Tetrahedron 68 (2012) 10406–10413

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Metallic chalcogenolates mediated modular Michael-aldol cascade reaction: an easy route to multi-functionalized chalcogenides and Morita–Baylis–Hillman adducts

Bruno A. Sousa [a], Arthur F. Keppler [b], Rogério A. Gariani [c], João V. Comasseto [a,d], Alcindo A. Dos Santos [a,*]

[a] Instituto de Química, Universidade de São Paulo, Av. Prof. Lineu Prestes, 748, Cx.P. 26077, CEP 05508-000 São Paulo, Brazil
[b] Centro de Ciências Naturais e Humanas, Universidade Federal do ABC, Avenida Dos Estados, 5001, CEP 09210-170 São Paulo, Brazil
[c] GAPAM – Departamento de Química, Universidade do Estado de Santa Catarina, R. Paulo Malschitzki, S/N, CEP 89219-710 Santa Catarina, Brazil
[d] Universidade Federal de São Pulo, Campus de Diadema, Instituto de Ciências Ambientais, Químicas e Farmacêuticas, Departamento de Ciências Exatas e da Terra, Setor de Química, Rua Prof. Artur Ridel, 275, CEP 09972-270, Jardim Eldorado, Diadema, SP, Brazil

ARTICLE INFO

Article history:
Received 9 July 2012
Received in revised form 28 August 2012
Accepted 4 September 2012
Available online 11 September 2012

Keywords:
Michael-aldol
Cascade reaction
Chalcogens
Organometallics
Morita–Baylis–Hillman

ABSTRACT

Chalcogenolate mediated Michael-aldol cascade reactions consists of a very efficient route to multi-functionalized γ-hydroxichalcogenides. Although, when selenolates are employed, these γ-hydroxichalcogenides can be readily converted into the corresponding Morita–Baylis–Hillman adducts by oxidative elimination of the selenium moiety. In this context, herein we present a complete study on the scope and limitations of this reaction.

1. Introduction

The Michael and the aldol reactions have always been amongst the most important and widely employed reactions in organic synthesis.[1] Another relevant feature of these two reactions is the fact that both transformations can be performed in a cascade fashion.[2–8] For this purpose, metallic organochalcogenolates consists on a key class of nucleophiles due to its high nucleophilicity and low basicity.[9] In special, when metallic selenolates are employed as initial nucleophiles, the resulting adduct can be easily converted into the corresponding Morita–Baylis–Hillman (MBH) adduct by *syn*-selenoxide elimination, as previously described by the group.[10] Since these kinds of nucleophiles can be generated in situ by the reductive cleavage of the elemental chalcogen by the corresponding organometallic, it is worth noting that this methodology completely avoids the manipulation of chalcogen nucleophiles with unpleasant odors and can be applied in many different situations.[11–15]

In this study we decided to evaluate the scope and the limitations of this protocol and its complementarity to the MBH reaction. Focusing in possible synthetic applications of this methodology, we have evaluated the behavior of different chalcogenolates, aldehydes, and Michael acceptors.

2. Results and discussion

Willing to investigate the cascade reaction, we proposed a systematic study in order to evaluate each of the three components involved in this protocol and the most important effects that might drive the reactivity (Fig. 1).

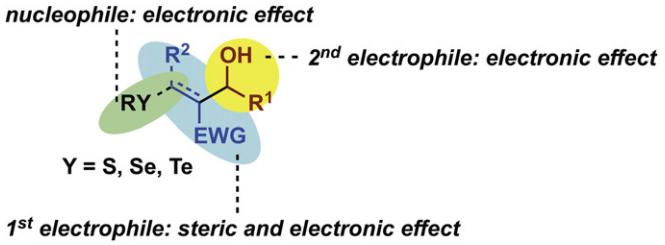


Fig. 1. The possible driving effects of each component of the cascade reaction.

* Corresponding author. Tel.: +55 01130919110; e-mail address: alcindo@iq.usp.br (A.A. Dos Santos).

0040-4020/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2012.09.027

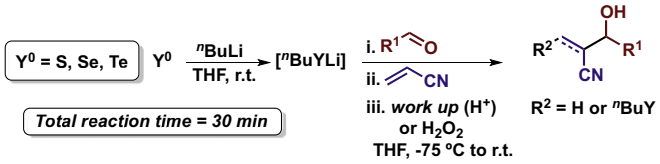
One of the most serious drawbacks of the MBH reaction is the fact that the reaction with electron rich aldehydes, such as alkyl- and electron-donating substituted aryl-aldehydes is quite slow in comparison to electron-poor aldehydes, such as nitro-aromatic ones.[16] Our initial study focused on the evaluation of the behavior of different aldehydes and chalcogenolates. In these initial experiments we have chosen acrylonitrile as the standard Michael acceptor. In order to verify the influence of the electronic effect on the secondary electrophile, some aromatic aldehydes were tested, in which the substituents were varied from electron donating- to electron withdrawing groups.

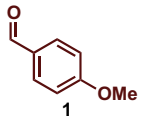
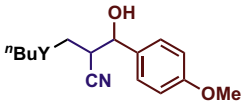
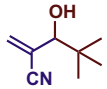
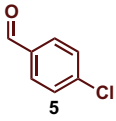
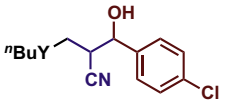
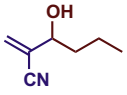
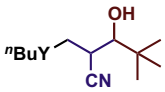
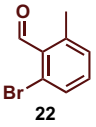
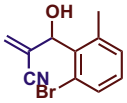
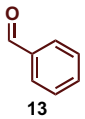
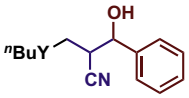
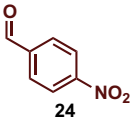
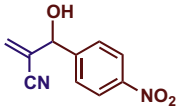
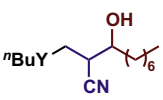
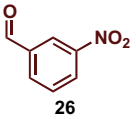
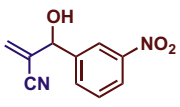
Amongst these examples, some selenides were converted into the corresponding MBH adducts by in situ oxidative elimination, by quenching the reaction with hydrogen peroxide solution (30%). The following Table 1 summarizes the obtained results.

A fair reactivity comparison can be made with aromatic aldehydes with different substituents and an alkyl aldehyde (Table 1, entries 1–4). In comparison to entry 4 (benzaldehyde), the presence of an electron donating group (methoxy, entry 1) or a weak electron-withdrawing group (chlorine, entry 2) does not strongly affect the conversion into the expected aldol product. However, a trend to lowest conversions can be observed when employing more electron deficient aldehydes, such as in entry 2. In this case, this is particularly important to the applicability of this protocol, since no aldehyde activation is necessary and common alkyl aldehydes can be readily employed, leading to the expected aldol products in good yields (Table 1, entries 3 and 5). As can be seen in Table 1 (entries 1–4), the average yield of the sulfides and the selenides produced by this protocol is the same, both leading to the aldol products in good yields. On the other hand, the corresponding tellurides were obtained in lower yields in all the cases. It is important to note that this observation on the tellurides yields is not only related to the reactivity of the intermediate lithium-tellurolate, but also on the stability of the product. In all cases, the cyano-tellurides have shown to be very unstable under various conditions.[17] It is possible to observe the decomposition of these compounds when in solution, during the chromatography and even when stored in low temperatures after purification. In this case, unfortunately it is not possible to affirm that the lower yields are due to a different reactivity without considering the pronounced decomposition during the extraction and isolation procedures.

