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Synthesis of 5-(1-Alkoxyalkylidene)tetronates by Direct Condensation Reactions of Tetronates with Thionolactones and Thionoesters

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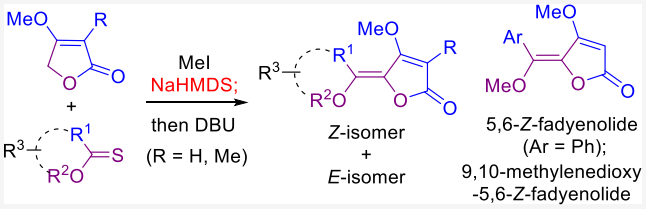
ABSTRACT: We report a two-step approach to bicyclic and monocyclic 5-(1-alkoxyalkylidene)tetronates starting from lactones/esters. The method features the use of thionolactones and thionoesters as activated forms of lactones/esters that allows the direct condensation with tetronates *via* one-pot enolate formation, nucleophilic addition, *S*-methylation, and DBU-promoted elimination. The value of the method was demonstrated by the stereoselective syntheses of two natural products: 5,6-*Z*-fadyenolide (*Z*/*E* ratio = 6:1) and 9,10-methylenedioxy-5,6-*Z*-fadyenolide (*Z*/*E* ratio = 9:1).



INTRODUCTION

5-(1-Alkoxyalkylidene)tetronates, namely, a tetronate connected to a lactone or an ester in the form of either an *E*- or a *Z*-ene diether (**1** in Figure 1), constitute a key structural feature of many bioactive natural products isolated from traditional medicinal plants. Salient examples are the structurally complex *Stemona* alkaloids[1] such as those that belong to the stemofoline groups **2**−**5** and protostemonamide (**6**), isolated from *Stemona* plants. The latter have been used in China and in East Asia for thousands of years as insecticides and anti-cough agents. Stemofoline (**2**) has been found to reverse multidrug resistance of certain types of cancer.[1a] Monocyclic 5-(1-alkoxyalkylidene)tetronates are found in some secondary metabolites isolated from *Piper* species.[2] For example, both 5,6-*E*- and 5,6-*Z*-fadyenolides **7** and **8** were isolated from *Piper fadyenii* collected from Jamaica in 1981[3a,b] and from *Piper malacophyllum* collected from Brazilian Atlantic Forest and Cerrado.[3c] Both geometric isomers fadyenolides **7** and **8** displayed antifungal activities.[3c] More recently, three such natural products including 9,10-methylenedioxy-5,6-*Z*-fadyenolide (**9**) and 5,6-*E*-fadyenolide (**7**) were isolated from the leaves of *Piper hispidum* Swingle (Piperaceae).[4] **8** and **9** were identified as the serotonin receptor 5-HT$_7$ and estrogen receptor agonists, respectively.[4] These activities are consistent with the Q'eqchi traditional use of the plant for the treatment of disorders associated with the female reproductive cycle including amenorrhea, dysmenorrhea, and pain.[4b]

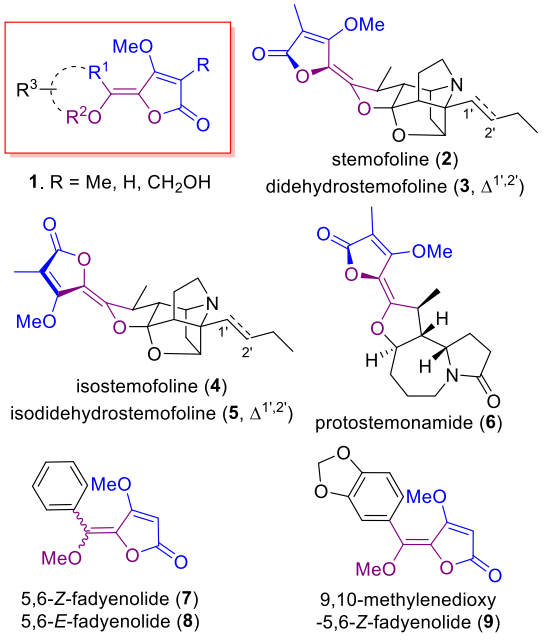


Figure 1. Representative bioactive natural products containing 5-(alkoxyalkylidene)tetronate motifs.

Although synthetic efforts toward 5-(1-alkoxyalkylidene)-tetronate motifs **1** can be traced back to the early 1980s,[3a] efficient construction of such motifs remains rare and challenging, yet in high demand.

For the synthesis of 5,6-*Z*/*E*-fadyenolides **7** and **8**, Pelter and co-workers developed a two-step (Scheme 1, a1) and a

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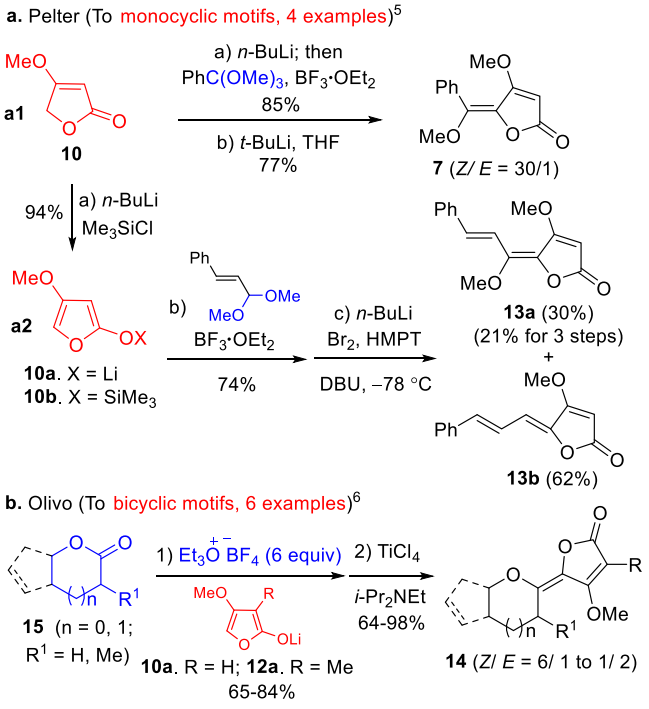
Scheme 1. Known Concise Methods for the Construction of 5-(Alkoxyalkylidene)tetronate Motifs



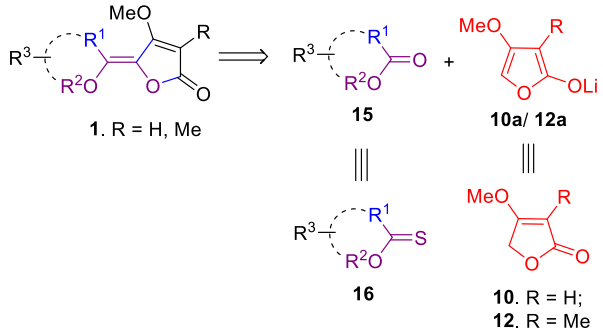
four-step (Scheme 1, a2) approach to *Z*- and *E*-diastereomer from methyl tetronate **10** and trimethyl orthobenzoate, respectively.[5] Although highly stereoselective, the methods suffer either from low efficiency (lengthy and low overall yield) or from the use of strong base *t*-BuLi, which renders the method of low functional group tolerance. Indeed, this method is limited to the synthesis of monocyclic 5-(1-alkoxyalkylidene)tetronate motifs with an aryl group.[6] For the motifs such as piperolide (**13a**) that bears a styryl group, it was formed as a minor product in only 30% yield (Scheme 1, a2). In 2002, Velázquez and Olivo reported a two-step method for the synthesis of bicyclic 5-(1-alkoxyalkylidene)tetronate motifs that feature the addition of methyl 5-lithiotetronate to highly electrophilic alkoxy oxonium ions, generated *in situ* from lactones and 6.0 equiv of trialkyloxonium tetrafluoroborate (Scheme 1, b).[6]

