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Phenyltelluroacrylonitriles and phenylselenoacrylonitriles as precursors of (*Z*)-α-phenylseleno-α,β-unsaturated aldehydes, β-amino-α-phenylselenonitriles and Diels–Alder adducts

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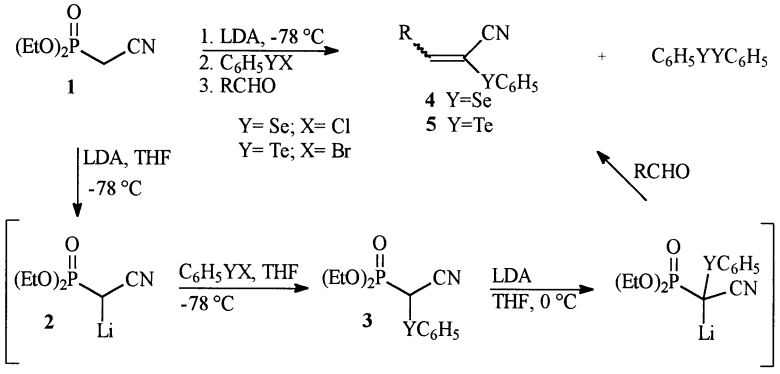
Abstract—Reaction of cyanomethylphosphonate with aryl selenenyl (or tellurenyl) halides and aldehydes, under basic conditions, provides α-phenylseleno or α-phenyltelluro acrylonitriles in good yields. Reaction of the α-phenylseleno acrylonitriles with dienes furnishes the corresponding adducts while reaction with amines furnishes α-phenylseleno-β-amino nitriles. Selective reduction of the cyano group with DIBAL-H results in the α-phenylseleno-α,β-unsaturated aldehydes. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Vinylic sulfides α-substituted by strong electron withdrawing groups have been synthetically used as potent Michael acceptors,[1] in a variety of cycloaddition reactions[2] and in studies as precursors of extended enolates.[3] The selenium analogs have been used as dienophiles in Diels–Alder reactions,[4] as Michael acceptors[5] and in the synthesis of 2,3-dihydroselenophenes and butadienes.[6]

α-Cyano substituted vinylic sulfides have been prepared by several different routes.[7] However, the preparation of α-phenylselenoacrylonitriles is scarcely known[8] and no methods to the corresponding α-phenyltelluroacrylonitriles were described up to date. To the best of our knowledge, the only method reported for preparing the α-phenylseleno-acrylonitriles involves the addition of benzeneselenenyl chloride or bromide to cyano olefins leading to α-seleno adducts, which are subjected to in situ dehydrohalogenation.[6,8]



Scheme 1.

Keywords: Wittig reactions; aldehydes; phenylseleno or phenyltelluroacrylonitriles; α-phenylseleno-β-amino nitriles.
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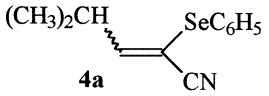
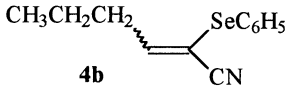
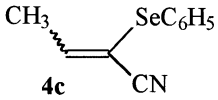
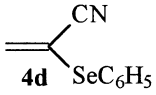
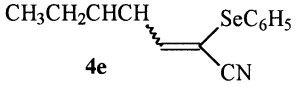
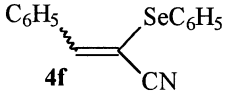
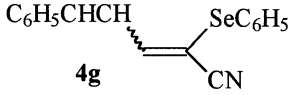
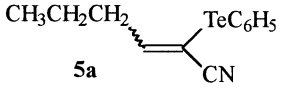
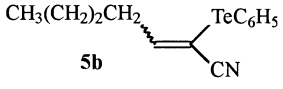
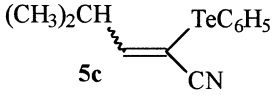
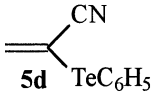
Table 1. α-Phenylseleno and α-phenyltelluro acrylonitriles obtained

Entry	R	Products	Reaction time (h)	Yield (%)	Ratio (*Z*/*E*)
1	$(CH_3)_2CH$	 **4a**	1.5	92	5.0:1
2	$CH_3CH_2CH_2$	 **4b**	1.5	80	5.2:1
3	CH_3	 **4c**	1.5	81	2.6:1
4	H	 **4d**	1.5	58	–
5	CH_3CH_2CHCH	 **4e**	1.5	81	2.7:1
6	C_6H_5	 **4f**	0.5	86	3.0:1
7	C_6H_5CHCH	 **4g**	0.5	78	6.8:1
8	$CH_3CH_2CH_2$	 **5a**	1.5	93	5.6:1
9	$CH_3(CH_2)_2CH_2$	 **5b**	1.5	81	4.5:1
10	$(CH_3)_2CH$	 **5c**	1.5	78	4.5:1
11	H	 **5d**	1.5	23	–

However, it is important to note that the chemical reactivity of this kind of compounds remains almost unexplored. On the basis of the described methods, one can state that the preparation of 2-(organylseleno)propenenitriles is more difficult than the preparation of the corresponding thio analogues.