We have also optimized this protocol for the one-pot preparation of the corresponding MBH adducts, by quenching the reaction with hydrogen peroxide solution. Some examples of MBH adducts have been produced (Table 1, entries 6–10) and as can be seen, alkyl and aromatics aldehydes are tolerated. It is also worth noting that when nitro aldehydes were employed (Table 1, entries 9 and 10) the lowest yields were observed. As depicted in the general reaction scheme in Table 1, the aldehyde is added first into the reaction media, since no reaction between the lithium chalcogenolate and the aldehyde is expected. In the case of the nitro aldehydes, a reaction between the aldehyde and the chalcogenolate clearly takes place. As well as being visually distinct, these reactions furnish the

Table 1
Evaluation of different aldehydes and lithium chalcogenolates



Entry	Aldehyde	Aldol product	Chalcogen yield	Entry	Aldehyde	MBH adduct	Yield
1	 1		a **2**, Y=S, 98% b **3**, Y=Se, 97% c **4**, Y=Te, 65%	6	 9		**19**, 87%
2	 5		a **6**, Y=S, 80% b **7**, Y=Se, 88% c **8**, Y=Te, 60%	7	 20		**21**, 79%
3	 9		a **10**, Y=S, 83% b **11**, Y=Se, 83% c **12**, Y=Te, 60%	8	 22		**23**, 87%
4	 13		a **14**, Y=S, 91% b **15**, Y=Se, 95% c **16**, Y=Te, 60%	9	 24		**25**, 40%
5	 17		**18**, Y=Se, 85%	10	 26		**27**, 32%

All the reactions were conducted under nitrogen atmosphere and in a 3 mmol scale.
In all the cases in which a diastereomeric mixture was obtained, *anti*:*syn*=3:2 d.r., calculated by ^{1}H and ^{77}Se NMR.

corresponding nitro-benzyl alcohol as major byproduct, probably by a Cannizzaro type disproportionation.[18]

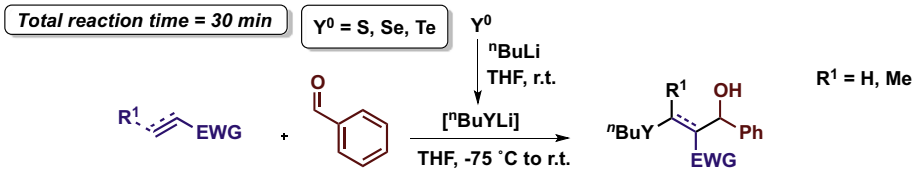
As demonstrated in this initial study on the scope of aldehydes, the methodology is versatile and allows the use of non-activated aldehydes. Unlike the MBH reaction, this methodology is limited by electron deficient aldehydes, which lead to the lower yields of the expected product. In this context, this methodology demonstrates an important complementarity regarding the MBH reaction.

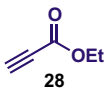
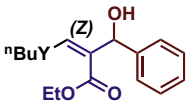
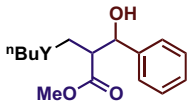
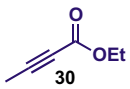
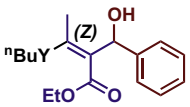
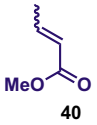
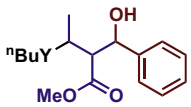
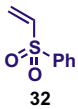
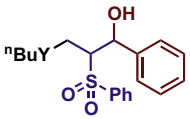
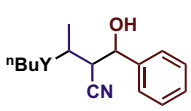
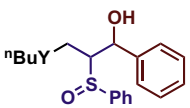
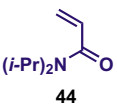
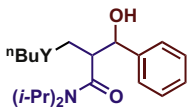
The other important component to be studied in this reaction is the Michael acceptor (or primary electrophile). The structure of these olefins is also of great importance regarding possible applications of this protocol in the synthesis of substances of interest.[19] In this study we have evaluated especially different electron withdrawing groups. As a standard secondary electrophile we have chosen benzaldehyde, since it has furnished good yields and, regarding electronic effects on the carbonyl group benzaldehyde can be considered as a neutral substrate. Within this study, we intended to evaluate Michael acceptors usually employed in the MBH reaction,[16] such as esters, amides, sulfones, sulfoxides, ketones, lactones, and nitriles. Also, in order to compare the stability of the cyano-tellurides shown in Table 1 (entries 1–4), we preferably produced the corresponding tellurides from the Michael-aldol reaction. In those cases in which the telluride has not been obtained in a reasonable yield, a different chalcogen was employed, giving priority to selenium and then sulfur, respectively. The following Table 2 summarizes some of the obtained results.

As depicted in Table 2, we have successfully obtained several tellurides from the Michael-aldol cascade reaction in very good yields. In fact, these tellurides shown in Table 2 are much more stable than the corresponding cyano-derivatives shown in Table 1. These observations lead us to conclude that all the three chalcogens are good nucleophiles in this Michael-aldol cascade reaction. The only exception was found when the vinyl-sulfoxide **35** was employed as the Michael acceptor (Table 2, entry 4). In this case, the corresponding telluride was not observed and the starting material was completely recovered. On the other hand, the corresponding selenide could be prepared from the sulfoxide **35** in a very good yield. However, when the analog sulfone **33** was employed, the expected telluride, as well as the selenide, was obtained in good yield. It is also worth noting that the secondary amide **44** was prepared and tested as a Michael-acceptor only its precursor (acrylamide) failed to give the expected products. When acrylamide was submitted to this established reaction conditions, the oligomerization of this substrate is observed as the temperature rises and there is no consumption of the secondary electrophile (aldehyde). The same behavior is observed when α,β-unsaturated ketones, such as methyl–vinyl ketone (MVK) were employed, suggesting that the enone itself is a more reactive secondary electrophile (by conjugate addition) then the aldehyde, leading to the oligomerization of the Michael acceptor (Scheme 1).

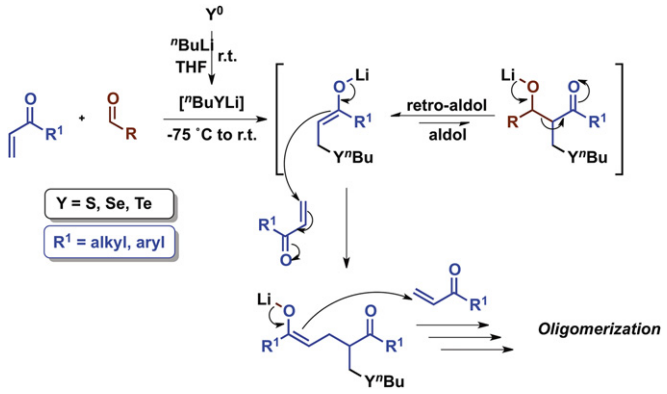
Not only vinylic Michael acceptors (Table 2, entries 3–8) were employed, but also acetylenic esters (Table 2, entries 1 and 2), which lead to the corresponding aldol product in very good yields. It is also very important to observe that the reaction of lithium chalcogenolates with Michael acceptors proceeded with high stereoselectivity, since the resulting double bond is obtained exclusively in the *Z* geometry.[8,20] The geometry of the double bonds in the compounds **29** and **31** (Table 2, entries 1 and 2) was determined by NOESY-NMR experiment and the NOE enhancement observed for these compounds is shown in Fig. 2.