For the construction of the 5-(1-alkoxyalkylidene)tetronate motifs **1** in the context of total synthesis of stemofoline (**2**) and/or isostemofoline (**3**), the early efforts of Thomas featuring the addition of a α-lithio α-benzenesulfonyl tetrahydropyran to a methyl 5-hydroxy-3-methyltetronate followed by elimination of benzenesulfinic acid resulted in a mixture of hydroxyspiroketals instead of the desired 5-(1-alkoxyalkylidene)tetronates.[7] In Kende's seminal total synthesis of (±)-isostemofoline (**4**),[8] in the last step of a four-step approach to generate the 5-(1-alkoxyalkylidene)tetronate motif, the dehydration reaction proceeded in only 12% yield. In 2003, Overman and co-workers accomplished the total synthesis of (±)-didehydrostemofoline (**3**) and (±)-isodidehydrostemofoline (**5**), in which a five-step protocol was established for building the 5-(1-alkoxyalkylidene)tetronate moiety.[9] This protocol was adopted by Huang and co-workers for the enantioselective total synthesis of methoxystemofoline and isomethoxystemofoline.[10a,c] In connection with our interest in the total synthesis of stemofoline alkaloids,[10] we report herein a two-step method for the versatile synthesis of both bicyclic and monocyclic 5-(alkoxyalkylidene)tetronate motifs **1** from lactones/esters.

RESULTS AND DISCUSSION

Retrosynthetically, the most straightforward method for the synthesis of 5-(alkoxyalkylidene)tetronates **1** would be the direct condensation of tetronate enolates **10a**/**12a** with esters/lactones **15** (Scheme 2). However, esters[3a,5] and lactones[6]

Scheme 2. Our Strategy for the Efficient Construction of (Alkoxyalkylidene)tetronates



turned out to be unreactive toward the lithium enolates (**10a**/**12a**) of tetronates (**10**/**12**). The previous reported methods used either the highly electrophilic alkoxyoxonium ions generated *in situ* from orthoesters/acetals or lactones[3a,5,6] or aldehydes[8,9] as alternates. Given that lactone/esters **15** are not reactive enough to serve as the electrophilic partners, we reasoned that thionolactones and thionoesters **16**, readily available from the formers using thionation[11] reagents such as Lawesson's reagent,[11,12] would serve as valuable reactive partners for the direct condensation reaction with lithium enolates **10a**/**12a** (Scheme 2).

At the outset, the known γ-thionolactone (**16a**)[13a] was selected as a model compound for our investigation. Dropwise addition of γ-thionolactone (**16a**) to a solution of lithium enolate **12a** in THF at −78 °C, followed by trapping the resulting lithium thiolate intermediated with MeI, afforded unexpectedly vinylic methyl sulfide **18** in 56% yield (Scheme 3, protocol A). On the basis of the consideration that **18** might be a retro-oxy-conjugate addition product generated from **17** under basic conditions, a base-promoted re-oxy-conjugate addition was attempted. Pleasantly, exposure of **18** to DBU in MeCN at reflux produced directly **1a** in 88% yield as a mixture of *Z*/*E*-geometric isomers in a 4:1 ratio (Scheme 3, protocol A). The stereochemistry of the major geometric isomer was determined to be *Z*- by NOESY experiments (see the Supporting Information). Furthermore, a modification of the protocol consisting of the addition of a mixture of **16a** and MeI in THF to enolate **12a** (0 °C, 10 min; rt, 30 min) led to the formation of a mixture of labile **17** and **1a**. Without separation, this mixture was treated with DBU in MeCN at reflux, and the desired product **1a** was obtained in 70% yield (Scheme 3, protocol B). Next, in the light of the work of Nicolaou,[14] a cascade addition−elimination reaction was envisioned. Thus, after the enolate addition, 1,4-diiodobutane was used to replace MeI to trap the presumed thiolate intermediate to generate **19**, which was followed by warming up in the presence of *N*-methyl-2,2,6,6-pentamethylpiperidine, a non-nucleophilic base[14] (Scheme 3, protocol C). In this manner,

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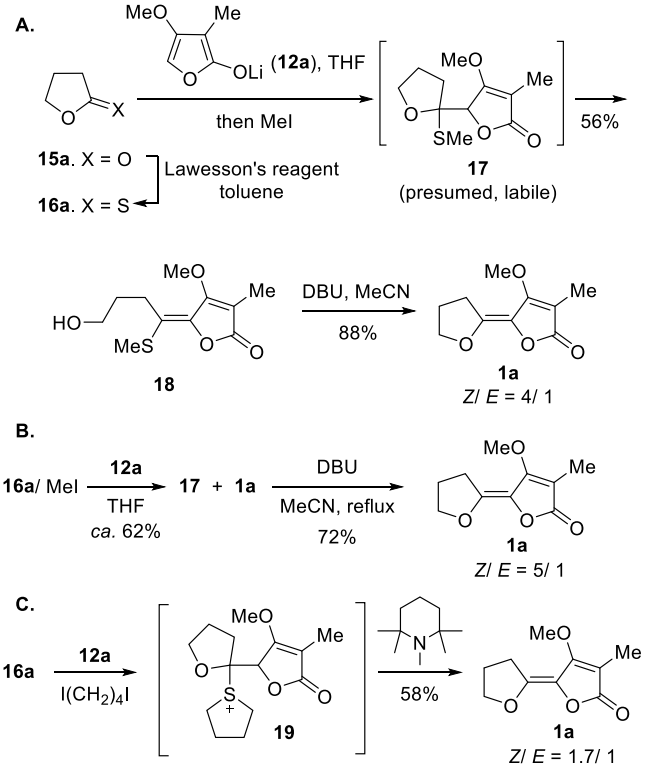
Scheme 3. Two-Step Protocols for the Synthesis of 1a from Thionolactone 16a

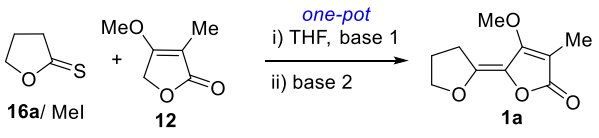


the desired product **1a** was directly obtained in 58% yield. However, the *Z*/*E* ratio dropped to 1.7:1, and this route was not pursued.

Next, our efforts were devoted to converting the two-step procedure (Scheme 3, B) into a one-pot reaction. Addition of 2 times the same base such as NaHMDS and KHMDS (2.0; 3.0 equiv) afforded the desired product **1a** in low yield and low geometric selectivity (Table 1, entries 1 and 2). The use of LiHMDS afforded a higher yield of 65%; however, the selectivity was still low (Table 1, entry 3). Employing LDA as the base provided a disappointing yield (Table 1, entry 4). Encouragingly, the strong base−weak base combination (LiHMDS + DBU; *n*-BuLi + DBU; NaHMDS + DBU) afforded satisfactory results in terms of both chemical yield and *Z*-selectivity (Table 1, entries 5−7). Finally, we found that the amount of DBU could be decreased to 1.0 equiv. Thus, the optimal conditions were determined as follows: by using 1.1 equiv of NaHMDS for the deprotonation of **12** (1.3 equiv), 1.5 equiv of MeI for *S*-methylation, and 1.0 equiv of DBU for the elimination reaction, the desired **1a**[15] was obtained in 68% yield with a *Z*/*E* stereoselectivity of 7:1 (Table 1, entry 8).

