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SYNTHETIC APPLICATIONS OF 2-PHENYLSELENENYL-ENONES—III

AN OVERVIEW

DENNIS LIOTTA,* MANOHAR SAINDANE, CHRISTOPHER BARNUM and GEORGE ZIMA
Department of Chemistry, Emory University, Atlanta, GA 30322, U.S.A.

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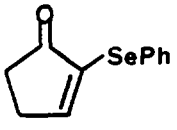
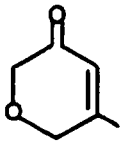
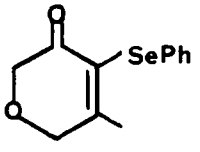
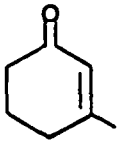
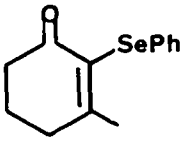
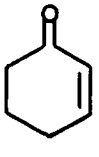
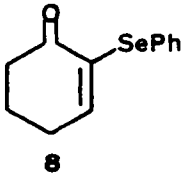
Abstract—2-Phenylselenenylenones are versatile species which can be selectively converted into a number of different ketones and enones in high overall yields.

The generation of specific enolates via Michael addition of nucleophiles to unsaturated ketones has proven to be an extremely useful process in organic synthesis. In this regard we felt that the incorporation of a phenylselenenyl group in the 2-position of an enone would: (a) enhance the ability of the enone to undergo Michael addition, (b) provide, after Michael addition, a stabilized enolate for the subsequent introduction of a substituent in the 2-position and (c) allow for the eventual introduction of a new double bond via the well-known selenoxide β-elimination reaction.[1] While a few 2-phenylselenenylenones had been previously reported in the literature, prior to our work in the area,[3a] no general method existed for their preparation.[3b–d,4]

By chance, we found that 2-phenylselenenylenones could be prepared easily and in high yield by simply exposing the enone in question to a 1:1 complex of phenylselenenyl chloride and pyridine.[3a] These reactions proved to be somewhat sensitive to the degree of steric hindrance at or near the β-carbon atom of the enone. Thus, while substrates such as **1** react smoothly with the complex to produce **5**, more-hindered enones such as **2** react quite sluggishly.[5] In most cases, however, this problem can be circumvented by simply running the reaction at temperatures ranging between $-20°$ and $0°$ for prolonged periods of time. Under these conditions most enones can be converted to their corresponding 2-phenylselenenyl derivatives in good to excellent yields. Some representative examples are given in Table 1.

2-Phenylselenenylenones have proven to be excellent

Table 1

Substrate	Product	Yield (%)	Time/Temp (°)
 **1**	 **5**	88	30 min/25
 **2**	 **6**	88	3 hr/25
 **3**	 **7**	45	3 days/25
 **4**	 **8**	71	2 hr/25

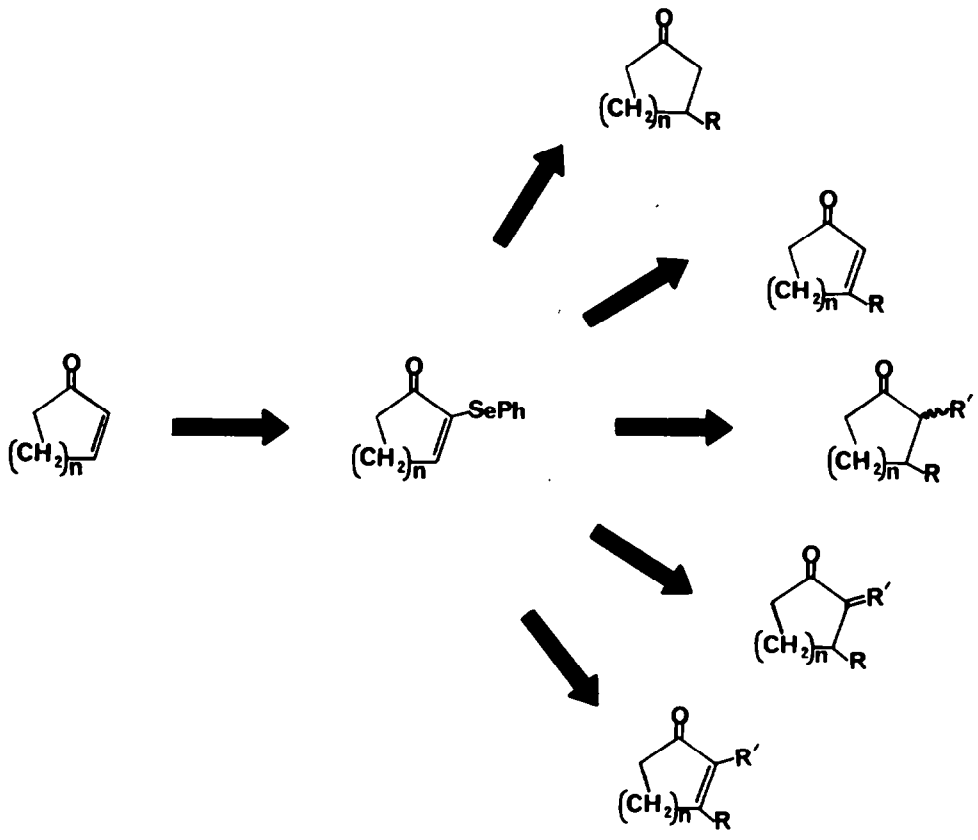
Michael acceptors. As a consequence, we have been able to develop simple procedures for converting these compounds into a variety of new ketones and enones in high overall yields.[6] A generalized illustration of the various transformations which can be accomplished using this methodology is given in Scheme 1.