Table 2
Evaluation of different Michael acceptors



Entry	Michael acceptor	Aldol product	Chalcogen, Yield	Entry	Michael acceptor	Aldol product	Chalcogen, Yield
1	 **28**		**29**, Y=Te, 84%	5	 **38**		**39**, Y=Te, 81%
2	 **30**		**31**, Y=Te, 92%	6	 **40**		**41**, Y=Te, 85%
3	 **32**		a **33**, Y=Te, 80% b **34**, Y=Se, 83%	7	 **42**		**43**, Y=Te, 75%
4	 **35**		a Y=Te, 0% b **36**, Y=Se, 93% c **37**, Y=S, 57%	8	 **44**		a **45**, Y=Te, 42% b **46**, Y=Se, 85%

All the reactions were conducted under nitrogen atmosphere and in a 3 mmol scale.
In the cases in which two diastereomers were formed, *anti*:*syn*=3:2 d.r., calculated by ^{1}H and ^{125}Te NMR.



Scheme 1. Proposed lithium chalcogenolate mediated oligomerization of enones.

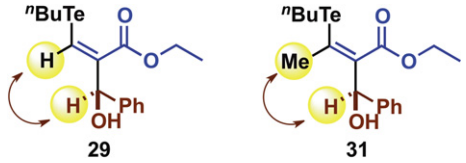
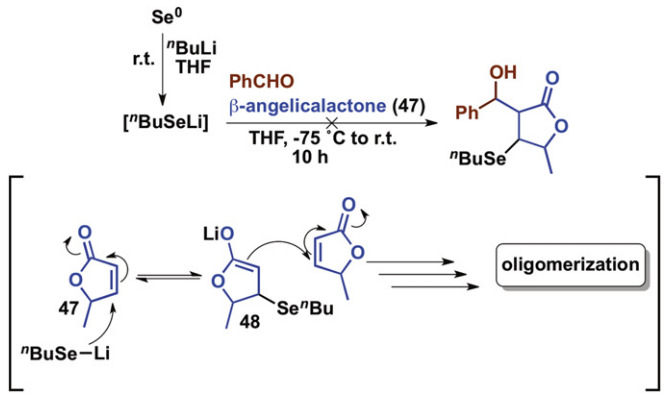


Fig. 2. Key NOE enhancements in the double bond geometry elucidation for compounds **29** and **31**.

A second drawback of the MBH reaction is the fact that β-substituted Michael acceptors cannot be employed when the reaction is performed under atmospheric pressure.[16] Crotonates, for example, requires very high pressures to be employed as Michael acceptors in a MBH reaction. As shown in Table 2 (entries 2, 6, and 7), β-substituted vinylic and acetylenic Michael acceptors have been successfully employed in this protocol, leading to the expected aldol products in very good yields.

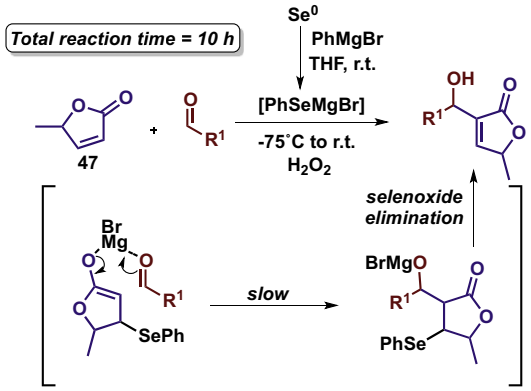
Another very interesting class of Michael acceptors is the α,β-unsaturated lactones. In special, the butenolides are of particular interest since its moiety is present in several classes of natural products that exhibit relevant biological activity.[21] Thus, we decided to test a simple butenolide as a Michael acceptor in this cascade reaction. The commercially available α-angelicalactone was converted into the corresponding α,β-unsaturated isomer **47** (β-angelicalactone). Initially we have submitted the β-angelicalactone to the previously established reaction conditions, employing lithium *n*-butylselenolate as the nucleophile and benzaldehyde as the secondary electrophile. Unfortunately, even within a 10 h reaction time, the aldehyde was not consumed and the oligomerization of the butenolide is observed when the solution warms back to room temperature (Scheme 2).

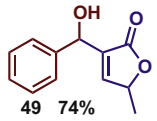
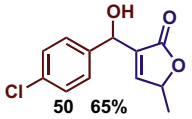
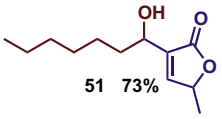
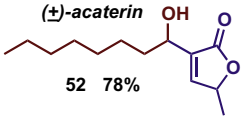
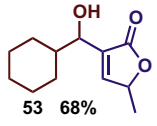
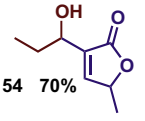
This result suggested that, as the intermediate enolate **48** was not capable of undergoing the aldol reaction with the aldehyde, this carbonyl compound could be activated when a magnesium counterpart is present, driving the intermediate enolate toward the aldol reaction with the carbonyl compound. As a proof of principle experiment, we decided to change the organometallic compounds used to generate the selenium nucleophile. In this case, we have tested the use of a Grignard reagent (PhMgBr) to generate a magnesium selenolate. Fortunately, our experiment was successful. However, the behavior of this butenolide as a Michael acceptor is very different from all the others tested substrates. The reaction still proceeded very slowly but in very reasonable yields. The following Table 3 summarizes the obtained results.



Scheme 2. Butenolide oligomerization lithium *n*-butylselenolate mediated reaction.

Table 3
Examples of β-hydroxi-butenolides



Entry	MBH adduct
1	 49 74%
2	 50 65%
3	 51 73%
4	 (±)-acaterin 52 78%
5	 53 68%
6	 54 70%

All the reactions were conducted under nitrogen atmosphere and in a 3 mmol scale. In all the cases the d.r. was about 1:1.

As can be seen in Table 3, despite the negligible diastereoselectivity, the β-hydroxi-butenolides could be obtained in very reasonable yields. Jauch reported a similar methodology employing the Feringa's lactone as a Michael acceptor in a lithium selenolate mediated MBH reaction.[22–24] In this protocol the elimination of the selenium moiety was thermally achieved. In our protocol, this could not be reproducibly observed, and for this reason the peroxide must be added after the consumption of the aldehyde in order to obtain the butenolide.

As the chalcogenolates presents a very low basicity, the products of γ- and α,γ-di-functionalization of the β-angelicalactone was not observed, unlike on the MBH reaction, in which the enolization of the lactone is quite pronounced.[16]

Like on the other cases, this protocol allows the use of alkyl (Table 3, entries 3–6) as well as aryl (Table 3, entries 1 and 2) aldehydes without the need of an activating group. Amongst the examples it is worth noting that it was possible to prepare the acaterin (Table 3, entry 4), a compound isolated from *Pseudomonas* sp. and an acyl-CoA inhibitor in its racemic form in a single step.

3. Conclusions

We have developed a fast and high yielding route to multifunctionalized chalcogenides and MBH adducts employing in situ generated metallic chalcogenolates. The presented methodology shows some interesting advantages in comparison to the classic MBH reaction, such as the short reaction times and the substrate scope, which presents smaller limitations. On the other hand, the MBH reaction is known to be a very experimentally simple reaction. In this context, our methodology is quite sensitive to the experimental conditions and needs to be performed under oxygen and moisture free conditions. Nevertheless, the complementarity of this protocol regarding the MBH reaction and the substrate scope makes this protocol a valuable alternative to MBH adducts and derivatives. In this context, the asymmetric version of this reaction is under development in our group, looking forward to apply this methodology in the stereoselective synthesis of natural products of interest.