With the optimized conditions for the one-pot reaction in hand, we proceeded to examine the scope of the one-pot reaction (Scheme 4), and the results are displayed in Table 2.

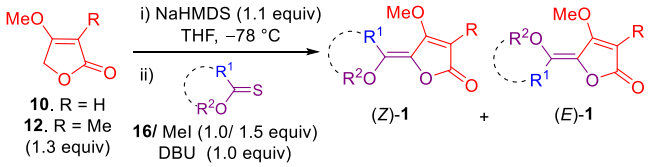
Table 1. Optimization of Reaction Conditions[a]



entry	base 1 (*n* equiv)	**12** (*n* equiv)	base 2 (*n* equiv)	product **1a** (% yield)
1	NaHMDS (2.0)	2.5	NaHMDS (3.0)	30%, *Z*/*E* = 1.3:1
2	KHMDS (2.0)	2.5	KHMDS (3.0)	25%, *Z*/*E* = 1.1:1
3	LiHMDS (2.0)	2.5	LiHMDS (3.0)	65%, *Z*/*E* = 1.5:1
4	LDA (2.0)	2.5	LDA (3.0)	19%, *Z*/*E* = 3:1
5	*n*-BuLi (2.0)	2.5	DBU (3.0)	59%, *Z*/*E* = 7:1
6	LiHMDS (2.0)	2.5	DBU (3.0)	54%, *Z*/*E* = 3:1
7	NaHMDS (2.0)	2.5	DBU (3.0)	62%, *Z*/*E* = 7:1
8[b]	NaHMDS (1.1)	1.3	DBU (1.0)	68%, *Z*/*E* = 7:1

[a]1.1 equiv of MeI used. [b]1.5 equiv of MeI used.

Scheme 4. One-Pot Synthesis of 1 from 10/12 and Thionolactones/Thionoesters 16



Extension of the reaction to oxepane-2-thione (**16b**) led to the formation of the corresponding **1b**[15] in a high yield of 81% (Table 2, entry 2), but the *Z*/*E* geometric isomeric ratio was low (2:1). Interestingly, the reaction of macrocyclic thionolactone **16c** not only gave the expected product **1c** in high yield (82%), but also the *Z*/*E* ratio was higher (4:1, entry 3). The enolate (**10c**) of the parent methyl tetronate (**10**) served also as a useful nucleophile in the coupling with **16c**, which produced **Z-1d**[15] in 60% yield [80% based on the recovered starting material (BRSM)] as a single geometric isomer (entry 4). Chromane-2-thione (**16e**) exhibited a low reactivity toward enolate **12c**, providing **1e**[15] in low yield. However, the yield was improved to 61% by replacing DBU with NaHMDS as the base for the elimination, and an excellent geometric isomeric selectivity was observed with only the *Z*-isomer obtained (entry 5). Next, the condensation reaction using esters as the electrophilic partner was examined. The condensation reaction of *O*-methyl benzothionoester (**16f**) with enolate **10c** proceeded smoothly to give stereoselectively (*Z*/*E* ratio = 6:1) the natural product 5,6-*Z*-fadyenolide (**7**) and 5,6-*E*-fadyenolide (**8**) in a combined yield of 62% (92% BRSM) (entry 6). The ^{1}H and ^{13}C{^{1}H} NMR data of our synthetic **7** and **8** fully matched those reported for the natural products.[3] *O*-Methyl benzothionoester with a methyl group at the *para*-position of the phenyl group (**16g**) led to a higher yield of 83% with a *Z*/*E* ratio = 2:1 (entry 7).[15] However, the reaction of the substrate with a *tert*-butyl group at the *para*-position (**16h**) resulted in a moderate yield of 55% (90% BRSM) and *Z*-selectivity (*Z*/*E* ratio = 1.6:1, entry 8). By modifying the reaction conditions consisting of trebling the equivalents of the main reagents as compared with those of the general procedure, the yield was increased to 80%, and a higher *Z*-selectivity was observed (*Z*/*E* ratio = 4.7:1, entry 8). The substrate bearing a methoxy group at the *para*-position (**16i**) reacted smoothly to afford **1i** in 88% yield in favor of the *Z*-isomer (*Z*/*E* ratio = 2:1, entry 9). The reaction of electron-rich substrate *O*-methyl benzo[*d*][1,3]dioxole-5-carbothionoester (**16j**) provided the natural product 9,10-methylenedioxy-5,6-*Z*-fadyenolide (**Z-9**) at a modest conversion (48% yield, 95% BRSM) but in high geometric selectivity (*Z*/*E* ratio = 9:1,

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Table 2. Scope of the Direct Condensation Reactions of Tetronates with Thionolactones/Thionoesters[a]

Entry[a]	Thionolactone/ Thionoester	Tetronate enolate	5-(1-Alkoxyalkylidene)tetronates[b]
1	X = O, **15a**; X = S, **16a** — 98%[13a]	**12c**	***Z*-1a** + ***E*-1a**; 68%, *Z*/*E* = 7/1[c,d]
2	X = O, **15b**; X = S, **16b** — 77%[13b]	**12c**	***Z*-1b** + ***E*-1b**; 81%, *Z*/*E* = 2/1[c]
3	X = O, **15c**; X = S, **16c** — 86%[13b]	**12c**	***Z*-1c** + ***E*-1c**; 82%, *Z*/*E* = 4/1[e]
4	X = O, **15c**; X = S, **16c** — 86%[13b]	**10c**	***Z*-1d**; 60% (80% BRSM), single *Z*-isomer[c]
5	X = O, **15e**; X = S, **16e** — 62%[13c]	**12c**	***Z*-1e**; 61%, single *Z*-isomer[c,f]
6	X = O, **15f**; X = S, **16f** — 85%[13d]	**10c**	**7** 5,6-*Z*-fadyenolide + **8** 5,6-*E*-fadyenolide; 62% (92% BRSM), *Z*/*E* = 6/1[e]
7	X = O, **15g**; X = S, **16g** — 82%[13e]	**12c**	***Z*-1g** + ***E*-1g**; 83%, *Z*/*E* = 2:1[c]
8	X = O, **15h**; X = S, **16h** — 88%[13d]	**12c**	***Z*-1h** + ***E*-1h**; 55% (90% BRSM), *Z*/*E* =1.6/1; 80%, *Z*/*E* = 4.7/1[d,e,g]
9	X = O, **15i**; X = S, **16i** — 95%[13e]	**12c**	***Z*-1i** + ***E*-1i**; 88%, *Z*/*E* = 2:1[e]
10	X = O, **15j**; X = S, **16j** — 75%	**10c**	***Z*-9** 9,10-methylenedioxy-5,6-*Z*-fadyenolide + ***E*-9**; 48% (95% BRSM), *Z*/*E* = 9/1[e]
11	X = O, **15k**; X = S, **16k** — 84%[13f]	**12c**	***Z*-1k** + ***E*-1k**; 63%, *Z*/*E* = 1/4[d,e]
12	X = O, **15l**; X = S, **16l** — 85%	**12c**	***Z*-1l** + ***E*-1l**; 88%, *Z*/*E* = 6/1[d,e,g]
13	X = O, **15m**; X = S, **16m** — 61%[13g]	**12c**	***Z*-1m** + ***E*-1m**; 80%, *Z*/*E* = 1/1[e]
14	X = O, **15n**; X = S, **16n** — 70%[13e]	**12c**	***Z*-1n** + ***E*-1n**; 83%, *Z*/*E* = 1/1.3[e]
15	X = O, **15o**; X = S, **16o** — 83%[13b]	**12c**	***Z*-1o** + ***E*-1o**; 87%, *Z*/*E* = 3.7/1[e,g]
16	X = O, **15p**; X = S, **16p** — 86%[13g]	**12c**	***Z* or *E*-1p** *ca.* 54%[h] + ***Z* or *E*-1p'** *ca.* 25%[h]
17	X = O, **15q**; X = S, **16q** — 65%	**12c**	***Z*-1q** + ***E*-1q**; 50%, *Z*/*E* = 3.7/1[e]
18	X = O, **15r**; X = S, **16r** — 58%	**12c**	***Z*-1r** + ***E*-1r**; 52%, *Z*/*E* = 2/1[c]

