.5 mmol), phenylacetylene (0.27 ml, 2.5 mmol), and heptan-4-one (0.28 ml, 2 mmol) in THF (15 ml). FC (AcOEt/hexane 1:4) of the crude products gave the alcohol as a clear oil (0.277 g, 64%). IR: 3389, 2959, 2872, 1489, 1466, 1456, 1379, 1284, 1140, 1070, 999, 912, 754, 690. ^{1}H-NMR ($CDCl_3$): 7.42–7.40 (*m*, 2 H); 7.31–7.28 (*m*, 3 H); 2.10 (*s*, 1 H); 1.73–1.56 (*m*, 8 H); 0.99 (*t*, *J* = 7.1, 6 H). ^{13}C-NMR: 131.7 (2 C); 128.2 (2 C); 122.9; 92.2; 84.3; 71.8; 44.4; 17.7 (2 C); 14.4 (2 C). LR-MS: 66, 71, 91, 102, 115, 129, 134, 155, 173, 198, 216. HR-MS: calc. for $C_{15}H_{20}O$: 216.1514; found: 216.1512.

[3-(Prop-2-en-1-yloxy)-3-propylhex-1-ynyl]benzene. The procedure for the synthesis of **10** was followed, using allyl bromide (0.285 ml, 3.3 mmol), KOH (0.22 g, 5.5 mmol), and the above alcohol (0.239, 1.1 mmol) in DMSO (10 ml). FC (AcOEt/hexane 1:4) of the crude products gave the allyl ether as a clear oil (0.22 g, 78%). IR: 2959, 2872, 1651, 1556, 1504, 1489, 1454, 1311, 1130, 1070, 993, 916, 756, 690. ^{1}H-NMR ($CDCl_3$): 7.45–7.42 (*m*, 2 H); 7.32–7.30 (*m*, 3 H); 6.08–5.93 (*m*, 1 H); 5.34 (*dd*, *J* = 17.2, 1.7, 1 H); 5.15 (*dd*, *J* = 10.3, 1.6, 1 H); 4.16 (*d*, *J* = 5.4, 2 H); 1.75 (*t*, *J* = 8.3, 4 H); 1.63–1.45 (*m*, 4 H); 0.97 (*t*, *J* = 7.3, 6 H). ^{13}C-NMR: 135.7; 131.1 (2 C); 128.3 (2 C); 128.2 (1 C); 123.1; 116.1 (2 C); 90.5; 86.1; 65.2; 41.0 (2 C); 17.4 (2 C); 14.4 (2 C). LR-MS: 71, 77, 91, 117, 132, 142, 155, 213: HR-MS: calc. for $C_{15}H_{17}O$ ($[M - C_3H_7]^+$): 213.1279; found: 213.1278.

*6-Phenyl-1,1-dipropyl-3a,4dihydro-1*H*,3*H*-cyclopenta[*c*]furan-5-one* (**11**). The procedure for the synthesis of **6** was followed, using $Co_2(CO_8)$ (307 mg, 0.9 mmol), the above enyne (0.14 g, 0.6 mmol) and NMO (0.422 g, 3.6 mmol) in CH_2Cl_2 (12 ml). FC (AcOEt/hexane 1:4) of the crude products gave **11** as a clear oil (80 mg, 47%). IR: 2957, 2870, 1713, 1682, 1660, 1651, 1645, 1495, 1464, 1454, 1149, 1026, 999, 760, 698. ^{1}H-NMR ($CDCl_3$): 7.40–7.30 (*m*, 2 H); 2.76 (*dd*, *J* = 7.6, 6.0, 1 H); 2.26 (*dd*, *J* = 7.6, 3.2, 1 H); 1.90–1.57 (*m*, 3 H); 1.52–1.38 (*m*, 2 H); 1.38–1.18 (*m*, 3 H); 1.00 (*t*, *J* = 7.2, 3 H); 0.58 (*t*, *J* = 7.0, 3 H). ^{13}C-NMR: 207.4; 183.0; 137.0; 131.1; 128.9 (2 C); 128.4 (3 C); 84.7; 71.3; 45.3; 43.9; 39.9; 18.0; 17.3; 14.6; 14.2. LR-MS: 64, 71, 132, 241. HR-MS: calc. for $C_{16}H_{17}O$ ($[M - C_3H_7]^+$): 241.1228; found: 241.1226.

*1a,3a,4,6-Tetrahydro-6-phenyl-1,1-dipropylcyclopenta[*c*]furan-5(3*H*)-one* (**13**). A soln. of **11** (8 mg) excess Bu_3SnH, and AIBN in 1 ml of benzene was heated at 80° for 12 h. After DBU workup, **13** (7.8 mg, 97%) was obtained. IR: 2960, 2880, 2361, 2339, 1734, 1716, 1699, 1684, 1653, 1558, 1539, 1522, 1506, 1471, 1456. ^{1}H-NMR ($CDCl_3$): 7.38–7.22 (*m*, 3 H); 7.13–7.10 (*m*, 2 H); 4.21 (*t*, *J* = 7.5, 1 H); 3.60 (*dd*, *J* = 4.7, 4.5, 1 H); 3.45 (*d*, *J* = 17.0, 1 H); 2.68 (*dd*, *J* = 21, 7.5, 1 H); 2.50–2.48 (*m*, 1 H); 1.65–1.05 (*m*, 8 H); 0.89 (*t*, *J* = 5.0, 3 H); 0.57 (*t*, *J* = 4.5, 3 H). ^{13}C-NMR: 217.5; 138.8; 128.9 (2 C); 127.1; 88.0; 71.9; 56.4; 55.2; 42.4; 38.0; 37.8; 36.1; 17.9; 17.0; 16.4; 14.7; 14.2. LR-MS: 43, 71, 129, 143, 171, 207, 243. HR-MS: calc. for $C_{16}H_{19}O$ ($[M - C_3H_7]^+$): 243.1385; found: 243.1385.

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