4. Experimental section

4.1. 2-((Butylthio)methyl)-3-hydroxy-3-(4-methoxyphenyl) propanenitrile (2)

To a stirred suspension of the elemental chalcogen (3 mmol) in THF (45 mL), a 2 mol L^{-1} solution of *n*-butyl-lithium in hexanes was added dropwise until the total consumption of the chalcogen (1.0 equiv). The resulting colorless solution was cooled down to −75 °C and then an equivalent amount of the aldehyde was added (4-anisaldehyde, 3 mmol, 0.36 mL), followed by the equimolar addition of the Michael acceptor (acrylonitrile, 3 mmol, 0.22 mL). The reaction is kept under stirring at −75 °C for 10 min and then the solution is allowed to warm back to room temperature (about 20 min). The reaction is then quenched with saturated NaCl solution (20 mL) and then extracted with AcOEt (3×20 mL). The combined organic phases were dried under $MgSO_4$ and concentrated under reduced pressure. In those cases in which the selenoxide elimination step was performed, hydrogen peroxide 30% solution (2 mL, 6 equiv) was added after quenching the reaction with NaCl solution and the reaction mixture was kept under stirring for an additional 10 min. The crude oil was purified by column chromatography using silica gel and a hexanes/ethyl acetate (4:1) mixture as eluent to afford **2** as a clear oil in 98% (0.8214 g) isolated yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.45–7.28 (m, 2H), 7.01–6.88 (m, 2H), 4.97 (dt, *J*=7.0, 3.8 Hz, 1H), 3.84 (s, 3H), 3.26–2.55 (m, 6H), 1.69–1.34 (m, 4H), 0.94 (t, *J*=7.1 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 159.92, 159.82, 132.03, 131.48, 127.69, 127.29, 119.33, 119.25, 114.15, 114.09, 72.48, 72.11, 55.28, 42.04, 41.43, 32.51, 31.46, 31.14, 30.35, 21.81, 13.59. IR (KBr, cm^{-1}): 833; 1033; 1176; 1249; 1512; 2931; 3452. HRMS: requires ($C_{15}H_{21}NNaO_2S$): 302.1191; found: 302.1188.

4.2. 2-((Butylselanyl)methyl)-3-hydroxy-3-(4-methoxyphenyl)propanenitrile (3)

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.45–7.28 (m, 2H), 7.00–6.86 (m, 2H), 4.85 (dt, *J*=7.0, 3.8 Hz, 1H), 3.80 (s, 3H), 3.22–2.52 (m, 6H), 1.72–1.45 (m, 4H), 1.10 (t, *J*=7.1 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 159.92, 159.82, 132.03, 131.48, 127.69, 127.29, 119.33, 119.25, 114.15, 114.09, 72.48, 72.11, 55.28, 42.04, 41.43, 32.51, 31.46, 31.14, 30.35, 21.81, 13.59. IR (KBr, cm^{-1}): 833; 1033; 1176; 1249; 1512; 1612; 2927; 2958; 3456. HRMS: requires ($C_{15}H_{21}NNaO_2Se$): 350.0635; found: 350.0633.

4.3. 2-((Butyltellanyl)methyl)-3-hydroxy-3-(4-methoxyphenyl)propanenitrile (4)

^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.53–7.18 (m, 2H), 7.10–6.78 (m, 2H), 4.93–4.74 (m, 1H), 3.82 (s, 3H), 3.16 (dddd, *J*=26.5, 11.8, 6.2, 2.8 Hz, 2H), 2.90–2.56 (m, 4H), 1.86–1.60 (m, 2H), 1.52–1.30 (m, 2H), 0.92 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 159.7, 132.0, 131.7, 127.8, 127.5, 120.3, 114.1, 114.0, 74.5, 55.3, 44.0, 43.6, 33.9, 24.9, 13.4, 4.9, −1.2, −1.9. ^{125}Te NMR (63 MHz, $CDCl_3$) δ: 262.44, 258.06. IR (KBr, cm^{-1}): 732; 833; 1033; 1176; 1249; 1303; 1512; 1612; 2835; 2870; 2927; 2958; 3452. HRMS: requires ($C_{15}H_{21}NNaO_2Te$): 400.0532; found: 400.0527.

4.4. 2-((Butylthio)methyl)-3-(4-chlorophenyl)-3-hydroxypropanenitrile (6)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.95 (t; *J*=7.3 Hz; 3H); 1.45 (sex, *J*=7.3 Hz, 2H); 1.64 (qui, *J*=7.3 Hz, 2H); 2.63–2.72 (m, 3H); 2.78–2.82 (m, 1H); 3.00–3.20 (q, *J*=7.0 Hz, 1H); 5.00 (d, *J*=6.5 Hz, 1H); 7.4 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 13.6; 21.8; 26.0; 30.2; 31.2; 32.6; 41.3; 41.9; 64.5; 71.6; 72.2; 119.0; 128.3; 129.2; 137.9. IR (film, cm^{-1}): 824, 1014, 1088, 1490, 2250, 2866, 2932, 2961, 3447. HRMS: requires ($C_{14}H_{19}NOSNa$): 306.0695; found: 306.0694.

4.5. 2-((Butylselanyl)methyl)-3-(4-chlorophenyl)-3-hydroxypropanenitrile (7)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.9 (t; *J*=7.3 Hz; 3H); 1.42 (sex, *J*=7.3 Hz; 2H); 1.63 (qui; *J*=7.3 Hz; 2H); 2.68–2.74 (m, 3H); 2.80–2.85 (m, 1H); 3.01–3.20 (q; *J*=7.0 Hz; 1H); 4.97–5.02 (d; *J*=6.5 Hz; 1H); 7.38 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 13.5; 20.5; 21.3; 22.8; 25.2; 32.3; 42.2; 42.7; 72.2; 72.5; 119.3; 119.5; 127.4; 127.9; 128.8; 128.9; 134.3; 134.4; 138.0; 138.6. ^{77}Se NMR (95.338 MHz, $CDCl_3$), δ: 161.8, 163.4. IR (film, cm^{-1}): 826, 1014, 1091, 1491, 2246, 2872, 2929, 2958, 3445. HRMS: requires ($C_{14}H_{19}NOSeNa$): 354.0139; found: 354.0132.

4.6. 2-((Butyltellanyl)methyl)-3-(4-chlorophenyl)-3-hydroxypropanenitrile (8)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.95 (t; *J*=7.3 Hz; 3H); 1.45 (sex, *J*=7.3 Hz; 2H); 1.64 (qui; *J*=7.3 Hz; 2H); 2.63–2.72 (m, 3H); 2.78–2.82 (m, 1H); 3.00–3.20 (q; *J*=7.0 Hz; 1H); 5.00 (d; *J*=6.5 Hz; 1H); 7.4 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 13.6; 21.8; 26.0; 30.2; 31.2; 32.6; 41.3; 41.9; 64.5; 71.6; 72.2; 119.0; 128.3; 129.2; 137.9. IR (film, cm^{-1}): 824, 1014, 1088, 1490, 2250, 2866, 2932,

2961, 3447. HRMS: requires ($C_{14}H_{19}NOSNa$): 306.0695; found: 306.0694.

4.7. 2-((Butylthio)methyl)-3-hydroxy-4.4-dimethylpentanenitrile (10)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.92 (t, J=7.2 Hz, 3H); 1.02 (s, 9H); 1.42 (sext, J=7.2 Hz, 2H); 1.58 (qt, J=7.2 Hz, 2H); 2.60 (t, J=7.2 Hz, 3H); 2.88–2.97 (m, 3H); 3.50 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 13.6; 21.8; 26.0; 31.5; 32.4; 34.0; 34.3; 35.5; 77.5; 119.7. IR (film, cm^{-1}): 743; 919; 1015; 1077; 1366; 1420; 1466; 1480; 1624; 1708; 2244; 2873; 2932; 2959; 3478.