[a]The reaction was carried out under the optimized reaction conditions featuring the following ratios: **10c** or **12c** (1.0 equiv)/MeI (1.5 equiv), NaHMDS (1.1 equiv); NaHMDS (1.0 equiv) (Scheme 4). [b]*Z*/*E* ratio determined by ^{1}H NMR of crude. [c]Stereochemistry determined by NOESY experiments. [d]*Z*/*E* geoisomers partially separable. [e]Stereochemistry determined by comparison of the ^{13}C{^{1}H} NMR data (*cf.* Supporting Information Table S4 and ref 3a). [f]MeI (1.5 equiv), NaHMDS (1.3 equiv), and NaHMDS (1.0 equiv) used. [g]MeI (4.5 equiv), NaHMDS (3.3 equiv), and DBU (3.0 equiv) used. [h]Two regioisomers could not be separated in a pure form.

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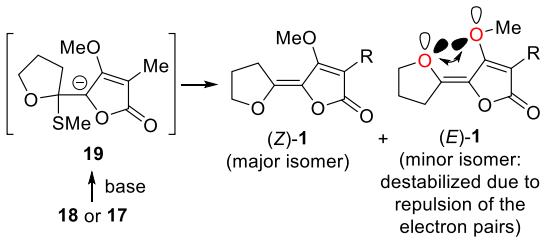
entry 10). The ^{1}H and $^{13}C\{^{1}H\}$ NMR data of our synthetic **9** fully matched those reported for the natural product.[4a] Considering the high *Z*-selectivity of the reaction (*Z*/*E* = 9:1), the yield of the *Z*-isomer obtained from **16j** is higher than that from **16i**. It is worth noting that *O*-methyl furan-2-carbothionoester (**16k**), an electron-rich substrate, reacted with **12c** to yield ***E*-1k** as the major geometric isomer in a *Z*/*E* ratio of 1:4 (combined yield: 63%, entry 11). Interestingly, as can been seen from entries 12−14, the reaction also tolerates electron-withdrawing groups such as F, CF_3, and Cl. In these cases, by modifying the reaction conditions consisting of trebling the equivalents of the main reagents, the reaction of *O*-methyl 4-fluorobenzothionoester (**16l**) furnished **1l** in excellent yield (88%) and in good *Z*-selectivity (*Z*/*E* ratio = 6:1) (entry 12). The reactions of *O*-methyl *p*-trifluoro and *p*-chloro-benzothionoesters produced ***Z*-1m** and ***Z*-1n** in 80 and 83% yields and with *Z*/*E* ratio = 1:1 and 1:1.3, respectively. Besides methyl ester, other esters such as *i*-propyl ester **16o** reacted similarly in terms of both yield (87%) and *Z*-selectivity (*Z*/*E* ratio = 3.7:1) (entry 15). As can be seen from entries 16−18, the reaction could be further extended to aliphatic thionoesters (**16p**−**16r**), and the desired products were obtained in moderate yields (50−58%) and *Z*-selectivity (*Z*/*E* ratio = 2:1 to 3.7:1). It is worth noting that due to the acidity of the benzylic protons, the reaction of *O*-methyl 2-phenylethanethionoester (**16p**, Table 2, entry 16) led to *ca.* 54% of the normal product **1p**, along with *ca.* 25% of the olefinic bond-migrated product **1p′**. We were unable to obtain pure samples of the two isomers; however, inspection of the ^{1}H NMR spectrum of the mixture **1p**/**1p′** allowed concluding that both isomers **1p** and **1p′** contain only one geometric isomer.

The preferential formation of the *Z*-isomer [(*Z*)-**1**] may be understood in terms of the destabilizing electronic effect due to repulsion by electron pair−electron pair interaction of the *E*-isomer[18] as indicated in Scheme 5. It is worth noting that such

Scheme 5. Plausible Reasons for the Preferential Formation of the *Z*-Isomer



a *Z*-selectivity is also found in both the natural products containing such motifs[1−3] and in synthetic methods featuring an elimination reaction as the last step for the formation of the motif.[5,6]

CONCLUSIONS

In summary, we have developed a practical protocol for the one-pot condensation of tetronates **10**/**12** with thionolactones/thionoesters **16**, which constitutes an efficient two-step approach to 5-(1-alkoxyalkylidene)tetronates **1** from feedstock lactones and esters. The method is broad in scope, allowing the synthesis of both monocyclic and bicyclic 5-(1-alkoxyalkylidene)tetronates from lactones as well as from aromatic and aliphatic esters. In most cases, *Z*-selectivity was observed (*Z*/*E* ratios = 2:1 to 100:0). The method has been applied to the stereoselective syntheses of natural products 5,6-*Z*-fadyenolide and 9,10-methylenedioxy-5,6-*Z*-fadyenolide. It is expectable that this method will find application in the total synthesis of *Stemona* alkaloids containing a 5-(1-alkoxyalkylidene)tetronate moiety.

EXPERIMENTAL SECTION

General. NMR spectra were recorded on a Bruker AV 400, AV 500, AV 600, or AV 850 spectrometer at 25 °C in the solvents indicated. NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as an internal standard. Chemical shifts (δ) are reported in ppm and referenced to the internal standard Me_4Si and solvent signals (Me_4Si, 0 ppm for ^{1}H NMR, and $CDCl_3$, 77.0 ppm for $^{13}C\{^{1}H\}$ NMR). Melting points were determined on a Büchi M560 automatic melting point apparatus and are uncorrected. HRMS spectra were recorded on a 7.0 T FT-MS apparatus using an ICR analyzer. Infrared spectra were measured with a Nicolet Avatar 330 FT-IR spectrometer using film KBr pellet technique. Silica gel (200−300 mesh) was used for flash column chromatography (FC), eluting (unless otherwise stated) with the ethyl EtOAc/*n*-hexane mixture. Structural assignments were made with additional information from NOESY experiments. All other commercially available compounds were used as received. THF and toluene were distilled over sodium benzophenone ketyl under N_2.

General Procedure for Synthesis of Thionolactone/Thionoester 16. A solution of lactone/ester **15** (10 mmol, 1.0 equiv) and Lawesson's reagent (8 mmol, 0.8 equiv) in refluxing xylene (30 mL) was stirred overnight (oil bath). The reaction mixture was filtered with diatomite and concentrated by reduced pressure to give the crude product. The residue was purified by FC on silica gel to afford the desired product **16**.