Consistent with previous studies involving cuprate additions to simple enones,[7] good donor solvents (e.g. THF or DME) retard the rate of conjugate additions of lithium dialkyl cuprates to phenylselenenylenones. Best results are obtained when the cuprate addition is performed in ether at $-20°$. As the data in Table 2 indicates, protonation of enolates resulting from cuprate additions to phenylselenenylenones results in the predominant formation of the corresponding *cis*-2-phenylselenenyl-3-alkylketone,[8] presumably to minimize Se–O interactions.[9] However, as we soon discovered, *the oxidative elimination of either the* cis *or* trans *isomers of these 2-phenylselenenyl-3-alkylketones can lead to the corresponding 3-alkylcycloalkenone in excellent yield, if the elimination process is carried out in the presence of a base.* The specific set of conditions which we prefer involve initial oxidation with ozone, followed by subsequent elimination in refluxing methylene chloride containing diethylamine. Since it is well-established that selenoxide eliminations occur in a *syn*-fashion,[10] epimerization at the α-carbon of the intermediate β-ketoselenoxide is probably occurring under the reaction conditions prior to elimination.[6,11] This is significant since both epimers can be simultaneously converted to product without any additional synthetic manipulations (see Table 2).

A summary of our results on the 2,3-dialkylations of 2-phenylselenenylenones is given in Table 3. These reactions can be performed in either a "one-pot" procedure or in a stepwise fashion.[12] Since in all cases these dialkylation reactions led to stereorandom mixtures of *cis*- and *trans*-2,3-dialkyl-2-phenylselenenylketones, the overall synthetic utility of this procedure for *selectively* preparing endocyclic and exocyclic enones at first appeared to be limited.[13] On the contrary, however, we have been able to selectively convert mixtures of these materials to either the endocyclic or exocyclic enones, irrespective of the relative amounts of the two isomers originally present.[14]

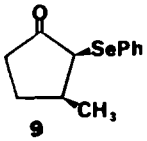
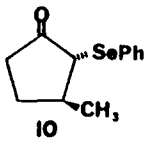
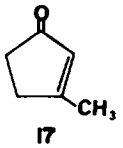
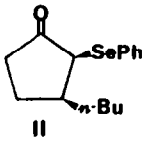
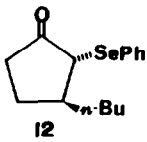
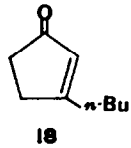
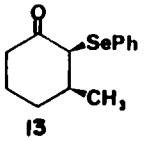
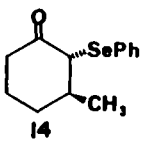
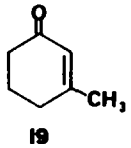
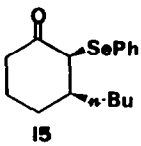
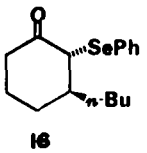
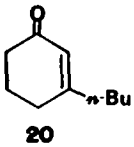
Exclusive formation of endocyclic enones is achieved in a two-step process. The first step simply involves a standard oxidative elimination of the mixture, which produces a mixture of both exocyclic and endocyclic enones. This mixture can then be completely isomerized to the endocyclic enone by exposure to acid (Tables 4 and 5).[15]

Our general approach to the production of exocyclic enones again involves a two step procedure. The first step involves the isomerization of an epimeric mixture entirely to the *trans*-isomer. We envisioned effecting the isomerization via an initial nucleophilic cleavage of the C—Se bond, followed by a re-selenation of the resulting enolate. Since in the selenation transition state, the



Scheme 1.

Table 2.

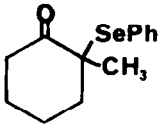
Substrate	Cuprate	Products	*Cis/trans* ratio[a]	Yield (%)	Oxidative elimination product	Yield (%)
5	$LiMe_2Cu$	 **9**  **10**	>99:1	95	 **17**	85
5	$Li(n\text{-}Bu)_2Cu$	 **11**  **12**	3:1	97	 **18**	97
8	$LiMe_2Cu$	 **13**  **14**	>99:1	96	 **19**	79
8	$Li(n\text{-}Bu)_2Cu$	 **15**  **16**	4:1	90	 **20**	85

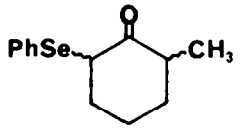
[a] Mixtures of these compounds (*cis* and *trans*) are readily separated by preparative TLC into their pure *cis* or pure *trans* isomers.

C—Se separation should be quite large, we reasoned that alkyl–alkyl repulsions would be most important in determining the stereochemistry of the product, thereby favoring the formation of the *trans* isomer (Scheme 2).