4.8. 2-((Butylselanyl)methyl)-3-hydroxy-4.4-dimethylpentanenitrile (11)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.95 (t, J=7.3 Hz, 3H); 1.02 (s, 9H); 1.42 (sext, J=7.3 Hz, 2H); 1.66 (qt, J=7.3 Hz, 2H); 2.51 (s, 1H); 2.68 (t, J=7.3 Hz, 2H); 2.88–3.00 (m, 3H); 3.46 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 13.5; 22.8; 24.8; 25.1; 26.0; 32.4; 35.0; 35.6; 78.6; 119.8. ^{77}Se NMR (95 MHz, $CDCl_3$), δ: 163.5. IR (film, cm^{-1}): 721; 929; 1022; 1080; 1476; 2244; 2871; 2935; 2958; 3450.

4.9. 2-((Butyltellanyl)methyl)-3-hydroxy-4.4-dimethylpentanenitrile (12)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.92 (t, J=7.3 Hz, 3H); 1.02 (s, 9H); 1.40 (sext, J=7.2 Hz, 2H); 1.75 (qt, J=7.3 Hz, 2H); 2.77 (t, 7.2 Hz, 3H); 2.91–3.04 (m, 3H); 3.50 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 2.9; 4.9; 13.4; 25.0; 26.0; 34.0; 35.7; 36.2; 80.6; 120.2. ^{125}Te NMR (157.79 MHz, $CDCl_3$), δ: 251.40. IR (film, cm^{-1}): 744; 921; 1077, 1362; 1466; 2244; 2870; 2931; 2962; 3466.

4.10. 2-((Butylthio)methyl)-3-hydroxy-3-phenylpropanenitrile (14)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.94 (dt; J=6.5 Hz; J=3.0 Hz; 3H); 1.43 (m; 2H); 1.54 (m; 2H); 2.63 (m; 2H); 2.75–2.87 (m; 2H); 3.00 (m, 1H); 3.61 (s; 3H); 5.03 (d, J=Hz; 1H); 7.26–7.31 (m, 5H) ^{13}C NMR (125 MHz, $CDCl_3$), δ: 21.8; 30.1; 31.2; 31.5; 32.5; 41.4; 42.0; 72.4; 72.8; 119.0; 119.3; 126.0; 126.4; 128.8; 128.9; 129.0; 139.4; 140.0. IR (film, cm^{-1}): 702; 1060; 1454; 1494; 1706; 1813; 1890; 1958; 2246; 2929; 2957; 3449.

4.11. 2-((Butylselanyl)methyl)-3-hydroxy-3-phenylpropanenitrile (15)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.91 (t; J=7.5 Hz; 3H); 1.39 (sext; J=7.5 Hz; 2H); 1.59–1.66 (m; 3H); 2.67–2.82 (m; 4H); 3.18–3.24 (m; 1H); 4.94–5.01 (m; 1H); 7.20 (d; J=7.5 Hz; 1H); 7.30 (dd; J=8.0 Hz; J=11.5 Hz; 2H); 7.37–7.45 (m; 2H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 13.5; 20.4; 21.5; 22.8; 25.2; 32.4; 42.7; 73.6; 119.4; 126.0; 126.4; 128.8; 129.5; 136.4; 136.9; 138.7; 139.4; 139.9. ^{77}Se NMR (95.338 MHz, $CDCl_3$), δ: 162.2 and 163.8. IR (film, cm^{-1}): 701; 1042; 1454; 1765; 1814; 1889; 1956; 2245; 2871; 2929; 2957; 3447. HRMS: requires ($C_{14}H_{19}NOSeNa$): 320.0529; found: 320.0517.

4.12. 2-((Butyltellanyl)methyl)-3-hydroxy-3-phenylpropanenitrile (16)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.91 (t; J=7.5 Hz; 3H); 1.36 (sext; J=7.5 Hz; 2H); 1.68–1.75 (m; 2H); 2.41–2.51 (m; 1H); 2.79–2.84 (m; 4H); 3.11–3.27 (m; 1H); 4.91–4.93 (m; 1H); 7.36–7.43 (m; 5H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 4.9; 5.0; 13.3; 24.9; 34.0; 43.5; 44.0; 74.9; 119.9; 120.1; 126.2; 126.5; 128.7; 128.8; 129.9; 139.5; 139.9. ^{125}Te NMR (157.79 MHz, $CDCl_3$), δ: 253.1 and 256.9. IR (film, cm^{-1}): 1040, 1454, 1812, 1888, 1956, 2244, 2870, 2957, 3449. HRMS: requires ($C_{14}H_{19}NOTeNa$): 370.0426; found: 370.0422.

4.13. 2-((Butylselanyl)methyl)-3-hydroxydecanenitrile (18)

^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.85 (dtt, J=6.7, 4.2, 2.5 Hz, 1H), 3.05–2.59 (m, 5H), 2.32 (dd, J=28.3, 6.3 Hz, 1H), 1.78–1.16 (m, 16H), 0.91 (q, J=7.1 Hz, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 120.08, 119.33, 71.47, 70.82, 40.89, 40.63, 35.62, 34.34, 32.41, 31.69, 29.26, 29.23, 29.10, 25.58, 25.38, 25.16, 22.84, 22.56, 21.61, 20.56, 14.03, 13.51. ^{77}Se NMR (38 MHz, $CDCl_3$) δ: 163.33, 161.47. IR (KBr, cm^{-1}): 1049; 1199; 1261; 1419; 1462; 2858; 2957; 2954; 3475. HRMS: requires ($C_{15}H_{29}NNaOSe$): 342.1312; found: 342.1309.

4.14. 3-Hydroxy-4.4-dimethyl-2-methylenepentanenitrile (19)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.00 (s; 9H); 2.00 (s; 1H); 3.95 (s; 1H); 5.96 (s; 1H); 6.00 (s; 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 25.6; 35.7; 79.8; 118.2; 124.7; 132.6. IR (film, cm^{-1}): 951; 1015; 1074; 1366; 1480; 1618; 1904; 2228; 2873; 2908; 2960; 3481.

4.15. 3-Hydroxy-2-methylenehexanenitrile (21)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.97 (t; J=7.4 Hz; 3H); 1.34–1.52 (m; 2H); 1.61–2.11 (m; 2H); 4.25 (dd; J=5.3 Hz; 1H); 5.97 (s; 1H); 5.99 (s; 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 13.7; 18.4; 37.8; 72.1; 117.0; 127.0; 129. IR (film, cm^{-1}): 948; 1466; 1713; 2227; 2875; 2936; 2962; 3444.

4.16. 2-((2-Bromo-6-methylphenyl)(hydroxy)methyl)acrylonitrile (23)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.83 (s; 3H); 5.50 (s; 1H); 6.02 (s; 2H); 6.78 (d; J=8.7 Hz; 1H); 7.41 (dd; J=2.4 Hz; 8.7 Hz; 1H); 7.48 (d; J=2.4 Hz; 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 55.7; 69.4; 112.7; 113.4; 116.9; 125.3; 129.4; 130.4; 130.5; 132.6; 155.6. IR (film, cm^{-1}): 622; 1026; 1254; 1487; 2228; 2849; 2925; 2962; 3441.

4.17. 2-(Hydroxy(4-nitrophenyl)methyl)acrylonitrile (25)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 5.4 (s; 1H); 6.1 (s; 1H); 6.2 (s; 1H); 7.6 (t; J=7.9 Hz; 1H); 7.7 (d; J=7.9 Hz; 1H); 8.2 (dd; J=7.9 Hz; 1.8 Hz; 1H); 8.2 (t; J=1.8 Hz; 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 73.4; 116.2; 124.1; 125.4; 127.4; 130.9; 145.9; 148.1. IR (film, cm^{-1}): 1062; 1348; 1520; 1607; 1715; 1804; 1935; 2230; 3081; 3113; 3456.