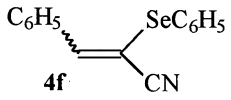
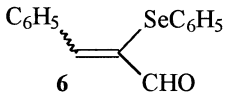
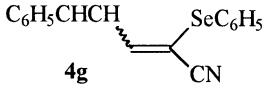
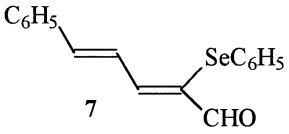
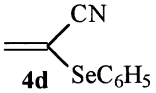
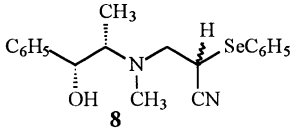
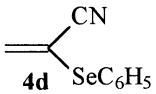
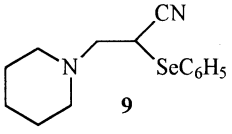
We have recently described practical methodologies for the preparation of vinyl chalcogenides based on Wittig and Wittig–Horner reactions.[9] Due to our continuous interest on the synthesis of functionalized vinylic chalcogenides, we report here the application of the Horner–Wittig reaction to make easier the synthesis of α-phenylseleno acrylonitriles and for the first synthesis of phenyltelluro acrylonitriles. Studies on the chemical reactivity of α-phenylseleno acrylonitriles in reactions with DIBAL-H, with amines and in a Diels–Alder-type reaction are also described.

2. Results and discussion

2.1. Preparation of α-phenylseleno or α-phenyltelluro acrylonitriles

Cyanomethylphosphonate **1** is easily available on a large scale by the Arbuzov reaction of triethylphosphite with chloromethyl acetonitrile[10] and it is a very useful intermediate in a variety of important transformations. Treatment of **1** with LDA generated the lithiated species **2** which, upon reaction with benzenetellurenyl bromide or benzeneselenenyl chloride in THF, afforded the α-phenylchalcogeno(cyano)phosphonate intermediates **3** as depicted in Scheme 1. Intermediate **3** was easily transformed into the desired product **4** or **5** in a one-pot process (without isolation) using LDA in excess followed by reaction with aldehydes. In most cases, good to excellent yields (78–93%) were obtained by using aromatic and aliphatic aldehydes.

Table 2. Products obtained from α-phenyl selenoacrylonitriles

Entry	Reagent	Products	Yield (%)	Ratio (*Z*/*E*)
1	 **4f**	 **6**	76	3.5 : 1
2	 **4g**	 **7**	55	100 : 0
3	 **4d**	 **8**	67	-
4	 **4d**	 **9**	82	-

However, the reactions with formaldehyde gave lower yields, particularly for the tellurium derivative case (entry 11, Table 1).

The sulfenylation of the diethyl cyanomethylphosphonate anion **2** with phenylsulfenyl chloride during the synthesis of α-phenylsulfenylacrylonitriles by a Horner–Emmons reaction modification, gave low yields (37–47%). All efforts to generate exclusively the intermediate $(EtO)_2POCH(SPh)CN$ (analogous to **3**) using 1:1 molar ratio of PhSCl and the anion **2** led to $(EtO)_2POC(SPh)_2CN$ as the major product.[11]

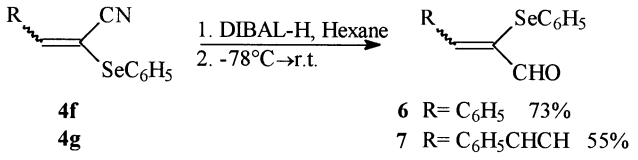
By contrast, we observed that phenyltellurenyl bromide excess was required to afford **5** in good yields. For example, intermediate **2** reacts with equimolar amounts of PhTeBr, followed by the addition of *n*-butyraldehyde, providing **5a** in 47% yield, while the yield increases to 67 and 93% by using 1.5 and 2.0 equiv. of the PhTeBr, respectively. On the other hand, using an excess of anion **2** (2.0 equiv.), the desired vinylic product was not formed. It was also observed that an excess of phenyl selenenyl chloride (1.5 equiv.) was required to afford good yields of **4**. The excess of these easily accessible reagents can be recovered at the purification step in the PhSeSePh or PhTeTePh form.

The method described here exhibits good generality to the phenylselenoacrylonitriles and it is successful with aromatic and aliphatic aldehydes, while for phenyltelluro acrylonitriles, the reaction was possible only with aliphatic aldehydes and the products from aromatic derivatives are unstable under the reaction employed. However, this is the first method to this potentially very useful, new class of tellurium compounds. It is noteworthy that by our method it was possible to prepare the simplest and new phenylseleno and phenyltelluro acrylonitriles **4d** and **5d** derived from formaldehyde, albeit in only 58 and 23% yield, respectively, as a consequence of low stability of these products.

Although most experiments were performed on a 1.0 mmol scale, these reactions can also be performed successfully on higher scales (up to 10 mmol) with comparable yields.

Concerning the stereochemistry of the obtained olefins, we usually observed the formation of *Z* and *E* isomer mixtures. In the case of aliphatic derivatives, the *Z* and *E* isomers ratios were directly obtained by ^1H NMR analysis (400 MHz). However, for **4f** and **g** products, this ratio could not be determined directly by ^1H NMR, because the vinylic proton signals overlaped with the aromatic hydrogens. For **4f** (reaction with benzaldehyde), the ratio was obtained by the analysis of their ^{13}C NMR spectra. The presence of *Z* and *E* isomers could be easily confirmed since two peaks relative to the CN group appeared at δ 97.9 and 104.0. The same ratio was observed for the aldehyde obtained by the reduction of the CN moiety with DIBAL-H (vide infra).

For product **4g** (entry 7, Table 1), the *Z*/*E* isomers (6.8:1) were easily separated by column chromatography and the major isomer was shown to have the *Z*-configuration by X-ray crystallography.[12]



Scheme 2.

An alternative experimental condition employing $BF_3{\cdot}OEt_2$ (2.3 equiv.) was applied in one experiment between *n*-butyraldehyde (1.2 equiv.) and the α-phenylseleno-α-cyanomethylphosphonate of type **3**. In this case, the proportion of the *Z*-isomer was increased (from 5.2:1 to 10:1), but the yield of **4b** was slightly lower (72% isolated yield). The effect of $BF_3{\cdot}OEt_2$ on the stereochemistry and the scope of the observed effect deserve further investigation.