In practice, the nucleophilic cleavage of the C—Se bonds of these mixtures is readily accomplished by exposing a mixture of these compounds to lithium phenylselenide in THF at temperatures between −78° and 25°.[6,2b] The resulting enolate can then be directly selenated using either PhSeCl or CH_3I. The latter reagent presumably reacts preferentially with the potent nucleophile, $PhSe^-$, thereby shifting the equilibrium back to the left. The use of this method results in the formation of new mixtures of selenated ketones, in which the *trans*-dialkyl isomer is by far the major component. In fact, in virtually all of the cases studied, the epimerized mixtures contain only trace amounts of the *cis*-dialkyl isomer (Table 3). Once isomerized, these mixtures could then be oxidized and eliminated under standard conditions to give excellent overall yields of the exocyclic enone.

Another useful aspect of these 2,3-dialkyl-2-phenylselenenylketones involves their ability to efficiently undergo a base-induced 1,3-selenium shift, such as the one shown in the conversion of **27** to **49** (Table 6).[16] Mechanistically, this reaction involves a series of *intermolecular* phenylseleno and proton exchange processes whose driving force is the production of increasingly more stable enolate ions. Steric interactions between properly placed alkyl groups and the phenylselenenyl group actually accelerate the exchange process. In cases in which there is relatively little steric repulsion (e.g. **56** → **57**), the reaction fails if lithium diisopropylamide is used as the base.[17] In these cases we have found that sodium hydride is an effective substitute, presumably because of the higher propensity for rearrangement of sodium enolates vs lithium enolates.[18]

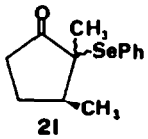
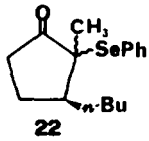
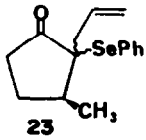
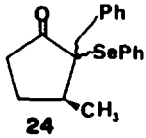
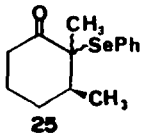
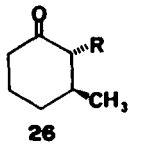
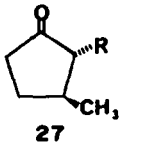

56


57

In general terms, this formal 1,3-selenium shift methodology further extends the versatility of these species to be regiospecifically functionalized in the α′-position.[12] For example, **51** is readily isomerized to **52**. Since the phenylseleno group stabilizes an adjacent negative charge, **52** can be regiospecifically alkylated at C-2, instead of the usually preferred position C-4.

Although obviously useful synthetically, the 1,3-selenium shift process described above also poses an intriguing mechanistic dilemma. α,α′-Rearrangements such as the conversion of **27** to **49** proceed smoothly in the presence of only 0.5 equiv of base. While the observation is completely consistent with an overall bimolecular process, one must question why rearrangement products were not also observed in

Table 3.

Substrate	Reagents	Products	*Cis/trans* ratio[a]	Yield (%)	Epimerized *cis/trans* ratio[a]	Yield (%)
5	(1) $LiMe_2Cu$ (2) MeI	 21	4:1	95	(1:16)	95
5	(1) $Li(n\text{-}Bu)_2Cu$ (2) MeI	 22	3:2	90	(1:99)	89
5	(1) $LiMe_2Cu$ (2) Allyl Br	 23	1:4	97	(1:99)	97
5	(1) $LiMe_2Cu$ (2) Benzyl Br	 24	1.5:5	90	(1:99)	73
8	(1) $LiMe_2Cu$ (2) MeI	 25	2.3:1	78	(1:4)	78
5	(1) $LiMe_2Cu$ (2) 1-Br-2-pentyne	 26	>99:1	90		
8	(1) $LiMe_2Cu$ (2) 1-Br-2-pentyne	 27	>99:1	96		

[a] These terms refer to the relative relationships of the alkyl substituents.
R = $-CH_2C{\equiv}CCH_2CH_3$.

the 2,3-dialkylation process discussed earlier. Our tentative rationale for this is as follows. We assume that selenium-stabilized enolate ions are incapable of abstracting the α-protons of ketones. This is a reasonable assumption since α-phenylseleno ketones exhibit pK_As which are approximately three units lower than their unselenated counterparts.[19] As a consequence, any process which directly generates a Se-stabilized enolate ion in the absence of other strong bases should not result in the α,α'-rearrangement. On