4.18. 2-(Hydroxy(3-nitrophenyl)methyl)acrylonitrile (27)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 5.4 (s; 1H); 6.1 (s; 1H); 6.2 (s; 1H); 7.6 (d; J=8.7 Hz; 2H); 8.2 (d; J=8.7 Hz; 2H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 73.4; 116.2; 124.1; 125.4; 127.4; 130.9; 145.9; 148.1. IR (film, cm^{-1}): 1057; 1351; 1530; 2230; 2873; 2926; 3092; 3450.

4.19. (*Z*)-Ethyl 3-(butyltellanyl)-2-(hydroxy(phenyl)methyl) acrylate (29)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.94 (t, J=7.5 Hz, 3H); 1.21 (t, J=7.2 Hz, 3H); 1.41 (sext, J=7.5 Hz, 2H); 1.81 (qt, J=7.5 Hz, 2H); 2.57 (t, J=7.5 Hz, 2H); 2.71 (d, J=4.8 Hz, 1H); 4.20 (q, J=7.5 Hz, 2H); 5.63 (d, J=4.2 Hz, 1H); 7.35–7.36 (m, 5H); 8.42 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 9.9; 13.5; 14.2; 25.0; 33.9; 61.1; 74.7; 126.7; 127.5; 128.2; 132.2; 136.2; 142.2; 167.1. ^{125}Te NMR (157.79 MHz, $CDCl_3$), δ: 385.3. IR (film, cm^{-1}): 699; 1025; 1183; 1281; 1559; 1679; 1806; 1887; 1950; 2871; 2925; 2957; 3456. HRMS: requires ($C_{16}H_{22}O_3TeNa$): 415.0529; found: 415.0515.

4.20. (*Z*)-Ethyl 3-(butyltellanyl)-2-(hydroxy(phenyl)methyl) but-2-enoate (31)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.94 (t, J=7.4 Hz, 3H); 1.02 (t, J=7.1 Hz, 3H); 1.44 (sext, J=7.4 Hz, 2H); 1.77 (qt, J=7.4 Hz, 2H); 2.51 (s, 3H); 2.63 (dt, J=3.2, 7.4 Hz, 2H); 3.40 (d, J=10.8 Hz, 1H); 4.05–4.16 (m, 2H); 6.00 (d, J=10.8 Hz, 1H); 7.19–7.34 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 7.9; 8.8; 13.4; 13.9; 23.4; 25.3; 32.9; 61.0; 70.4; 124.9; 126.7; 128.1; 131.7; 143.1; 146.7; 167.7. ^{125}Te NMR (157.79 MHz, $CDCl_3$), δ: 628.5. IR (film, cm^{-1}): 708; 747; 765; 1012; 1810; 1887; 1953; 2980; 3472. HRMS: requires ($C_{17}H_{24}O_3TeNa$): 429.0685; found: 429.0684.

4.21. 3-(Butyltellanyl)-1-phenyl-2-(phenylsulfonyl)propan-1-ol (33)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.78 (t, J=7.2 Hz, 3H); 1.12 (sext, J=7.2 Hz, 2H); 1.36 (qt, J=7.2 Hz, 2H); 2.19 (t, J=7.2 Hz, 2H); 2.79 (dd, J=5.1, 13.2 Hz, 1H); 3.02 (dd, J=6.6, 13.2 Hz, 1H); 3.56 (d, J=2.7 Hz, 1H); 3.71 (t, J=6.6 Hz, 1H); 5.53 (s, 1H); 7.28–7.33 (m, 5H); 7.52–8.10 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 6.1; 13.3; 24.9; 33.7; 69.5; 75.2; 125.7; 128.5; 128.6; 128.9; 129.5; 133.7; 134.3; 137.2; 139.3. ^{125}Te NMR (157.9 MHz, $CDCl_3$), δ: 379.5. IR (film, cm^{-1}): 689; 746; 1305; 1447; 2870; 2926; 2956; 3503. HRMS: requires ($C_{19}H_{24}O_3STeNa$): 485.0406; exp: 485.0404.

4.22. 3-(Butylselanyl)-1-phenyl-2-(phenylsulfonyl)propan-1-ol (34)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.76 (t, J=7.5 Hz, 3H); 1.04–1.25 (m, 4H); 1.93–2.08 (m, 2H); 2.89 (t, J=6.6 Hz, 2H); 2.89 (t, J=6.6 Hz, 2H); 3.53–3.57 (m, 1H); 5.62 (s, 1H); 7.27–7.37 (m, 5H); 7.59–7.75 (m, 3H); 7.98–8.00 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 13.5; 13.6; 22.9; 25.6; 25.7; 32.1; 69.6; 73.8; 125.7; 128.0; 128.6; 129.0; 129.6; 134.4; 137.5; 139.5. ^{77}Se NMR (95 MHz, $CDCl_3$), δ: 220.9. IR (film, cm^{-1}): 689; 734; 1319; 1448; 1700; 1774; 1816; 2871; 2927; 2956; 3505. HRMS: requires ($C_{17}H_{24}O_3TeNa$): 435.0509; found: 435.0510.

4.23. 3-(Butylselanyl)-1-phenyl-2-(phenylsulfinyl)propan-1-ol (36)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.82 (t, J=7.0 Hz, 3H); 1.12 (m, 3H); 1.37 (qt, J=7.0 Hz, 2H); 2.28–2.39 (m, 4H); 3.38 (dt, J=5.5, 9.0 Hz, 1H); 5.20 (d, J=9.0 Hz, 1H); 7.30–7.43 (m, 5H); 7.54–7.56 (m, 3H); 7.83–7.85 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 25.8; 55.5; 120.7; 124.0; 124.7; 126.9; 129.2; 129.3; 129.4; 130.0; 131.1; 131.2; 142.8; 143.0; 143.3. ^{77}Se NMR (95 MHz, $CDCl_3$), δ: 154.4. HRMS: requires ($C_{19}H_{24}O_2SSeNa$): 419.0560; found: 419.0548.

4.24. 3-(Butylthio)-1-phenyl-2-(phenylsulfinyl)propan-1-ol (37)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.85 (t, J=7.2 Hz, 3H); 1.30–1.35 (m, 4H); 2.34–2.42 (m, 2H); 2.65–2.69 (m, 1H); 2.88 (dd, J=3.0, 14.7 Hz, 1H); 3.22 (dd, J=10.8, 14.7 Hz, 1H); 5.27 (s, 1H); 7.04–7.06 (m, 2H); 7.23–7.32 (m, 3H); 7.61–7.77 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 13.5; 21.8; 25.5; 31.3; 32.3; 70.2; 70.8; 124.4; 125.2; 127.5; 128.4; 129.6; 131.3; 140.3; 141.7. HRMS: requires ($C_{19}H_{24}O_2SSeH$): 349.1296; found: 349.1287.

4.25. Methyl-2-((butyltellanyl)methyl)-3-hydroxy-3-phenylpropanoate (39)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.90 (t; J=7.5 Hz; 3H); 1.35 (sext; J=7.5 Hz; 2H); 1.68 (quint; J=7.5 Hz; 2H); 2.63 (tap, J=7.5 Hz; 2H); 2.68 (d; J=11.5 Hz; 1H); 2.91 (d; J=11.5 Hz; 1H); 3.19 (d; J=5.0 Hz; 1H); 3.73 (s, 3H); 4.90 (dap; J=5.0 Hz; 1H); 7.27–7.31 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 11.1; 13.4; 19.2; 24.8; 34.0; 52.1; 52.9; 78.9; 127.4; 127.9; 128.0; 139.8; 176.2. ^{125}Te NMR (157.79 MHz, $CDCl_3$), δ: 171.5; 192.8. IR (film, cm^{-1}): 704, 1021, 1154, 1452, 1715, 2871, 2930, 2955, 3421.