*O-Methyl benzo[d][1,3]dioxole-5-carbothionoester (**16j**).* Ester **15j** (1.80 g, 10 mmol, 1.0 equiv) and Lawesson's reagent (3.23 g, 8 mmol, 0.8 equiv) were used. The residue was purified by flash chromatography (eluent: *n*-hexane) to afford **16j** (1.47 g, yield: 75%) as a yellow solid. mp: 74−75 °C; IR (film) ν_{max}: 2940, 1501, 1486, 1435, 1261, 1236, 1103, 1033, 810, 671 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.68 (d, *J* = 1.8 Hz, 1H), 6.78 (d, *J* = 8.3 Hz, 1H), 6.03 (s, 2H), 4.26 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 210.6, 151.8, 147.5, 133.0, 124.9, 109.0, 107.5, 101.9, 59.1 ppm; HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd for $C_9H_8O_3SNa$, 219.0086; found, 219.0077.

*O-Methyl 4-Fluorobenzothionoester (**16l**).* Ester **15l** (1.54 g, 10 mmol, 1.0 equiv) and Lawesson's reagent (3.23 g, 8 mmol, 0.8 equiv) were used. The residue was purified by flash chromatography (eluent: *n*-hexane) to afford **16l** (1.45 g, yield: 85%) as an orange oil. ^{1}H NMR and $^{13}C\{^{1}H\}$ NMR data of **16l** matched those reported.[13h]

*O-Methyl Hexadecanethionoester (**16q**).* Ester **15q** (2.75 g, 10 mmol, 1.0 equiv) and Lawesson's reagent (3.23 g, 8 mmol, 0.8 equiv) were used. The residue was purified by flash chromatography (eluent: *n*-hexane) to afford **16q** (1.86 g, yield: 65%) as a pale yellow oil. IR (film) ν_{max}: 2924, 2853, 1441, 1266, 1189, 1151, 1086, 429 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.06 (s, 3H), 2.72 (t, *J* = 7.6 Hz, 2H), 1.77−1.69 (m, 2H), 1.31−1.24 (m, 24H), 0.88 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 225.4, 58.8, 46.7, 31.9, 29.7 (3C), 29.6 (3C), 29.4, 29.3 (2C), 28.8, 28.7, 22.7, 14.1 ppm; HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{17}H_{35}OS$, 287.2403; found, 287.2407.

*O-Hexadecyl Hexadecanethionoester (**16r**).* Ester **15r** (2.87 g, 10 mmol, 1.0 equiv) and Lawesson's reagent (3.23 g, 8 mmol, 0.8 equiv) were used. The residue was purified by flash chromatography (eluent: *n*-hexane) to afford **16r** (2.21 g, yield: 58%) as a pale yellow oil. IR (film) ν_{max}: 2924, 2853, 1466, 1378, 1276, 1181, 1088, 721, 411 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.42 (t, *J* = 6.6 Hz, 2H), 2.72 (t, *J* = 7.6 Hz, 2H), 1.80−1.68 (m, 4H), 1.42−1.24 (m, 50H), 0.88 (t, *J* = 6.8 Hz, 6H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 224.9, 72.5, 47.2, 31.9 (2C), 29.7 (12C), 29.6 (2C), 29.5 (2C), 29.4 (2C), 29.3,

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29.2, 28.8, 28.6, 28.1, 22.7 (2C), 14.1 (2C) ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{32}H_{64}OSNa$, 519.4570; found, 519.4569.

Detailed Procedure for the Synthesis of Thionolactone/Thionoester 16. Dihydrofuran-2(3*H*)-thione (**16a**),[13a] oxepane-2-thione (**16b**),[13b] oxacyclohexadecane-2-thione (**16c**),[13b] chromane-2-thione (**16e**),[13c] *O*-methyl benzothionoester (**16f**),[13d] *O*-methyl 4-methylbenzothionoester (**16g**),[13g] *O*-methyl 4-(*tert*-butyl)-benzothionoester (**16h**),[13f] *O*-methyl 4-methoxybenzothionoester (**16i**),[13e] *O*-methyl furan-2-carbothionoester (**16k**),[13f] *O*-isopropyl benzothionoester, *O*-methyl 4-(trifluoromethyl)benzothioate (**16m**),[13g] *O*-methyl 4-chlorobenzothioate (**16n**),[13e] *O*-isopropyl benzothionoester (**16o**),[13b] and *O*-methyl 2-phenylethanethionoester (**16p**)[13g] were prepared according to the reported procedures.

General Procedure for the Synthesis of 5-(1-Alkoxyalkylidene)tetronates. 4-methoxy-3-methylfuran-2(5*H*)-one (**12**)[16] and 4-methoxyfuran-2(5*H*)-one (**10**)[17] were prepared according to the reported procedures.

Method A. To a cooled solution (−78 °C) of compound **12** or **10** (1.3 mmol) in anhydrous THF (5 mL) under a nitrogen atmosphere was added NaHMDS (1.1 mmol, 2.0 M in THF) dropwise. After stirring for 30 min, a solution of **16** (1.0 mmol) and MeI (1.5 mmol) in the THF (5 mL) was added dropwise. The reaction mixture was stirred at the same temperature for 10 min; then, DBU (1.0 mmol) was added. The mixture was warmed to reflux and then stirred for 2 h (oil bath). Then, the reaction was quenched with a saturated aqueous solution of NH_4Cl (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by FC on silica gel to afford the desired product.

Method B. To a cooled solution (−78 °C) of compound **12** or **10** (1.3 mmol) in anhydrous THF (5 mL) under a nitrogen atmosphere was added NaHMDS (1.1 mmol, 2.0 M in THF) dropwise. After stirring for 30 min, a solution of **16** (1.0 mmol) and MeI (1.5 mmol) in THF (5 mL) was added dropwise. The reaction mixture was stirred at the same temperature for 10 min; then, NaHMDS (1.0 mmol) was added. The mixture was warmed to reflux and then stirred for 2 h (oil bath). Then, the reaction was quenched with a saturated aqueous solution of NH_4Cl (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by FC on silica gel to afford the desired product.

Method C. To a cooled solution (−78 °C) of compound **12** or **10** (3.9 mmol) in anhydrous THF (5 mL) under a nitrogen atmosphere was added NaHMDS (3.3 mmol, 2.0 M in THF) dropwise. After stirring for 30 min, a solution of **16** (1.0 mmol) and MeI (4.5 mmol) in THF (5 mL) was added dropwise. The reaction mixture was stirred at the same temperature for 10 min; then, DBU (3.0 mmol) was added. The mixture was warmed to reflux and then stirred for 2 h (oil bath). Then, the reaction was quenched with a saturated aqueous solution of NH_4Cl (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by FC on silica gel to afford the desired product.

*5-(4-Hydroxy-1-(methylthio)butylidene)-4-methoxy-3-methylfuran-2(5H)-one (**18**).* To a cooled solution (−78 °C) of compound **12a** (320 mg, 2.5 mmol) in anhydrous THF (5 mL) under a nitrogen atmosphere was added *n*-BuLi (2 mmol, 2.5 M in hexane) dropwise. After stirring for 30 min, **16a** (102 mg, 1 mmol) in THF (5 mL) was added dropwise. The reaction mixture was stirred at the same temperature for 10 min. The mixture was warmed to room temperature and MeI (3 mmol) was added. Then, the reaction was quenched with a saturated aqueous solution of NH_4Cl (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by FC (eluent: EtOAc/*n*-hexane = 1:1) on silica gel to afford compound **18** (136.6 mg, yield: 56%) as a pale yellow solid. mp: 59−60 °C; IR (film) ν_{max}: 3436, 2928, 2869, 1743, 1615, 1353, 1218, 1063, 974, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.18 (s, 3H), 3.65 (t, J = 6.2 Hz, 2H), 2.74−2.68 (m, 2H), 2.40 (s, 3H), 2.04 (s, 3H), 1.96 (br s, 1H), 1.82−1.74 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.7, 162.1, 138.0, 126.3, 100.0, 61.7, 59.2, 32.6, 25.3, 15.1, 9.0 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{11}H_{16}O_4SNa$, 267.0662; found, 267.0670.