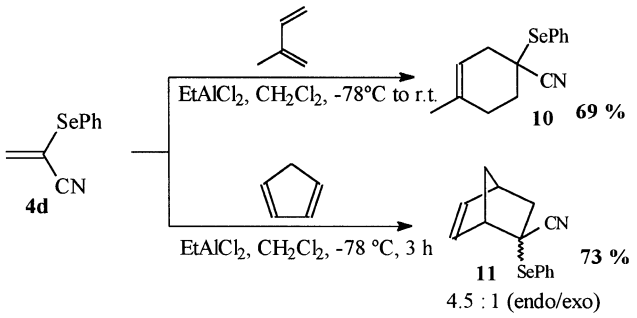
2.2. Selective reduction of the nitrile moiety

α-Phenylseleno-α,β-unsaturated aldehydes have recently been prepared by the reaction of 1-lithio-2-ethoxy vinyl selenides with aldehydes and ketones, followed by acid-catalyzed dehydration.[13] Some other methods were also described for the preparation of this class of compounds.[14a,b] They have been used to access selenobutadienes[15a] and in a Diels–Alder-type reaction.[15b,14b]

In the present work, we decided to study the selectivity on the reduction of the CN moiety from α-phenylseleno acrylonitriles. For this purpose, some of the obtained α-phenylseleno acrylonitriles were reacted with DIBAL-H at −78°C, warming up the solution slowly to room temperature and keeping the reaction at this temperature for 1 h, followed by aqueous quenching. It was observed that the use of 2 equiv. of DIBAL-H was crucial to afford good yields of **6** or **7**.

Concerning to the stereochemistry of the obtained products, in the case of the α-phenylselenocinnamaldehyde **6** (entry 1, Table 2), we observed the formation of *Z* and *E* isomers mixture in a 3.5:1 ratio. The *Z* and *E* isomers were easily separable by column chromatography (entry 1, Table 2) and should be noted that the reaction occurred with nearly total retention of configuration since the starting material used (**4f**) was a mixture of *Z* and *E* isomers in a ca. 3:1 ratio (entry 6, Table 1) (Scheme 2).

In the other example studied, the *Z*-isomer of compound **4g** was employed furnishing the corresponding α-phenylseleno-α,β,γ,δ-unsaturated aldehyde **7** in 55% yield (entry 2, Table 2). This reaction occurred with complete retention of the *Z*-configuration as confirmed by ^{1}H NMR (400 MHz),



Scheme 4.

NOESY experiment and by the ^{13}C NMR spectra where single peaks for all carbons were observed.

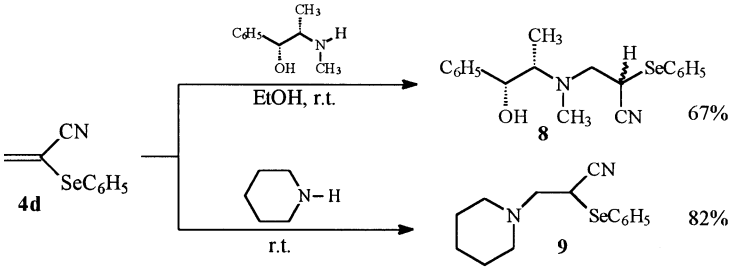
2.3. Preparation of α-phenylseleno-β-amino nitriles

The α-phenylseleno-β-amino esters have attracted considerable attention due to their utility as precursors of modified β-amino esters,[16] oligopeptides[17] and α-phenylseleno-β-lactams.[18] The presence of the organoselenium functional group provides an entry into radical chemistry.[16,17,19]

The addition of the amines to olefins bearing an electron-withdrawing substituent has been known for a long time. The addition takes place probably involving a typical 1,4-addition mechanism. In this way, we decided to perform the reaction of nitrile **4d** with two different amines. Performing the reaction with an ethanolic solution of (1*R*,2*S*)-(−)-ephedrine, the product **8** was easily obtained in 67% isolated yield, as a 1:1 mixture of diastereoisomers. In the case of reaction with morpholine, this amine was added neat to the nitrile **4d** at room temperature and the corresponding product was isolated in 82% yield. This reaction furnishes an easy access to the highly functionalized nitriles **8** and **9** directly from the readily available α-phenylseleno acrylonitrile **4d** (Scheme 3; Table 2, entries 3 and 4).

2.4. Study on the reactivity of 4d in a Diels–Alder reaction

The Diels–Alder reaction is one of the most useful and powerful tools in preparative organic chemistry.[20] With this in mind, we decided to perform studies on the reaction of α-phenylseleno α,β-unsaturated esters as dienophiles in Diels–Alder reactions with commercially available dienes. For our study, we decided to use the simplest reagent of this class of compounds (**4d**) (Scheme 4).



Scheme 3.

Compound **4d** was reacted with a small excess of isoprene and 1.4 equiv. of the $EtAlCl_2$, using dichloromethane (4 mL) as solvent. This reaction proceeded regioselectively to give **10** in 69% isolated yield. The formation of the *para* isomer was confirmed by a NOESY NMR study and no other regioisomer was detected.

The reaction of **4d** with cyclopentadiene, under the conditions described above, showed a low stereoselectivity, and the adduct **11** was obtained in a 4.5:1 (*endo*/*exo*) ratio, in 73% yield. The preferential formation of the *endo* isomer was confirmed by a NOESY NMR experiment. For both dienes, the best results were obtained with $EtAlCl_2$ as the Lewis acid.