4.26. Methyl 3-(butyltellanyl)-2-(hydroxy(phenyl)methyl)butanoate (41)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.90 (t; J=7.3 Hz; 3H); 1.38 (sext; J=7.3 Hz; 2H); 1.55–1.61 (m; 6H); 2.48–2.55 (m; 2H); 2.83 (dd; J=7.5, 5.7 Hz; 1H); 2.95 (qt; J=7.5 Hz; 1H); 3.60 (s; 3H); 5.07 (d; J=5.7 Hz; 1H); 7.31 (s; 5H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 13.5; 22.0; 23.0; 23.4; 32.3; 33.0; 51.7; 59.0; 64.1; 72.6; 127.5; 128.2; 128.5; 133.5; 140.3; 173.5. ^{77}Se NMR (95.34 MHz, $CDCl_3$), δ: 170.2; 189.7 IR (film, cm^{-1}): 828; 1163; 1491; 1733; 3461; 2871; 2927; 2956.

4.27. 3-(Butyltellanyl)-2-(hydroxy(phenyl)methyl)butanenitrile (43)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.93 (qt, J=7.5 Hz, 3H); 1.31–1.45 (m, 2H); 1.67–1.86 (m, 5H); 1.69–2.83 (m, 2H); 3.08 (dd, J=5.1, 7.2 Hz, 1H); 3.19 (qt, J=1.0, 7.2 Hz, 1H); 3.32–3.48 (m, 1H); 5.11 (d, J=5.1 Hz, 1H); 7.46–7.50 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 4.2; 4.5; 10.2; 12.3; 13.3; 13.4; 20.9; 22.4; 25.1; 34.1; 50.8; 51.2; 73.4; 74.3; 118.2; 118.3; 125.9; 126.5; 128.9; 129.0; 129.1; 140.1; 140.3. ^{125}Te NMR (157.9 MHz, $CDCl_3$), δ: 454.6; 472.4. IR (film, cm^{-1}): 701; 762; 1025; 1042; 1454; 2240; 2870; 2925; 2957; 3455. HRMS: requires ($C_{15}H_{21}NOTeNa$): 384.0583; found: 384.0569.

4.28. 2-((Butylselanyl)methyl)-3-hydroxy-*N*,*N*-diisopropyl-3-phenylpropanamide (45)

^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.43 (d, J=6.6 Hz, 3H); 0.91 (t, J=7.3 Hz, 3H); 1.11 (d, J=6.6 Hz, 3H); 1.21 (d, J=6.8 Hz, 3H); 1.34 (d, J=6.8 Hz, 3H); 1.38 (sext, J=7.3 Hz, 2H); 1.67 (s, 1H); 1.74 (qt, J=7.3 Hz, 2H); 2.71 (t, J=7.3 Hz, 2H); 3.10 (dd, J=3.6, 7.4 Hz, 2H); 3.17–3.23 (m, 2H); 3.70 (qt, J=7.0 Hz, 1H); 4.90 (dd, J=2.9, 8.8 Hz, 1H); 5.67 (d, J=8.8 Hz, 1H); 7.18–7.25 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 3.0; 4.2; 13.4; 20.0; 20.3; 20.4; 21.0; 25.0; 34.2; 46.4; 49.3; 49.8; 76.6; 125.7; 127.2; 128.2; 143.7; 173.7. ^{125}Te NMR (157.79 MHz, $CDCl_3$), δ: 212.0. HRMS: requires ($C_{20}H_{33}NO_2TeNa$): 472.1471; found: 472.1469.

4.29. 2-((Butyltellanyl)methyl)-3-hydroxy-*N*,*N*-diisopropyl-3-phenylpropanamide (46)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.88 (t, J=7.5 Hz, 3H); 0.97 (d, J=6.5 Hz, 3H); 1.27 (d, J=6.5 Hz, 3H); 1.33 (d, J=6.5 Hz, 3H); 1.34 (qt, J=7.5 Hz, 2H); 1.43 (d, J=6.5 Hz, 3H); 1.51–1.58 (m, 2H); 2.42–2.54 (m, 2H); 2.79 (dd, J=4.0, 12.0 Hz, 1H); 3.00 (dd, J=11.0, 12.0 Hz, 1H); 3.20 (dt, J=4.0, 11.0 Hz, 1H); 3.42 (s, 1H); 4.15 (hept, J=6.5 Hz, 2H); 4.90 (d, J=4.0 Hz, 1H); 7.24–7.40 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 13.5; 20.5; 20.6; 20.7; 20.8; 20.9; 22.9; 24.9; 32.5; 46.3; 49.2; 50.3; 75.2; 126.2; 127.5; 128.3; 141.7; 173.7. ^{77}Se NMR (95 MHz, $CDCl_3$), δ: 144.4. HRMS: requires ($C_{20}H_{33}NO_2SeNa$): 422.1574; found: 422.1570.

4.30. 3-(Hydroxy(phenyl)methyl)-5-methylfuran-2(5*H*)-one (49)

To a stirred suspension of elemental selenium (3 mmol) in THF (30 mL), a 2 M solution of PhMgBr in THF was added dropwise until the total consumption of the chalcogen (1.0 equiv). The resulting colorless solution was cooled down to −75 °C and then an equivalent amount of the aldehyde was added (benzaldehyde, 3 mmol, 0.30 mL), followed by the equimolar addition of the β-angelicalactone (3 mmol, 0.294 g). The reaction is kept under stirring at

−75 °C for 10 min and then the solution is allowed to warm back to room temperature (about 20 min). The reaction is then quenched with saturated NaCl solution (20 mL) and then hydrogen peroxide 30% solution (2 mL, 6 equiv) was added and the reaction mixture was kept under stirring for an additional 10 min. The mixture was extracted with AcOEt (3×20 mL). The combined organic phases were dried under $MgSO_4$ and concentrated under reduced pressure. The crude oil was purified by column chromatography using silica gel and a hexanes/ethyl acetate (1:1) mixture as eluent to afford **49** as a colorless oil in 74% (0.4533 g) isolated yield. ^{1}H NMR (200 MHz, $CDCl_3$), δ: 7.52–7.32 (m, 6H), 7.09 (dt, J=7.4, 1.5 Hz, 1H), 5.60 (t, J=1.6 Hz, 1H), 5.08 (qq, J=6.9, 1.8 Hz, 1H), 3.23 (s, 2H), 1.45 (d, J=11.9 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$), δ: 172.47, 150.58, 150.48, 140.17, 136.22, 136.11, 128.70, 128.36, 126.51, 126.46, 78.16, 69.14, 69.07, 18.81, 14.21. IR (KBr, cm^{-1}): 702; 829; 1014; 1083; 1195; 1319; 1747; 3414. HRMS: requires ($C_{12}H_{12}NaO_3$): 227.0684; found: 227.0684.

4.31. 3-((4-Chlorophenyl)(hydroxy)methyl)-5-methylfuran-2(5*H*)-one (50)

^{1}H NMR (200 MHz, $CDCl_3$), δ: 7.40 (s, 4H), 7.06 (t, J=1.5 Hz, 1H), 5.60 (dt, J=3.5, 1.6 Hz, 1H), 5.11 (qt, J=6.9, 1.6 Hz, 1H), 1.77 (d, J=6.9 Hz, 1H), 1.49–1.41 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$), δ: 172.30, 150.54, 138.61, 135.83, 134.18, 128.90, 127.88, 78.22, 68.55, 18.80. IR (KBr, cm^{-1}): 540; 1014; 1087; 1195; 1319; 1408; 1489; 1747; 2981; 3414. HRMS: requires ($C_{12}H_{11}ClNaO_3$): 261.0294; found: 261.0285.