*(Z)-5-(Dihydrofuran-2(3H)-ylidene)-4-methoxy-3-methylfuran-2(5H)-one (**Z-1a**) and (E)-5-(Dihydrofuran-2(3H)-ylidene)-4-methoxy-3-methylfuran-2(5H)-one (**E-1a**).* Following the general method B, the reaction of the thionolactone **16a** (102 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 2:3), ***Z*-1a** and ***E*-1a** (133 mg, yield: 68%, Z/E = 7:1) as a colorless oil. ***Z*-1a**: IR (film) ν_{max}: 2925, 1736, 1694, 1613, 1461, 1332, 1147, 1064, 1024, 966 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.29 (t, J = 6.9 Hz, 2H), 4.12 (s, 3H), 2.89 (t, J = 7.7 Hz, 2H), 2.17−2.09 (m, 2H), 2.05 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.4, 163.9, 144.2, 122.8, 95.7, 72.3, 58.9, 27.9, 24.6, 9.0 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{10}H_{12}O_4Na$, 219.0628; found, 219.0634. ***E*-1a**: IR (film) ν_{max}: 2921, 1752, 1686, 1668, 1612, 1394, 1330, 1160, 1047, 989 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) data of the minor isomer read from the spectrum of the mixture of ***E*-1a** and starting material **12c**: δ 4.37 (t, J = 6.8 Hz, 2H), 4.14 (s, 3H), 2.94 (t, J = 7.7 Hz, 2H), 2.09 (t, J = 7.3 Hz, 2H), 2.04 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) data of the minor isomer read from the spectrum of the mixture of ***E*-1a** and starting material **12c**: δ 170.9, 163.0, 148.2, 124.8, 97.9, 74.1, 59.4, 29.0, 23.5, 8.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{10}H_{12}O_4Na$, 219.0628; found, 219.0633.

*(Z)-4-Methoxy-3-methyl-5-(oxepan-2-ylidene)furan-2(5H)-one (**Z-1b**) and (E)-4-Methoxy-3-methyl-5-(oxepan-2-ylidene)furan-2(5H)-one (**E-1b**).* Following the general method A, the reaction of the thionolactone **16b** (130 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), ***Z*-1b** and ***E*-1b** (182 mg, yield: 81%, Z/E = 2:1) as a white solid. ***Z*-1b**: mp: 125−127 °C; IR (film) ν_{max}: 2926, 2857, 1731, 1682, 1463, 1393, 1329, 1260, 1186, 970 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.24−4.20 (m, 2H), 4.10 (s, 3H), 2.84−2.80 (m, 2H), 2.05 (s, 3H), 1.82−1.75 (m, 2H), 1.70−1.65 (m, 4H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.6, 163.8, 146.8, 126.9, 98.0, 69.9, 59.2, 30.1, 29.1, 27.3, 26.0, 9.2 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{16}O_4Na$, 247.0941; found, 247.0950. ***E*-1b**: mp: 87−89 °C; IR (film) ν_{max}: 2928, 2867, 1732, 1679, 1463, 1393, 1332, 1187, 968 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.19−4.16 (m, 2H), 4.09 (s, 3H), 2.77−2.73 (m, 2H), 2.02 (s, 3H), 1.82−1.78 (m, 2H), 1.73−1.66 (m, 4H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.4, 163.8, 150.0, 128.9, 99.9, 70.6, 59.6, 30.2, 29.1, 27.7, 26.6, 8.7 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{16}O_4Na$, 247.0941; found, 247.0940.

*(Z)-5-(Oxacyclohexadecan-2-ylidene)-4-methoxy-3-methylfuran-2(5H)-one (**Z-1c**) and (E)-5-(Oxacyclohexadecan-2-ylidene)-4-methoxy-3-methylfuran-2(5H)-one (**E-1c**).* Following the general method A, the reaction of the thionolactone **16c** (256 mg, 1.0 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), ***Z*-1c** and ***E*-1c** (287 mg, yield: 82%, Z/E = 4:1) as a white solid. ***Z*-1c**: mp: 88−89 °C; IR (film) ν_{max}: 2929, 2857, 1749, 1649, 1621, 1458, 1361, 1153, 1064, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.29 (t, J = 5.8 Hz, 2H), 4.10 (s, 3H), 2.46 (t, J = 7.6 Hz, 2H), 2.05 (s, 3H), 1.65−1.59 (m, 2H), 1.57−1.49 (m, 2H), 1.47−1.41 (m, 2H), 1.37−1.28 (m, 18H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.1, 164.7, 146.5, 126.9, 97.0, 73.0, 59.2, 30.3, 29.5, 27.5, 27.4, 27.1, 26.9, 26.7, 26.6, 26.05, 26.01, 25.9, 25.5, 24.6, 9.1 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{21}H_{34}O_4Na$, 373.2349; found, 373.2360. ***E*-1c**: mp: 86−87 °C; IR (film) ν_{max}: 2929, 2857, 1754, 1622, 1457, 1397, 1362, 1205, 1062, 754 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.09 (s, 3H), 3.81 (t, J = 6.3 Hz, 2H), 2.47 (t, J = 7.7 Hz, 2H), 2.02 (s, 3H), 1.71−1.67 (m, 2H), 1.57−1.51 (m, 2H), 1.50−1.44 (m, 2H), 1.39−1.28 (m, 18H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.3, 163.3, 147.9, 133.8, 100.6, 71.0, 59.5, 28.9, 28.1, 27.34, 27.29, 27.1, 26.6, 26.4, 26.3, 26.2, 25.9, 25.8, 25.7, 24.5, 8.7 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{21}H_{34}O_4Na$, 373.2349; found, 373.2357.

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*(Z)-5-(Oxacyclohexadecan-2-ylidene)-4-methoxyfuran-2(5H)-one (**Z-1d**).* Following the general method A, the reaction of the thionolactone **16c** (256 mg, 1 mmol) with **10c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), **Z-1d** (202 mg, yield: 60%, BRSM 80%, single *Z*-isomer) as a colorless oil. IR (film) ν_{max}: 2930, 2856, 1747, 1652, 1588, 1443, 1384, 1203, 1088, 903, 784 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.06 (s, 1H), 4.37 (t, J = 5.7 Hz, 2H), 3.89 (s, 3H), 2.48 (t, J = 7.5 Hz, 2H), 1.67−1.60 (m, 2H), 1.58−1.51 (m, 2H), 1.48−1.40 (m, 2H), 1.40−1.28 (m, 18H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 172.0, 168.1, 147.0, 126.0, 85.9, 73.1, 59.1, 30.3, 29.5, 27.4, 27.2, 27.0, 26.9, 26.7, 26.4, 25.9 (3C), 25.5, 24.5 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{20}H_{32}O_4Na$, 359.2193; found, 359.2210.