3. Conclusions

We have developed a new and simple methodology to the synthesis of α-phenylseleno and α-phenyltelluro acrylonitriles and studies on the reactivity of the seleno compounds by reaction with DIBAL-H, with amines and with dienes were also described here.

4. Experimental

4.1. General remarks

^1H and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded with a 200, 300 or a 400 MHz spectrometer as noted. Chemical shifts are expressed as parts per million (ppm) downfield from tetramethylsilane as an internal standard. Mass spectra (EI) were obtained at 70 eV with a Hewlett Packard EM/CG HP-5988A spectrometer, infra-red spectra were acquired on a Perkin–Elmer 1310 spectrometer and elemental analyses were performed with a Vario EL Elementar Analysis System. Merck's silica gel (230–400 mesh) was used for flash chromatography. THF was distilled over sodium/benzophenone immediately before use.

4.2. General procedure for the synthesis of α-phenylseleno and α-phenyltelluro acrylonitriles 4–5

A solution of **1** (0.177 g, 1 mmol) in THF (1 mL) was added dropwise to a solution of LDA (2.1 mmol) in THF (3 mL) at −78°C under nitrogen. The reaction was stirred at this temperature for 20 min, then a solution of C_6H_5SeCl (0.287 g, 1.5 mmol) in THF (1 mL) or C_6H_5TeBr (2 mmol) in THF (2 mL) was added at −78°C. The temperature was raised to 0°C for 30 min, the aldehyde (1 mmol) was then added and the stirring continued for 30 min at 0°C and for an additional 30–90 min at rt (see Table 1). The reaction mixture was treated with water and extracted with ethyl acetate (3×25 mL). The organic layer was dried over $MgSO_4$ and the solvent removed in vacuo. The residue was purified by column chromatography (SiO_2) using hexane/ethyl acetate (99:1) as eluent. Spectral data of **4a–g** and **5a–d** are listed below.

4.2.1. (*Z*+*E*)-4-Methyl-2-phenylselanyl-pent-2-enenitrile (4a). Yield 0.230 g (92%). MS *m*/*z* (rel. int.) 251 (M^++1, 100.0), 155 (31.7), 94 (25.7), 77 (87.1); IR (film, cm^{-1}): 2210 (CN). ^1H NMR (300 MHz, $CDCl_3$) δ (*Z*+*E*) 1.02–1.10 (m, 6H); 2.76–3.05 (m, 1H); 6.64 (*Z*) and 6.65 (*E*) (2d, *J*=9.9 Hz, 1H); 7.20–7.37 (m, 3H); 7.42–7.60 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.3, 21.6, 31.9, 33.5, 97.9, 101.4, 115.8, 117.3, 127.2, 127.9, 128.6, 128.8, 129.6, 133.4, 134.2, 160.2, 163.6. Anal. calcd for $C_{12}H_{13}NSe$: C, 57.61; H, 5.24. Found: C, 57.91; H, 5.14.

4.2.2. (*Z*+*E*)-2-Phenylselanyl-hex-2-enenitrile (4b). Yield 0.201 g (80%). MS *m*/*z* (rel. int.) 251 (M^++1, 100.0), 157 (66.0), 77 (89.1); IR (film, cm^{-1}): 2211 (CN). ^1H NMR (300 MHz, $CDCl_3$) δ (*Z*+*E*) 0.88–1.00 (m, 3H); 1.42–1.58 (m, 2H); 2.30–2.45 (m, 2H); 6.79 (*Z*) and 6.84 (*E*) (2t, *J*=7.8 Hz, 1H); 7.25–7.35 (m, 3H); 7.50–7.60 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.4, 13.6, 21.3, 21.5, 34.1, 35.5, 100.2, 103.7, 115.9, 117.3, 127.2, 127.9, 128.6, 128.8, 129.5, 133.5, 134.1, 154.1, 157.3. Anal. calcd for $C_{12}H_{13}NSe$: C, 57.61; H, 5.24. Found: C, 57.82; H, 5.05.

4.2.3. (*Z*+*E*)-2-Phenylselanyl-but-2-enenitrile (4c).[8b] Yield 0.180 g (81%). ^1H NMR (200 MHz, $CDCl_3$) δ 1.97 (*E*) and 2.03 (*Z*) (2d, *J*=7.0 Hz, 3H); 6.83 (*Z*) and 6.89 (*E*) (2q, *J*=7.0 Hz, 1H); (*Z*+*E*) 7.19–7.32 (m, 3H); 7.51–7.56 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.0, 19.1, 100.7, 104.2, 115.6, 117.2, 127.0, 127.6, 128.4, 128.6, 129.4, 133.3, 133.8, 149.5, 152.5.

4.2.4. 2-Phenylselanyl-acrylonitrile (4d).[8] Yield 0.121 g (58%). MS *m*/*z* (rel. int.) 209 (M^+, 56.4), 157 (79.5), 91 (100.0), 77 (75.9), 51 (62.5); IR (film, cm^{-1}): 2216 (CN). ^1H NMR (200 MHz, $CDCl_3$) δ 6.06 (d, *J*=0.8 Hz, 1H); 6.43 (d, *J*=0.8 Hz, 1H); 7.29–7.40 (m, 3H); 7.52–7.63 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 110.6, 116.3, 125.9, 129.3, 129.6, 134.6, 134.9.