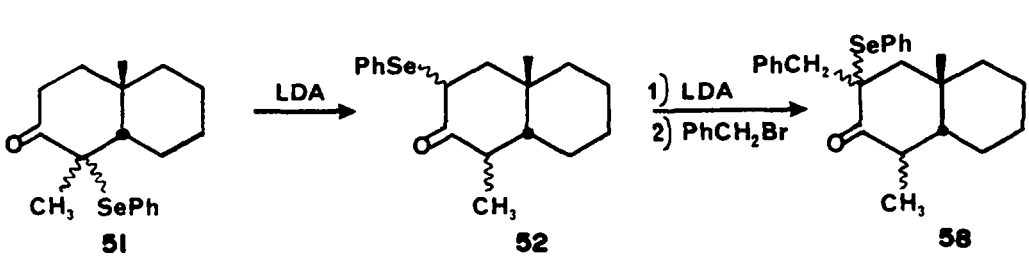
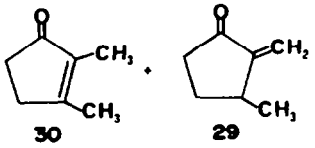
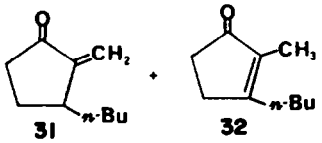
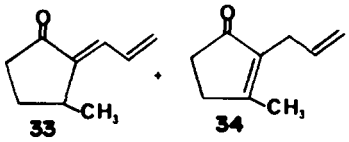
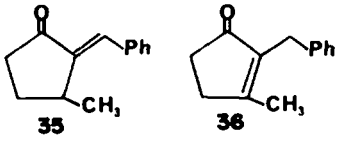
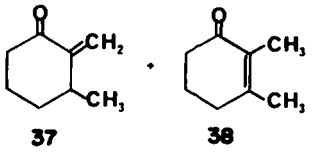
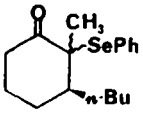
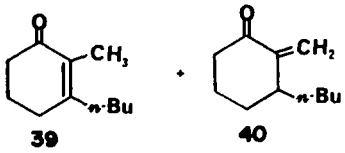
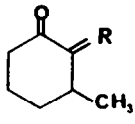
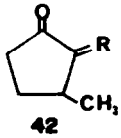


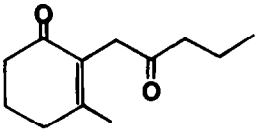
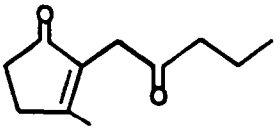
Table 4.

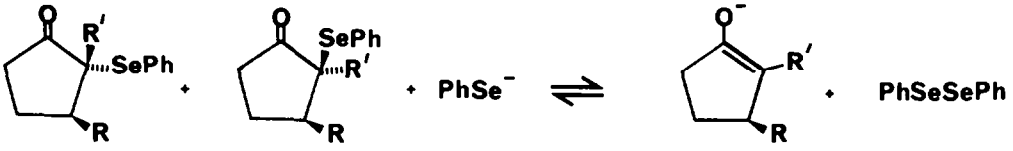
Substrate	Conditions[a]	Products	Product ratio	Yield (%)
21	A	 **30** + **29**	78:22	85
22	A	 **31** + **32**	33:50	88
23	A	 **33** + **34**	53:13	66
23	B	**34** + **33**	<1:99	62
24	A	 **35** + **36**	63:9	86
25	A	 **37** + **38**	22:51	94
25	B	**37** + **38**	14:60	91
 **28**	A	 **39** + **40**	78:16	94
26	A	 **41**	>99:1	67
26	B	**41**	>99:1	95
27	A	 **42**	>99:1	100

R = −CHC≡CCH$_2$CH$_3$

[a]A, O_3–Et_2NH–CH_2Cl_2; B, H_2O_2–CH_2Cl_2.

Table 5.

Substrates	Conditions	Product	Yield (%)
29+30	HCl–n-BuOH (90°)	30	97
31+32	HCl–n-BuOH (90°)	32	90
33+34	HCl–n-BuOH (90°)	Complex mixture	—
35+36	HCl–n-BuOH (90°)	36	90
37+38	HCl–n-BuOH (90°)	38	58
39+40	HCl–n-BuOH (90°)	39	95
41	HCl–n-BuOH (90°)	 43	95
42	HCl–n-BuOH (90°)	 44	90



Scheme 2.

Table 6.

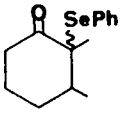
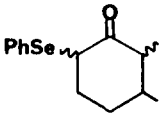
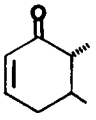
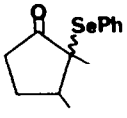
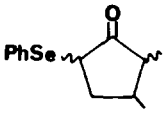
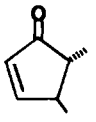
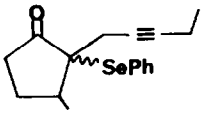
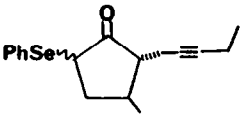
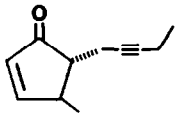
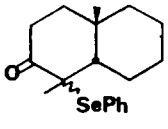
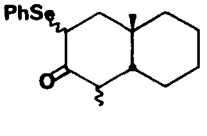
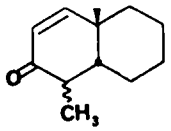
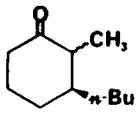
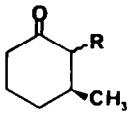
Substrate	Migration product	Yield (%)	Enone	Yield (%)
 25	 45	100	 46	90
 21	 47	95	 48	85
 27	 49	100	 50	100
 51	 52	100	 53	90

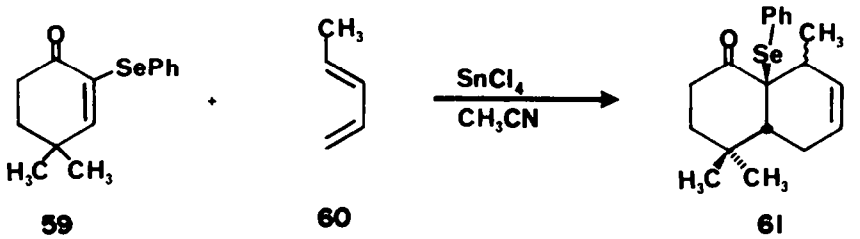
Table 7.