*(Z)-5-(Chroman-2-ylidene)-4-methoxy-3-methylfuran-2(5H)-one (**Z-1e**).* Following the general method B, the reaction of the thionolactone **16e** (164 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), **Z-1e** (157 mg, yield: 61%, single *Z*-isomer) as a white solid. mp: 176−177 °C; IR (film) ν_{max}: 2922, 1743, 1689, 1622, 1455, 1282, 1260, 1223, 1009, 757 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.21−7.19 (m, 1H), 7.09−7.04 (m, 2H), 6.99−6.95 (m, 1H), 4.17 (s, 3H), 3.05−3.01 (m, 2H), 2.84−2.80 (m, 2H), 2.11 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.6, 163.6, 151.7, 137.8, 128.5, 125.1, 126.9, 122.7, 122.6, 116.8, 98.8, 59.2, 23.4, 21.4, 9.2 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{14}O_4Na$, 281.0784; found, 281.0794.

*5,6-Z-Fadyenolide (**7**) and 5,6-E-Fadyenolide (**8**).* Following the general method A, the reaction of the thionoester **16f** (152 mg, 1 mmol) with **10c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), 5,6-*Z*-fadyenolide (**7**) and 5,6-*E*-fadyenolide (**8**) (144 mg, yield: 62%, BRSM 92%, Z/E = 6:1) as a white solid. 5,6-*Z*-Fadyenolide (**7**): mp: 131−132 °C; IR (film) ν_{max}: 2944, 1742, 1658, 1589, 1439, 1388, 1215, 1131 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45−7.37 (m, 5H), 5.12 (s, 3H), 3.75 (s, 3H), 3.60 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.8, 167.9, 144.0, 130.6, 130.1, 130.1, 129.0, 127.9, 87.5, 60.5, 58.9, 58.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{12}O_4Na$, 255.0628; found, 255.0637. 5,6-*E*-Fadyenolide (**8**): mp: 130−131 °C; IR (film) ν_{max}: 2926, 1770, 1747, 1590, 1438, 1376, 1213, 1133 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) data of the minor isomer read from the spectrum of the mixture of geometric isomers **7** and **8**: δ 7.74−7.70 (m, 3H), 7.48−7.40 (m, 2H), 5.28 (s, 1H), 3.99 (s, 3H), 3.65 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (400 MHz, $CDCl_3$) data of the minor isomer read from the spectrum of the mixture of geometric isomers **7** and **8**: δ 171.6, 168.1, 144.6, 134.9, 131.1, 129.9, 129.0 (2C), 128.5 (2C), 88.8, 60.5, 59.5 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{12}O_4Na$, 255.0628; found, 255.0636.

*(Z)-4-Methoxy-5-(methoxy(p-tolyl)methylene)-3-methylfuran-2(5H)-one (**Z-1g**) and (E)-4-Methoxy-5-(methoxy(p-tolyl)-methylene)-3-methylfuran-2(5H)-one (**E-1g**).* Following the general method C, the reaction of the thionoester **16g** (166 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:5), **Z-1g** and **E-1g** (216 mg, yield: 83%, Z/E = 2:1) as a white solid. **Z-1g**: mp: 136−137 °C; IR (film) ν_{max}: 2922, 1748, 1674, 1621, 1456, 1390, 1273, 1211, 1149, 983 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29−7.25 (m, 2H), 7.23−7.18 (m, 2H), 3.70 (s, 3H), 3.67 (s, 3H), 2.40 (s, 3H), 2.02 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.8, 163.6, 142.9, 139.9, 130.0 (2C), 129.6, 128.5 (2C),128.0, 99.9, 58.9, 58.6, 21.4, 8.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}O_4Na$, 283.0941; found, 283.0950. **E-1g**: mp: 93−94 °C; IR (film) ν_{max}: 2928, 1748, 1615, 1455, 1392, 1357, 1216, 1162, 1060, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.62−7.57 (m, 2H), 7.24−7.19 (m, 2H), 4.18 (s, 3H), 3.61 (s, 3H), 2.37 (s, 3H), 2.10 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.3, 164.2, 143.5, 139.8, 134.9, 129.2 (2C), 128.73 (2C), 128.68, 100.6, 60.4, 59.7, 21.4, 8.9 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}O_4Na$, 283.0941; found, 283.0949.

*(Z)-5-((4-(tert-Butyl)phenyl)(methoxy)methylene)-4-methoxy-3-methylfuran-2(5H)-one (**Z-1h**) and (E)-5-((4-(tert-Butyl)phenyl)-(methoxy)methylene)-4-methoxy-3-methylfuran-2(5H)-one (**E-1h**).* Following the general method A, the reaction of the thionoester **16h** (208 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), **Z-1h** and **E-1h**: (166 mg, yield: 55%, BRSM 90%, Z/E = 1.6:1) as a colorless oil. Following the general method C, the reaction of the thionoester **16h** (208 mg, 1 mmol) with **12c** (3.3 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), **Z-1h** and **E-1h**: (242 mg, yield: 80%, Z/E = 4.7:1). **Z-1h** and **E-1h**: IR (film) ν_{max}: 2961, 2869, 1748, 1621, 1456, 1394, 1361, 1268, 1162, 1060, 994 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, data of two geometric isomers, ratio Z/E = 1.5:1): δ 7.64−7.61 (m, 0.8H), 7.44−7.37 (m, 2H), 7.32−7.27 (m, 1.2H), 4.19 (s, 1.2H), 3.68 (s, 1.8H), 3.64 (s, 1.8H), 3.62 (s, 1.2H), 2.10 (s, 1.2H), 2.00 (s, 1.8H), 1.33 (s, 5.4H), 1.32 (s, 3.6H) ppm; $^{13}C\{^1H\}$ NMR (500 MHz, $CDCl_3$, data of two geometric isomers, ratio = Z/E = 1.5:1): δ 170.4, 169.9, 164.3, 163.7, 153.2, 152.9, 143.6, 143.0, 135.0, 129.9 (2C), 129.7, 128.72, 128.65 (2C), 128.1, 125.5 (2C), 124.7 (2C), 100.7, 100.6, 60.6, 59.8, 58.9, 58.8, 34.83, 34.81, 31.22 (3C), 31.16 (3C), 9.0, 8.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{22}O_4Na$, 325.1410; found, 325.1415.

*(Z)-4-Methoxy-5-(methoxy(4-methoxyphenyl)methylene)-3-methylfuran-2(5H)-one (**Z-1i**) and (E)-4-Methoxy-5-(methoxy(4-methoxyphenyl)methylene)-3-methylfuran-2(5H)-one (**E-1i**).* Following the general method A, the reaction of the thionoester **16i** (182 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), **Z-1i** and **E-1i** (243 mg, yield: 88%, Z/E = 2:1) a white solid. **Z-1i**: mp: 78−79 °C; IR (film) ν_{max}: 2942, 1747, 1606, 1511, 1456, 1362, 1252, 1175, 1063, 1036 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.29 (m, 2H), 6.95−6.89 (m, 2H), 3.86 (s, 3H), 3.72 (s, 3H), 3.68 (s, 3H), 2.02 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.7, 163.6, 160.7, 142.7, 131.5 (2C), 129.4, 123.0, 113.1 (2C), 99.6, 58.9, 58.5, 55.2, 8.7 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}O_5Na$, 299.0890; found, 299.0895. **E-1i**: mp: 96−97 °C; IR (film) ν_{max}: 2935, 1746, 1605, 1510, 1456, 1359, 1255, 1178, 1062, 1029 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.69−7.64 (m, 2H), 6.95−6.90 (m, 2H), 4.19 (s, 3H), 3.84 (s, 3H), 3.63 (s, 3H), 2.10 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.3, 164.3, 160.6, 143.4, 134.4, 130.4 (2C), 124.0, 113.9 (2C), 100.5, 60.6, 59.7, 55.8, 8.9 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}O_5Na$, 299.0890; found, 299.0897.