4.2.5. (1*Z*+1*E*,3*E*)-2-Phenylselanyl-hepta-2,4-dienenitrile (4e). Yield 0.213 g (81%). MS *m*/*z* (rel. int.) 263 (M^++1, 25.1), 157 (32.7), 106 (18.9), 77 (100.0); IR (film, cm^{-1}): 2204 (CN). ^1H NMR (300 MHz, $CDCl_3$) δ (1*Z*+1*E*,3*E*) 0.98–1.10 (m, 3H); 2.15–2.30 (m, 2H); 6.18 (1*Z*,3*E*) and 6.28 (1*E*,3*E*) (2dt, *J*=14.9, 6.5 Hz, 1H); 6.45 (1*Z*,3*E*) and 6.61 (1*E*,3*E*) (2ddt, *J*=14.9, 10.8, 1.5 Hz, 1H); 7.12 (1*Z*,3*E*) and 7.16 (1*E*,3*E*) (2d, *J*=10.8 Hz, 1H); 7.20–7.40 (m, 3H); 7.50–7.60 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.5, 25.9, 26.2, 96.6, 98.4, 116.2, 118.4, 126.2, 127.7, 127.9, 128.4, 128.5, 129.4, 133.3, 147.7, 149.0, 149.7, 152.2. Anal. calcd for $C_{13}H_{13}NSe$: C, 59.55; H, 5.00. Found: C, 59.46; H, 5.16.

4.2.6. (*Z*+*E*)-3-Phenyl-2-phenylselanyl-acrylonitrile (4f). Yield 0.245 g (86%). MS *m*/*z* (rel. int.) 285 (M^++1, 53.7), 204 (55.9), 157 (29.1), 77 (100.0); IR (film, cm^{-1}): 2203 (CN). ^1H NMR (400 MHz, $CDCl_3$) δ (*Z*+*E*) 7.35–7.60 (m, 6H); 7.52 (s, 1H); 7.64–7.66 (m, 2H); 7.74–7.77 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 97.9, 104.0, 117.2, 117.5, 127.7, 127.8, 128.6, 128.8, 128.9, 129.0, 129.6, 129.6, 129.7, 129.7, 130.1, 130.9, 133.8, 134.1, 134.4, 135.5, 145.8, 150.1. Anal. calcd for $C_{15}H_{11}NSe$: C, 63.39; H, 3.90. Found: C, 63.36; H, 3.52.

4.2.7. (1*Z*,3*E*)-5-Phenyl-2-phenylselanyl-penta-2,4-dienenitrile (4g). Yield 0.211 g (68%). MS *m*/*z* (rel. int.) 311

(M^++1, 78.5), 230 (59.0), 154 (100.0), 127 (86.4), 77 (43.4); IR (film, cm^{-1}): 2200 (CN). ^1H NMR (300 MHz, $CDCl_3$) δ 6.82 (d, J=14.9 Hz, 1H); 7.11 (dd, J=14.9, 11.3 Hz, 1H); 7.22 (d, J=11.3 Hz, 1H); 7.27–7.39 (m, 6H); 7.40–7.50 (m, 2H); 7.55–7.62 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 99.4, 116.4, 124.4, 127.5, 127.7, 129.0, 129.6, 129.7, 133.9, 135.3. Anal. calcd for $C_{17}H_{13}NSe$: C, 65.81; H, 4.22. Found: C, 65.84; H, 4.12.

4.2.8. (1*E*,3*E*)-5-Phenyl-2-phenylselanyl-penta-2,4-dienenitrile (4g). Yield 0.031 g (10%). IR (KBr, cm^{-1}): 2202 (CN). ^1H NMR (300 MHz, $CDCl_3$) δ 7.02 (d, J=14.5 Hz, 1H); 7.02 (dd, J=14.5, 11.0 Hz, 1H); 7.30 (d, J=11.0 Hz, 1H); 7.34–7.45 (m, 6H); 7.50–7.57 (m, 2H); 7.58–7.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 101.3, 118.6, 124.7, 125.9, 127.7, 128.9, 129.0, 129.7, 129.9, 133.8, 135.6, 142.5, 149.0. Anal. calcd for $C_{17}H_{13}NSe$: C, 65.81; H, 4.22. Found: C, 66.04; H, 4.27.

4.2.9. (*Z*+*E*)-2-Phenyltellanyl-hex-2-enenitrile (5a). Yield 0.280 g (93%). MS *m*/*z* (rel. int.) 299 (M^+, 56.8), 205 (83.3), 142 (31.9), 129 (42.8), 77 (100.0); IR (film, cm^{-1}): 2201 (CN). ^1H NMR (300 MHz, $CDCl_3$) δ (*Z*+*E*) 0.90–1.00 (m, 3H); 1.42–1.58 (m, 2H); 2.22–3.33 (*E*) and 2.38–2.48 (*Z*) (2m, 2H); 6.88 (*E*) and 6.96 (*Z*) (2t, J=7.1 Hz, 1H); 7.24–7.42 (m, 3H); 7.78–7.88 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.2, 13.5, 21.1, 21.3, 37.1, 38.2, 79.2, 86.2, 112.1, 112.8, 117.8, 118.9, 128.8, 129.0, 129.5, 138.6, 139.3, 158.5, 164.1. Anal. calcd for $C_{12}H_{13}NTe$: C, 48.23; H, 4.38. Found: C, 48.50; H, 4.27.

4.2.10. (*Z*+*E*)-2-Phenyltellanyl-hept-2-enenitrile (5b). Yield 0.255 g (81%). MS *m*/*z* (rel. int.) 313 (M^+, 35.8), 207 (59.0), 142 (49.7), 129 (27.7), 77 (100.0); IR (film, cm^{-1}): 2202 (CN). ^1H NMR (300 MHz, $CDCl_3$) δ (*Z*+*E*) 0.87–0.98 (m, 3H); 1.28–1.55 (m, 4H); 2.26–2.35 (*E*) and 2.40–2.52 (*Z*) (2m, 2H); 6.89 (*E*) and 6.98 (*Z*) (2t, J= 7.4 Hz, 1H); 7.25–7.43 (m, 3H); 7.78–7.90 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.5, 13.6, 21.9, 22.1, 29.8, 30.1, 35.0, 36.1, 79.0, 86.0, 112.1, 112.8, 117.9, 119.0, 128.9, 129.1, 129.6, 138.7, 139.5, 158.8, 164.5. Anal. calcd for $C_{13}H_{15}NTe$: C, 49.91; H, 4.83. Found: C, 49.89; H, 4.75.