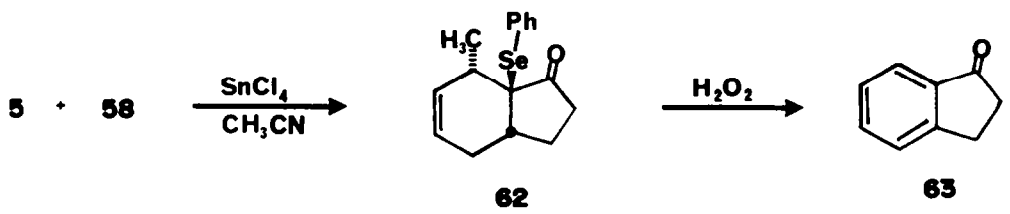
Substrate	Reagent	Electrophile	Products	*Cis/trans* ratio	Yield (%)
28	LiSePh–HMPA	NH_4Cl	 **54**	1:1	80
26	LiSePh–HMPA	NH_4Cl	 **55** $R = -CH_2C{\equiv}CCH_2CH_3$	>99:1	85

the other hand, the energy barrier for phenylseleno and proton exchange processes which result in unstabilized enolate ions should be quite small. Since a reasonable mechanism can be put forth for the α,α′-rearrangement which only requires these types of exchange reactions, we believe that the choice of the reaction pathway which is followed is almost totally a function of the nature of the enolate ion which is initially formed, rather than the enolate ion which is ultimately produced. From a synthetic viewpoint this means that one can use any of the procedures described above without having to worry about possible mechanistic cross-overs.

In addition to the reactions discussed above, 2-phenylselenenylenones could, in principle, also serve as dienophiles in Diels–Alder reactions. Since this type of Diels–Alder reaction would provide us with a new way of accessing α-phenylselenenylketones, this possibility was quite intriguing to us. Our first attempts to carry out Diels–Alder reactions with these compounds were a complete failure. We observed absolutely no reaction, irrespective of the temperature or diene used. Since Diels–Alder reactions are facilitated by the presence of acceptor groups on the dienophile and since the selenium species is actually a donor group, our failure was not surprising.

We reasoned, however, that this problem could be circumvented as follows. The presence of an electron-rich species in the 2-position should permit efficient complexation of a Lewis acid through chelation by both the oxygen and the selenium moieties. In essence, complexation of this sort converts the selenium group from a donor group to an acceptor group. In fact, many 2-phenylselenenylenones undergo Lewis acid-catalyzed Diels–Alder reactions with dienes.[18] Some representative examples are shown below. Of the Lewis acids studied, we have found stannic chloride to be the most effective. Boron trifluoride, boron trichloride, diethylaluminum chloride and titanium tetrachloride also catalyze these Diels–Alder reactions, but are far less effective. The major side reaction which is observed is deselenation of the Diels–Alder adduct. In addition to the type of synthetic manipulations which were described above, this method may also prove to be an effective benzoannulation procedure. For example, **5** can be converted to **63** in two steps in 88% overall yield.





CONCLUSION

In this article we have described a number of synthetically useful processes, all of which can be accomplished in high overall yields and usually under very mild conditions. Due to space limitations, our review of the chemistry of 2-phenylselenenylenones is by no means complete. Instead, we have focused on some selective aspects of the chemistry of these compounds which we feel provide significant advantages over other methods and which depend heavily for their success on one or more of the unique properties of selenium.

EXPERIMENTAL

General method for the conversion of enones to 2-phenylselenenylenones

To a CH_2Cl_2 or $CHCl_3$ soln of phenylselenenyl chloride (typically 1–5% by wt) was added 1.05 equiv of pyridine in one portion at room temp. Over a period of 10 min a slightly exothermic reaction ensued and the color of the soln changed from deep red to orange. At this point 0.95 equiv of the enone was added in one portion to the soln of the complex and the resulting mixture was allowed to react at room temp for varying lengths of time, depending upon the substrate (Table 1). In a crude way the progress of a reaction can be followed by observing the gradual color change of the soln from orange to light yellow. A more accurate appraisal of reaction in an NMR tube ($CDCl_3$–pyridine-d_5). Work-up typically entails washing the soln with a 10% HCl soln, drying ($MgSO_4$) and evaporating of the solvent *in vacuo*. Purification is achieved via chromatography on silica gel, followed either by distillation or recrystallization of the product.