4.32. 3-(1-Hydroxyheptyl)-5-methylfuran-2(5*H*)-one (51)

^{1}H NMR (200 MHz, $CDCl_3$), δ: 7.22 (d, J=1.4 Hz, 1H), 5.10 (qt, J=6.8, 1.6 Hz, 1H), 4.51 (dt, J=6.9, 3.5 Hz, 1H), 2.72 (s, 1H), 1.57–1.21 (m, 9H), 0.96–0.86 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$), δ: 172.68, 149.33, 136.23, 77.99, 67.05, 35.49, 31.74, 29.05, 25.24, 22.60, 18.97, 14.08. IR (KBr, cm^{-1}): 1022; 1080; 1114; 1203; 1319; 1454; 1747; 2858; 2927; 3441. HRMS: requires ($C_{12}H_{20}NaO_3$): 235.1310; found: 235.1308.

4.33. 3-(1-Hydroxyoctyl)-5-methylfuran-2(5*H*)-one (52)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 7.14 (t, J=1.5 Hz, 1H), 5.03 (qq, J=6.8, 1.7 Hz, 1H), 4.48 (ddq, J=8.2, 5.0, 1.7 Hz, 1H), 1.83–1.64 (m, 2H), 1.43 (d, J=6.8 Hz, 4H), 1.40–1.23 (m, 11H), 0.91–0.85 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$), δ: 172.32, 148.89, 136.43, 77.70, 67.12, 35.57, 31.71, 29.28, 29.09, 25.18, 22.52, 18.87, 13.89.

4.34. 3-(Cyclohexyl(hydroxy)methyl)-5-methylfuran-2(5*H*)-one (53)

^{1}H NMR (200 MHz, $CDCl_3$), δ: 7.18 (t, J=1.4 Hz, 1H), 5.08 (qt, J=6.8, 1.6 Hz, 1H), 4.27 (d, J=5.5 Hz, 1H), 1.73 (tdd, J=15.8, 8.0, 3.2 Hz, 7H), 1.46 (d, J=6.8 Hz, 3H), 1.33–0.99 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 172.70, 150.55, 134.73, 78.03, 71.88, 42.01, 29.51, 27.29, 26.29, 26.02, 25.84, 19.08. IR (KBr, cm^{-1}): 663; 1026; 1072; 1107; 1199; 1261; 1319; 1373; 1450; 1647; 1743; 2854; 2927; 2978; 3441. HRMS: requires ($C_{12}H_{18}NaO_3$): 233.1153; found: 233.1147.

4.35. 3-(1-Hydroxypropyl)-5-methylfuran-2(5*H*)-one (54)

^{1}H NMR (200 MHz, $CDCl_3$), δ: 7.20 (t, J=1.5 Hz, 1H), 5.17–4.96 (m, 1H), 4.44 (q, J=5.9, 5.4 Hz, 1H), 2.60 (t, J=5.0 Hz, 1H), 1.98–1.67 (m, 2H), 1.45 (d, J=6.8 Hz, 3H), 0.99 (t, J=7.4 Hz, 3H). 13C NMR (50 MHz, $CDCl_3$), δ: 172.61, 149.51, 135.89, 77.98, 68.28, 28.46, 18.99, 9.50. IR (film, cm^{-1}): 1114; 1319; 1743; 2920; 2920; 2966; 3417. HRMS: requires ($C_8H_{12}NaO_3$): 179.0684; found: 179.0679.

Acknowledgements

The authors would like to thank Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for the financial support and Universidade de São Paulo (USP) for the provided infrastructure.

Supplementary data

Supplementary data (copies of the ^{1}H, ^{13}C, ^{77}Se and ^{125}Te NMR spectra) is available free of charge on www.journals.elsevier.com. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.09.027.

References and notes

1. (a) Kürti, L.; Czakó, B. *Strategic Applications of Named Reactions in Organic Synthesis*; Elsevier Academic: Amsterdam, 2005, pp 286–287, p 628; (b) Tokoroyama, T. *Eur. J. Org. Chem.* **2010**, *10*, 2009.
2. Azevedo, M. B. M.; Murta, M. M.; Greene, A. E. *J. Org. Chem.* **1992**, *57*, 4567.
3. Zhu, G.; Lu, X. *J. Org. Chem.* **1995**, *60*, 1087.
4. Quinn, K. J.; Isaacs, A. K.; De Christopher, B. A.; Szklarz, S. C.; Arvary, R. A. *Org. Lett.* **2005**, *7*, 1243.
5. Ono, M.; Nishimura, K.; Nagaoka, Y.; Tomioka, K. *Tetrahedron Lett.* **1999**, *40*, 6979.
6. Ono, M.; Nishimura, K.; Tsubouchi, H.; Nagaoka, Y.; Tomioka, K. *J. Org. Chem.* **2001**, *66*, 8199.
7. Nishimura, K.; Tomioka, K. *Yakugaku Zasshi* **2003**, *123*, 9.
8. Marino, J. P.; Nguyen, H. N. *J. Org. Chem.* **2002**, *67*, 6291.
9. Iwaoka, M. Nucleophilic Selenium In *Organoselenium Chemistry: Synthesis and Reactions*; Wirth, T., Ed.; Wiley: New York, NY, 2011.
10. Keppler, A. F.; Gariani, R. A.; Lopes, D. G.; Comasseto, J. V. *Tetrahedron Lett.* **2009**, *50*, 2181.
11. Ferrarini, R. S.; Comasseto, J. V.; Dos Santos, A. A. *Tetrahedron: Asymmetry* **2009**, *20*, 2043.
12. Gariani, R. A.; Dos Santos, A. A.; Comasseto, J. V. *Synth. Commun.* **2008**, *38*, 789.
13. Ferrarini, R. S.; Dos Santos, A. A.; Comasseto, J. V. *Tetrahedron Lett.* **2010**, *51*, 6843.
14. Silva, M. S.; Ferrarini, R. S.; Sousa, B. A.; Toledo, F. T.; Comasseto, J. V.; Gariani, R. A. *Tetrahedron Lett.* **2012**, *53*, 3556.
15. Sousa, B. A.; Dos Santos, A. A. *Eur. J. Org. Chem.* **2012**, *18*, 3431.
16. (a) Satyanarayana, T.; Rao, A. J.; Basavaiah, D. *Chem. Rev.* **2003**, *103*, 811; (b) Basavaiah, D.; Reddy, B. S.; Badsara, S. S. *Chem. Rev.* **2010**, *110*, 5447; Basavaiah, D.; Veeraraghavaiah, G. *Chem. Soc. Rev.* **2012**, *41*, 68.
17. Ouchi, A.; Hyugano, T.; Liu, C. *Org. Lett.* **2009**, *11*, 5870.
18. Kürti, L.; Czakó, B. *Strategic Applications of Named Reactions in Organic Synthesis*; Elsevier Academic: Amsterdam, 2005; p 74.
19. Singh, V.; Batra, S. *Tetrahedron* **2008**, *64*, 4511.
20. Huang, X.; Xie, M. *Org. Lett.* **2002**, *4*, 1331.
21. Ugurchieva, T. M.; Veselovsky, V. V. *Russ. Chem. Rev.* **2009**, *78*, 337.
22. Jauch, J. *Synlett* **1999**, 1325.
23. Jauch, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2764.
24. Jauch, J. *J. Org. Chem.* **2001**, *66*, 609.