4.2.11. (*Z*+*E*)-4-Methyl-2-phenyltellanyl-pent-2-enenitrile (5c).[21] Yield 0.235 g (78%). MS *m*/*z* (rel. int.) 299 (M^+, 33.6), 207 (54.7), 77 (100.0); IR (film, cm^{-1}): 2202 (CN). ^1H NMR (200 MHz, $CDCl_3$) δ 1.04 (*E*) and 1.06 (*Z*) (2d, J=6.6 Hz, 6H); 2.55–2.73 (*E*) and 2.74–2.96 (2m, 1H); 6.66 (*E*) and 6.80 (*Z*) (2d, J=9.6 Hz, 1H); (*Z*+*E*) 7.23–7.40 (m, 3H); 7.77–7.87 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.1, 21.5, 35.1, 36.2, 76.9, 83.4, 112.1, 112.8, 117.8, 119.0, 128.9, 129.2, 129.7, 138.7, 139.6, 164.6, 170.4.

4.2.12. 2-Phenyltellanylacrylonitrile (5d).[21] Yield 0.060 g (23%). MS *m*/*z* (rel. int.) 259 (M^++2, 35.8), 207 (68.0), 129 (66.4), 77 (100.0), 51 (47.0); IR (film, cm^{-1}): 2206 (CN). ^1H NMR (200 MHz, $CDCl_3$) δ 6.30 (s, 1H); 6.95 (s, 1H); 7.20–7.50 (m, 3H); 7.86–7.93 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 90.5, 112.0, 118.7, 129.7, 130.1, 140.2, 142.6.

4.2.13. Synthesis of (*Z*+*E*)-2-phenylseleno-3-phenyl-2-propen-1-al 6 from 4f. A solution of diisobutylaluminum hydride (DIBAL-H) (2.0 mL, 2 mmol, 1.0 M solution in toluene) was added dropwise to a solution of nitrile **4f** (1.0 mmol) in hexane (10.0 mL) at −78°C under nitrogen. The temperature was allowed to reach rt for 1 h and stirred for 30 min at rt. The mixture was poured into aq. NH_4Cl solution and after 20 min, aq. sulfuric acid was added and the product was extracted with ethyl acetate (3×25 mL). The organic layer was dried over $MgSO_4$ and the solvent removed in vacuo. The residue was purified by column chromatography over silica gel and eluted with hexane/ethyl acetate (99:1), yielding **6** (*Z*+*E*).

(**6*Z***): Yield 0.170 g (59%). MS *m*/*z* (rel. int.) 288 (M^+, 57.4), 157 (34.6), 131 (100.0), 103 (74.4), 77 (87.5); IR (film, cm^{-1}): 1690 (CO). ^1H NMR (400 MHz, $CDCl_3$) δ 7.16–7.20 (m, 3H); 7.30–7.45 (m, 5H); 7.83–7.87 (m, 2H); 8.00 (s, 1H); 9.50 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 127.1, 128.3, 129.1, 130.7, 130.9, 131.7, 132.1, 134.0, 152.5, 191.2. Anal. calcd for $C_{15}H_{12}OSe$: C, 62.73; H, 4.21. Found: C, 62.25; H, 4.31.

(**6*E***) Yield 0.050 g (17%). IR (KBr, cm^{-1}): 1660 (CO). ^1H NMR (200 MHz, $CDCl_3$) δ 7.20–7.45 (m, 9H), 7.60–7.70 (m, 2H); 9.78 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 126.6, 128.5, 129.0, 129.3, 129.5, 129.8, 134.7, 136.4, 138.4, 145.4, 188.8. Anal. calcd For $C_{15}H_{12}OSe$: C, 62.73; H, 4.21. Found: C, 62.72; H, 4.21.

4.2.14. (2*Z*,4*E*)-2-Phenylseleno-5-phenyl-2,4-pentadien-1-al 7 from (*Z*)-4g. Yield 0.173 g (55%). MS *m*/*z* (rel. int.) 314 (M^+, 42.0), 157 (21.6), 128 (100.0), 77 (20.1); IR (film, cm^{-1}): 1679 (CO). ^1H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, J=15.6 Hz, 1H); 7.14–7.22 (m, 3H); 7.28–7.35 (m, 3H); 7.38–7.43 (m, 4H); 7.47 (dd, J=15.6, 10.8 Hz, 1H); 7.63 (d, J=10.8 Hz, 1H); 9.44 (s,1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 125.8, 126.9, 127.7, 128.7, 129.1, 129.7, 129.8, 131.5, 132.9, 135.4, 144.5, 154.2, 190.5. Anal. calcd for $C_{17}H_{14}OSe$: C, 65.18; H, 4.50. Found: C, 64.99; H, 4.65.