Preparation of cis- *and* trans - 2,3 - *dimethyl* - 2 - *phenylselenenylcyclopentanone*, **21**

To a 500 ml round bottom flask containing a magnetic stirring bar was added under N_2 5.77 g (30.4 mmol) oven dried cuprous iodide and 50 ml dry ether. 36.5 ml (1.8 M, 65.8 mmol) was added dropwise via a syringe to the stirred suspension at 0°. The color changed from yellow to light grey. After 15 min the mixture was cooled to −20° and 6 g (25.3 mmol) **5** was added dropwise in 25 ml ether. After 30 min to the resulting yellow suspension was added, in succession, 14.4 g (101.3 mmol) MeI, 300 ml dry THF and 9.06 g (50.6 mmol) hexamethylphosphoramide (HMPA). The reaction was allowed to warm to room temp and stirred for 8 hr. 1 ml sat NH_4Cl aq was added and the bulk of the THF was evaporated on a rotary evaporator. The residue was taken up in 600 ml ether and washed with 3 × 125 ml sat NH_4Cl–NH_4OH (1 : 1) (until the washes were no longer blue). The blue aqueous phase was extracted with 2 × 100 ml ether and the combined ether extracts were washed with 5 × 100 ml H_2O, dried over $MgSO_4$, decolorized and the solvent was evaporated leaving 7.30 g red oil. Methyl phenylselenide (produced in the reaction) was removed by bulb to bulb distillation (60–70° at 0.5 mm) leaving 5.50 g (20.6 mmol) **21**, as a red oil in 81% yield. The C-2 epimers were separated by preparative TLC chromatography (silica gel) using 10% ether in hexanes as the eluent. ^{1}H-NMR ($CDCl_3$) *trans* isomer: 7.35–7.95 (m, 5), 1.5–2.8 (m, 5), 1.40 (s, 3), 2.30 (d, J = 5 Hz, 3); *cis* isomer: 7.30–7.80 (m, 5), 1.48–2.60 (m, 5), 1.32 (s, 3), 1.00 (d, J = 7 Hz, 3). Mass spectrum: *m/e* = 268. ^{80}Se precise mass (mixture): calc 268.03661; found 268.03418. IR ($CHCl_3$): 3060, 2920, 1720 cm^{-1}.

Preparation of 3-methyl-2-phenylselenenylcyclopentanone, **9**

To a 250 ml round bottom flask containing a magnetic stirring bar was added under N_2 4.83 g (25.4 mmol) cuprous iodide and 125 ml dry ether. 34.4 ml (1.6 M, 51.6 mmol) MeLi was added dropwise via syringe to the stirred soln at 0°. The color changed from yellow to grey. After 20 min the mixture was cooled to −20° and a soln of 5.0 g of **5**, in 25 ml of dry ether was added in a dropwise fashion. After 30 min the reaction was quenched by pouring it into 300 ml of 1 : 1 NH_4OH–sat NH_4Cl. The mixture was subjected to continuous (lighter than water) extraction with ether overnight. The extract was washed with 1 × 150 ml water, dried over $MgSO_4$ and the solvent was stripped, resulting in 4.85 g (19.2 mmol) of the desired product **9**, isolated as an orange oil (91% yield). ^{1}H-NMR ($CDCl_3$): 7.3–7.9 (m, 5), 3.25 (d, J = 7 Hz, 1), 2.0–2.8 (m, 5), 1.19 (d, J = 6 Hz, 3). IR ($CHCl_3$): 3060, 2940, 1730 cm^{-1}. ^{80}Se precise mass: calc 254.02096; found 254.02101.

Conversion of cis- *and* trans - 2,3 - *dimethyl* - 2 - *phenylselenenylcyclopentanone to* trans - 2,2 - *dimethyl* - 2 - *phenylselenenylcyclopentanone*

To a 50 ml round bottom flask containing 15 ml THF at room temp 162 mg (1.03 mmol) benzeneselenol was added under N_2. 0.57 ml (1.8 M, 1.03 mmol) MeLi was added via syringe and stirred for 15 min. The flask was cooled to −78° and 250 mg (0.936 mmol) *cis*- and *trans*-**21**, was added in 3 ml THF, followed by 336 mg (1.89 mmol) hexamethylphosphoramide. After 15 min 2.6 mg (1.13 mmol) phenylselenenyl chloride in 3 ml THF was added with rapid dissipation of the red color. The reaction was allowed to warm to room temp and the THF was stripped. The residue was taken up in 50 ml ether, washed with 2 × 15 ml water, dried over $MgSO_4$ and the solvent was removed *in vacuo*. After chromatography on a silica gel prep plate with 5% ether in hexanes, 230 mg (0.860 mmol) *trans*-2,3-dimethyl-2-phenylselenenylcyclopentanone was obtained in 95% yield.

Oxidation/elimination of cis- *and* trans-2,3-*dimethyl*-2-*phenylselenenylcyclopentanone*

To a 50 ml 3-neck round bottom flask fitted with a stopper, a gas dispersion tube and a drying tube was added 25 ml CH_2Cl_2 and 400 mg (1.50 mmol) *cis*- and *trans*-**21**. The reaction was cooled to −78° and O_3, generated via a Welsbach ozonator, was bubbled through the soln until the soln turned blue. The mixture was purged with N_2 (to remove the excess O_3) until colorless. The contents of the flask were poured directly into 50 ml refluxing CH_2Cl_2 containing 220 mg (3.0 mmol) Et_2NH under N_2. After 20 min at reflux the reaction was cooled and washed with 2 × 15 ml 10% HCl and 1 × 15 ml water, dried over $MgSO_4$ and the solvent was removed. The residue was subjected to bulb to bulb distillation (50° at 0.5 mm) yielding 140 mg colorless distillate. GLC analysis (OV-17) indicated 22% exocyclic enone **30** and 78% endocyclic enone **29**. The overall yield of the mixture was 85%. The above mixture was converted to **29** by the method of Abdula and Fuhr.