4.2.15. Preparation of 8. A solution (1*R*, 2*S*)-(−)-ephedrine (0.165 g, 1 mmol) in EtOH (1.0 mL) was added dropwise to a solution of the **4d** (0.208 g, 1 mmol) in EtOH (1.0 mL) at rt. The reaction was stirred at this temperature for 3 h. The solvent was removed in vacuo and the residue incorporated into SiO_2 and purified by flash column chromatography, eluted with hexane/ethyl acetate (85:15), to afford **8**.[21]

Yield 0.250 g (67%). MS *m*/*z* (rel. int.) 118 (M^+−1, $-C_{10}H_{11}N_2Se$ and OH, 19.2), 110 (17.2), 105 (60.3), 77 (100.0), 58 (63.4); IR (film, cm^{-1}): 2232 (CN). ^1H NMR (200 MHz, $CDCl_3$) δ 0.95 (d, J=7.0 Hz, 3H); 2.33 and 2.34 (2s, 3H); 2.53 (s, broad, 1H); 2.75–3.10 (m, 3H); 3.63 (dd, J=9.0, 6.4 Hz, 0.5H); 3.73 (t, J=7.4 Hz, 0.5H); 4.75–4.78 (m, 1H); 7.20–7.45 (m, 8H); 7.66–7.74 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 9.8, 9.9, 26.3, 26.6, 38.9, 39.0, 56.9, 57.1, 64.6, 64.7, 74.4, 74.7, 119.7, 125.9, 126.0, 126.0, 126.1, 127.2, 128.1, 129.5, 136.2, 142.2, 142.4. Anal. calcd for $C_{19}H_{22}N_2OSe$: C, 61.12; H, 5.94. Found: C, 59.49; H, 5.72.

4.2.16. Preparation of 9. The same procedure as above was

followed using piperidine (0.085 g, 1 mmol). The reaction was performed solvent-free and was stirred at rt for 5 min. The compound **9** was obtained as a yellow oil.[21]

Yield 0.240 g (82%). MS *m/z* (rel. int.) 209 (M^+-1, $-C_5H_{10}N$, 6.6), 182 (7.1), 98 (100.0), 77 (35.5); IR (film, cm^{-1}): 2232 (CN). ^1H NMR (200 MHz, $CDCl_3$) δ 1.35–1.48 (m, 2H); 1.50–1.65 (m, 4H); 2.30–2.52 (m, 4H); 2.77 (d, J=7.4 Hz, 2H); 3.80 (t, J=7.4 Hz, 1H); 7.25–7.40 (m, 3H); 7.68–7.74 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.9, 25.3, 25.7, 54.3, 60.1, 119.9, 126.3, 129.5, 136.2. Anal. calcd for $C_{14}H_{18}N_2Se$: C, 57.34; H, 6.19. Found: C, 56.79; H, 5.97.

4.2.17. Preparation of 2-phenylselanyl-bicyclo[2.2.1]-hept-5-ene-2-carbonitrile (11). A solution of $EtAlCl_2$ (1.4 mmol, 1.0 M solution in hexane) was added dropwise to a solution of nitrile **4d** (1.0 mmol) in dichloromethane (3.0 mL) at −78°C under nitrogen. The reaction was stirred at this temperature for 5 min, cyclopentadiene (0.2 mL) was added, and the mixture was stirred for 2.5 h. The mixture was poured into water and the product was extracted with ethyl acetate (3×25 mL). The organic layer was dried over $MgSO_4$ and the solvent removed in vacuo. The residue was purified by column chromatography over silica gel and eluted with hexane/ethyl acetate (98:2), yielding **11**.

Yield 0.200 g (73%). MS *m/z* (rel. int.) 275 (M^++1, 13.2), 209 (100.0), 182 (67.5), 157 (36.5), 91 (70.8), 77 (48.1); IR (KBr, cm^{-1}): 2229 (CN). ^1H NMR (400 MHz, $CDCl_3$) δ (*endo*) 1.41 (dd, J=12.8, 2.1 Hz, 1H); 1.73–1.75 (m, 2H); 2.45 (dd, J=12.8, 3.7 Hz, 1H); 3.07–3.13 (m, 1H); 3.15–3.17 (m, 1H); 6.15 and 6.31 (2dd, J=5.6, 3.0 Hz, 2H); (*exo*) 1.63–1.67 (m, 1H); 1.89 (dd, J=12.7, 2.5 Hz, 1H); 2.04 (dd, J=12.7, 3.5 Hz, 1H); 2.04–2.07 (m, 1H); 3.00–3.02 (m, 1H); 3.04–3.07 (m, 1H); 6.12 and 6.35 (2dd, J=5.6, 3.0 Hz, 2H); (*endo*+*exo*) 7.35–7.50 (m, 6H); 7.74–7.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (*endo*) 38.6, 40.4, 42.5, 47.8, 52.2, 124.0, 126.9, 129.3, 129.6, 133.5, 136.8, 138.0, (*exo*) 37.9, 41.6, 43.3, 46.7, 50.9, 123.4, 127.1, 129.4, 129.8, 133.5, 137.1, 139.9. Anal. calcd for $C_{14}H_{13}NSe$: C, 61.32; H, 4.78. Found: C, 61.22; H, 4.80.

4.2.18. Preparation of 4-methyl-1-phenylselanyl-cyclohex-3-ene-carbonitrile (10).[21] The same procedure as above was followed using isoprene (0.2 mL). However, the reaction was stirred at −78°C for 1 h and was allowed to reach rt for 1 h and stirred for 2 h at this temperature.

Yield 0.190 g (69%). MS *m/z* (rel. int.) 277 (M^++1, 18.0), 157 (18.7), 120 (79.0), 93 (100.0); IR (film, cm^{-1}): 2225 (CN). ^1H NMR (400 MHz, $CDCl_3$) δ 1.68 (s, 3H); 1.89–1.97 (m, 1H); 2.05–2.26 (m, 3H); 2.48 (AB, J=17.3 Hz, 2H); 5.25–5.30 (m, 1H); 7.35–7.40 (m, 2H); 7.42–7.47 (m, 1H); 7.76–7.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.4, 28.2, 32.4, 34.8, 36.2, 117.0, 122.3, 125.6, 129.4, 130.1, 134.4, 137.9. Anal. calcd For $C_{14}H_{15}NSe$: C, 60.87; H, 5.47. Found: C, 61.63; H, 5.48.