Compound **29**: ^{1}H-NMR ($CDCl_3$): 6.08 (d, J = 3 Hz, 1), 2.25–2.75 (m, 5), 1.25 (d, J = 6 Hz, 3); Compound **30**: ^{1}H-NMR ($CDCl_3$): 2.45 (m, 4), 2.10 (s, 3), 1.85 (s, 3).

Conversion of **27** *to* **49**

To a 100 ml round bottom flask containing 0.25 g (2.5 mmol) of diisopropylamine in 20 ml of anhyd THF at −78° was added 1.2 ml of 1.5 M n-BuLi (1.8 mmol) in hexane via syringe. The resulting soln was allowed to stir for 15 min, at which time 1.0 g (3.14 mmol) of **27** and 2 ml of HMPA were added. The reaction mixture was allowed to stir at −78° for 30 min and then allowed to slowly warm to room temp. After being stirred at room temp for 1 hr, the mixture was quenched with 1 ml of a sat NH_4Cl aq soln. The THF was removed via a rotary evaporator, and the resulting residue was partitioned between ether (50 ml) and water (15 ml). The aqueous layer was washed twice with ether (25 ml). The combined ether layers were dried with $MgSO_4$ and stripped of solvent to give 1 g of **49** (100% yield). This material was used in the next step of the sequence without any additional purification. ^{1}H-NMR ($CDCl_3$): 7.79–7.20 (m, 5), 3.97–3.51 (m, 1), 2.85–1.50 (m, 8), 1.33–0.85 (m, 6).[3]

Conversion of **49** *to* **50**

To a 25 ml soln of CH_2Cl_2 containing 1 g (3.14 mmol) of **49** were added six 1 ml portions of 30% H_2O_2 at 10 min intervals. 5 min after the final peroxide addition, the mixture was

transferred to a separatory funnel, and the layers were separated. The organic layer was washed with water (5 ml). The soln was dried over $MgSO_4$ and evaporated to give 0.54 g of **50**, which contained virtually no impurities. Complete purification was achieved via silica gel chromatography (0.51 g, 100% yield). ^{1}H-NMR ($CDCl_3$): 7.63–7.52 (dd, J = 7 Hz, J' = 2 Hz, 1), 6.17–6.05 (dd, J = 7 Hz, J = 1.5 Hz, 1), 3.03–1.85 (m, 6), 1.27 (d, J = 7 Hz, 3). IR ($CHCl_3$): 1700, 1620, 1597 cm^{-1}. Mass spectrum: *m/e* = 162. Precise mass: calc for $C_{11}H_{14}O$: *m/e* 162.10466; found 162.10766.

Conversion of **59** *to* **61**

500 mg (1.79 mmol) of **59**, was dissolved in 25 ml of deoxygenated, freshly distilled acetonitrile. The mixture was cooled to 0° under a N_2 atmosphere and 700 mg (1.5 equiv) of *dry* $SnCl_4$ was slowly introduced to the system via syringe. The system was allowed to stir at 0° for 10–12 min and then 490 mg (4 equiv) of piperylene was injected into the mixture. The temperature was allowed to rise to 25° and the soln was stirred for 24 hr. At this point, the mixture was quenched with 10 ml of sat $NaHCO_3$ aq. The acetonitrile was then removed under vacuum and the aqueous residue was diluted with 75 ml of ether. The organic layer was washed with 2 × 50 ml of sat $NaHCO_3$ aq and then with 2 × 50 ml of water. The ether layer was dried over $MgSO_4$ and then conc under vacuum to yield 0.54 g of **61** (yellow–orange oil, 87% yield). ^{1}H-NMR ($CDCl_3$): 7.68–7.15 (m, 5), 5.75–5.41 (m, 2), 3.05–2.83 (m, 1), 2.20–1.05 (m, 6), 1.03 (s, 6), 0.99 (d, J = 7 Hz, 3).

Selected spectral data

Compound **9**. ^{1}H-NMR ($CDCl_3$): 7.9–7.3 (m, 5), 3.25 (d, J = 7 Hz, 1), 2.8–2.0 (m, 5), 1.19 (d, J = 6 Hz, 3); IR ($CHCl_3$): 1730 cm^{-1}; mass spectrum: *m/e* = 254. Precise mass: calc for $C_{12}H_{14}O^{80}Se$: *m/e* 254.02096, found 254.02101.

Compound **11**. ^{1}H-NMR ($CDCl_3$): 7.92–7.23 (m, 5), 3.37 (d, J = 7 Hz, 1), 2.73–0.72 (m, 14); IR ($CHCl_3$): 1725 cm^{-1}; mass spectrum: *m/e* = 296.