References

1. Zhou, F.; Rosen, J.; Zebrowski-Young, J. M.; Freihammer, P. M.; Detty, M. R. *J. Org. Chem.* **1998**, *63*, 5403. Bella, M.; D'Onofrio, F.; Margarita, R.; Parlanti, G.; Piancatelli, G.; Mangoni, A. *Tetrahedron Lett.* **1997**, *38*, 7917.
2. Aggarwal, V. K.; Anderson, E. S.; Elfyn Jones, D.; Obierey, K. B.; Giles, R. *J. Chem. Soc., Chem. Commun.* **1998**, 1985. Boucher, J.-L.; Stella, L. *Tetrahedron* **1986**, *42*, 3871. Boucher, J.-L.; Stella, L. *Tetrahedron Lett.* **1985**, *26*, 5041. Stella, L.; Boucher, J.-L. *Tetrahedron Lett.* **1982**, *23*, 953. Pochat, F. *Tetrahedron Lett.* **1983**, *24*, 5073. De Cock, Ch.; Piettre, S.; Lahousse, F.; Janousek, Z.; Merényi, R.; Viehe, H. G. *Tetrahedron* **1985**, *41*, 4183.
3. Brownbridge, P.; Durman, J.; Hunt, P. G.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1947. Durman, J.; Hunt, P. G.; Warren, S. *Tetrahedron Lett.* **1983**, *24*, 2113.
4. Martin, C.; Mailliet, P.; Maddaluno, J. *Org. Lett.* **2000**, *2*, 923. Silveira, C. C.; Nunes, M. R. S.; Wendling, E.; Braga, A. L. *J. Organomet. Chem.* **2001**, *623*, 131.
5. Bella, M.; Margarita, R.; Orlando, C.; Orsini, M.; Parlanti, L.; Piancatelli, G. *Tetrahedron Lett.* **2000**, *41*, 561. D'onofrio, F.; Margarita, R.; Parlanti, L.; Piancatelli, G.; Sbraga, M. *J. Chem. Soc., Chem. Commun.* **1998**, 185. D'Onofrio, F.; Parlanti, L.; Piancatelli, G. *Synlett* **1996**, 63. Angoh, A. G.; Clive, D. L. J. *J. Chem. Soc., Chem. Commun.* **1985**, 941.
6. Döpp, D.; Sturm, T. *Liebigs Ann./Recueil* **1997**, 541.
7. Han, D. I.; Oh, D. Y. *Synth. Commun.* **1988**, *18*, 2111. Pochat, F. *Tetrahedron Lett.* **1978**, 2683.
8. (a) Janousek, Z.; Piettre, S.; Gorissen-Hervens, F.; Viehe, H. G. *J. Organomet. Chem.* **1983**, *250*, 197. (b) Piettre, S.; Janousek, Z.; Merényi, R.; Viehe, H. G. *Tetrahedron* **1985**, *41*, 2527.
9. Silveira, C. C.; Perin, G.; Braga, A. L.; Dabdoub, M. J.; Jacob, R. G. *Tetrahedron* **1999**, *55*, 7421 and references therein.
10. Dawson, N. D.; Burger, A. *J. Am. Chem. Soc.* **1952**, *74*, 5312.
11. Dinizo, S. E.; Freerksen, R. W.; Edward Pabst, W.; Watt, D. S. *J. Org. Chem.* **1976**, *41*, 2846.
12. Silveira, C. C.; Perin, G.; Lang, E. S.; Braga, A. L., to be published.
13. Yoshimatsu, M.; Oguri, K.; Ikeda, K.; Gotoh, S. *J. Org. Chem.* **1998**, *63*, 4475.
14. (a) Lerouge, P.; Paulmier, C. *Bull. Soc. Chim. Fr.* **1985**, 1225. (b) Uneyama, K.; Takano, K.; Torii, S. *Tetrahedron Lett.* **1982**, *23*, 1161. (c) Reich, H. J.; Shah, S. K.; Gold, P. M.; Olson, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 3112. (d) Back, T. G.; Dyck, B. P. *Tetrahedron Lett.* **1992**, *33*, 4725.
15. (a) Back, T. G.; Dyck, B. P. *Tetrahedron Lett.* **1992**, 4725. (b) Uneyama, K.; Takano, K.; Torii, S. *Bull. Chem. Soc. Jpn* **1983**, *56*, 2867.
16. Hanessian, S.; Yang, H.; Schaum, R. *J. Am. Chem. Soc.* **1996**, *118*, 2507.
17. Hanessian, S.; Yang, H. *Tetrahedron Lett.* **1997**, *38*, 3155.
18. Torchiarolo, G. C.; D'Onofrio, F.; Margarita, R.; Parlanti, L.; Piancatelli, G.; Bella, M. *Tetrahedron* **1998**, *54*, 15657.
19. Berlin, S.; Engman, L. *Tetrahedron Lett.* **2000**, *41*, 3701.
20. (a) Fringhelli, F.; Taticchi, A. *Dienes in the Diels–Alder Reaction*, Wiley: New York, 1990. (b) Aggarwal, V. K.; Ali, A.; Coogan, M. P. *Tetrahedron* **1999**, *55*, 293.
21. Some of the prepared compounds were not stable to get correct elemental analysis, although they were pure as indicated by ^1H and ^{13}C NMR spectra (exception for **8** and **9**, always contaminated by a very small amount of **4d** formed by a retro-Michael reaction during silica gel column chromatography purification).