Compound **12**. ^{1}H-NMR ($CDCl_3$): 7.92–7.23 (m, 5), 3.82 (d, J = 4.5 Hz, 1), 2.73–0.72 (m, 14); IR ($CHCl_3$): 1725 cm^{-1}; mass spectrum: *m/e* = 296.

Compound **22** (cis). ^{1}H-NMR ($CDCl_3$): 7.71–7.3 (m, 5), 2.24–1.15 (m, 11), 1.28 (s, 3), 1.00–0.75 (t, 3); IR ($CHCl_3$): 1730 cm^{-1}; mass spectrum: *m/e* = 306. Precise mass: calc for $C_{16}H_{22}O^{76}Se$: *m/e* 306.08626; found 306.08699.

Compound **22** (trans). ^{1}H-NMR ($CDCl_3$): 7.80–7.21 (m, 5), 2.20–1.15 (m, 11), 1.39 (s, 3), 1.10–0.80 (t, 3); IR ($CHCl_3$): 1720 cm^{-1}; mass spectrum: *m/e* = 306. Precise mass: calc for $C_{16}H_{22}O^{76}Se$: *m/e* 306.08626; found 306.08689.

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[1] For a detailed outline of the scope and limitations of selenoxide eliminations, see: [a]H. J. Reich, *Acc. Chem. Res.* **12**, 22 (1979); [b]D. L. J. Clive, *Tetrahedron* **34**, 1049 (1978); [c]H. J. Reich, *Oxidation in Organic Chemistry* (Edited by W. Trahanovsky), Part C, p. 1. Academic Press, New York (1978); [d]D. Liotta, *Acc. Chem. Res.* **17**, 28 (1984).

[2a] H. J. Reich and S. K. Shah, *J. Am. Chem. Soc.* **99**, 263 (1977); [b]H. J. Reich, J. M. Renga and I. L. Reich, *Ibid.* **97**, 5434 (1975).

[3a] G. Zima and D. Liotta, *Synth. Commun.* **9**, 697 (1979); [b]D. J. Buckley, S. Kulowit and A. McKervey, *J. Chem. Soc. Chem. Commun.* 506 (1980); [c]M. Schumizer, R. Takeda and I. Kuwajima, *Tetrahedron Lett.* 3461 (1979); [d]for a method for converting enoates to their corresponding 2-phenylselenenyl enoates, see: T. A. Hase and P. Kukkola, *Synth. Commun.* **10**, 451 (1980).

[4] A number of acyclic 2-phenylselenenylenones have been prepared via propargyl selenoxide rearrangements (ref. 3*b*). This methodology is, of course, not applicable in the preparation of cyclic 2-phenylselenenylenones.

[5] Ley has shown that exposure of enones to 3 equiv of the complex leads to the formation of the corresponding 2-chloroenones. 2-Phenylselenenylenones were shown to be intermediates in this process. See: S. V. Ley and A. J. Whittle, *Tetrahedron Lett.* 3301 (1981).

[6] G. Zima, C. Barnum and D. Liotta, *J. Org. Chem.* **45**, 2737 (1980).

[7] H. O. House and J. Wilkins, *Ibid.* **43**, 2443 (1978).

[8] Addition of HMPA, prior to protonation of the enolate, did not significantly alter the observed product ratios.

[9] The preference which certain alpha substituents exhibit for the axial orientation is of course well known for alpha-haloketones. See: E. J. Corey, *J. Am. Chem. Soc.* **75**, 2301 (1953).

[10] K. B. Sharpless, M. W. Young and R. F. Lauer, *Tetrahedron Lett.* 1979 (1973).

[11] H. J. Reich, J. M. Renga and I. L. Reich, *J. Org. Chem.* **39**, 2133 (1974).

[12] The "one-pot" procedure involves the addition of an equal vol of THF and at least 3 molar equiv of HMPA after the cuprate addition is complete, followed by the addition of the appropriate electrophile. In our experience, however, carrying out the conjugate addition and the alkylation reactions in two separate steps, results in slightly higher overall yields.

[13] Typically, oxidative elimination of *cis*-2,3-dialkyl-2-phenylselenenylketones results primarily in the formation of endocyclic enones, whereas oxidative elimination of the corresponding *trans*-isomer results in the exclusive formation of exocyclic enones.

[14] Reductive removal of the phenylselenenyl group from these materials produces a mixture of epimers whose ratios typically reflect the thermodynamic stability of the materials in question. Thus, the actual stereochemistry of these materials actually plays no role in determining the product stereochemistry (see Table 7).

[15a] M. P. L. Caton, E. C. J. Coffee and G. L. Watkins, *Tetrahedron Lett.* 773 (1972); [b]R. F. Abdulla and K. H. Fuhr, *J. Org. Chem.* **43**, 4248 (1978); [c]T. Wakamatsu, K. Hashimoto, M. Ogura and Y. Ban, *Synth. Commun.* **8**, 319 (1978).

[16] For an interesting synthetic application of this 1,3-selenium shift methodology, see: D. Liotta, C. S. Barnum and M. Saindane, *J. Org. Chem.* **46**, 4301 (1981).

[17] D. Liotta, M. Saindane and D. Brothers, *Ibid.* **47**, 1598 (1982).

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