*9,10-Methylenedioxy-5,6-Z-fadyenolide (**Z-9**) and 9,10-Methylenedioxy-5,6-E-fadyenolide (**E-9**).* Following the general method A, the reaction of the thionoester **16j** (196 mg, 1 mmol) with **10c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:2), **Z-9** and **E-9** (132 mg, yield: 48%, BRSM 95%, Z/E = 9:1) as a white solid. **Z-9**: mp: 164−165 °C; IR (film) ν_{max}: 2918, 1746, 1590, 1505, 1490, 1236, 1213, 1099, 1038, 906 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.91 (dd, J = 8.0, 1.4 Hz, 1H), 6.85 (d, J = 1.4 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.03 (s, 2H), 5.13 (s, 1H), 3.75 (s, 3H), 3.66 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.8, 167.8, 149.2, 147.4, 146.8, 129.0, 124.9, 124.2, 110.2, 107.9, 101.5, 87.6, 58.92, 58.90 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{14}H_{12}O_6Na$, 299.0526; found, 299.0532. **E-9**: mp: 140−141 °C; IR (film) ν_{max}: 2919, 1748, 1591, 1489, 1380, 1252, 1236, 1104, 1037, 988 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.30 (dd, J = 8.1, 1.2 Hz, 1H), 7.25 (d, J = 1.2 Hz, 1H), 6.88 (d, J = 8.1 Hz, 1H), 6.02 (s, 2H), 5.26 (s, 1H), 3.99 (s, 3H), 3.66 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 171.6, 168.1, 149.1, 148.0, 144.3, 134.4, 125.1, 123.9, 108.9, 108.5, 101.5, 88.6, 60.8, 59.5 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{14}H_{12}O_6Na$, 299.0526; found, 299.0531.

*(Z)-5-(Furan-2-yl(methoxy)methylene)-4-methoxy-3-methylfuran-2(5H)-one (**Z-1k**) and (E)-5-(Furan-2-yl(methoxy)methylene)-4-methoxy-3-methylfuran-2(5H)-one (**E-1k**).* Following the general method A, the reaction of the thionoester **16k** (142 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), **Z-1k** and **E-1k**: (149 mg, yield: 63%, Z/E = 1:4) as a brown red oil. **Z-1k**: IR (film) ν_{max}: 2924, 1749, 1673, 1622, 1456, 1394, 1360, 1219, 1157, 1038, 1021, 994 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) data of the major read from the spectrum of the mixture of geometric isomers **Z-1k** and **E-1k**: δ 7.53 (dd, J = 1.8, 0.8 Hz, 1H), 6.64 (dd, J = 3.4, 0.8 Hz, 1H), 6.52 (dd, J = 3.4, 1.8 Hz, 1H), 3.87 (s, 3H), 3.72 (s, 3H), 2.04 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) data of the major read from the spectrum of the mixture of geometric isomers **Z-**

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1k and ***E*-1k**: δ 169.3, 163.0, 144.6, 144.2, 132.5, 132.0, 114.8, 111.1, 100.7, 59.2 (2C), 8.9 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{12}O_5Na$, 259.0577; found, 259.0587. ***E*-1k**: IR (film) ν_{max}: 2921, 1748, 1680, 1614, 1397, 1360, 1202, 1162, 1065, 1017, 977 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (dd, J = 1.7, 0.7 Hz, 1H), 6.98 (dd, J = 3.4, 0.7 Hz, 1H), 6.52 (dd, J = 3.4, 1.7 Hz, 1H), 4.17 (s, 3H), 3.80 (s, 3H), 2.10 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.8, 164.0, 146.8, 144.0, 134.8, 134.5, 114.9, 112.3, 101.3, 62.5, 59.8, 9.0 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{12}O_5Na$, 259.0577; found, 259.0587.

*(Z)-5-((4-Fluorophenyl)(methoxy)methylene)-4-methoxy-3-methylfuran-2(5H)-one (**Z-1l**) and (E)-5-((4-Fluorophenyl)-(methoxy)methylene)-4-methoxy-3-methylfuran-2(5H)-one (**E-1l**).* Following the general method C, the reaction of the thionoester **16l** (170 mg, 1 mmol) with **12c** (3.3 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), ***Z*-1l** and ***E*-1l**: (232 mg, yield: 88%, Z/E = 6:1) as a white solid. ***Z*-1l** and ***E*-1l**: mp: 119−120 °C; IR (film) ν_{max}: 2925, 2854, 1755, 1622, 1456, 1366, 1273, 1211, 1149, 846 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, data of two geometric isomers, ratio Z/E = 1.2:1): δ 7.73−7.68 (m, 0.9H), 7.38−7.34 (m, 1.1H), 7.12−7.05 (m, 2.0H), 4.20 (s, 1.3H), 3.72 (s, 1.7H), 3.70 (s, 1.7H), 3.61 (s, 1.3H), 2.11 (s, 1.3H), 2.02 (s, 1.7H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, data of two geometric isomers, ratio Z/E = 1.2:1): δ 170.1, 169.6, 164.1, 163.5 (d, J_{C-F} = 250.0 Hz, 1C), 163.3, 163.2 (d, J_{C-F} = 251.1 Hz, 1C), 142.2, 141.4, 135.3, 132.1 (d, J_{C-F} = 8.1 Hz, 2C), 130.9 (d, J_{C-F} = 8.5 Hz, 2C), 129.8, 127.9 (d, J_{C-F} = 3.7 Hz, 1C), 127.4 (d, J_{C-F} = 3.3 Hz, 1C), 115.6 (d, J_{C-F} = 21.3 Hz, 2C), 114.9 (d, J_{C-F} = 22.0 Hz, 2C), 100.9, 99.8, 60.6, 59.7, 59.0, 58.8, 9.0, 8.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{14}H_{13}FO_4Na$, 287.0690; found, 287.0693.

*(Z)-4-Methoxy-5-(methoxy(4-(trifluoromethyl)phenyl)-methylene)-3-methylfuran-2(5H)-one (**Z-1m**) and (E)-4-Methoxy-5-(methoxy(4-(trifluoromethyl)phenyl)methylene)-3-methylfuran-2(5H)-one (**E-1m**).* Following the general method B, the reaction of the thionoester **16m** (220 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), ***Z*-1m** and ***E*-1m** (251 mg, yield: 80%, Z/E = 1:1) as a white solid. ***Z*-1m**: mp: 119−120 °C; IR (film) ν_{max}: 2949, 1756, 1623, 1456, 1325, 1273, 1163, 1068, 996, 856 cm^{-1}; ^1H NMR (850 MHz, $CDCl_3$): δ 7.63 (m, 2H), 7.51 (m, 2H), 3.73 (s, 6H), 2.03 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (212.5 MHz, $CDCl_3$): δ 169.5, 162.9, 140.7, 135.3, 131.4 (q, J_{C-F} = 33.0 Hz, 1C), 130.5 (3C), 124.6 (2C), 123.8 (q, J_{C-F} = 272.2 Hz, 1C), 99.7, 59.3, 58.8, 8.9 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{13}F_3O_4Na$, 337.0658; found, 337.0658. ***E*-1m**: mp: 101−102 °C; IR (film) ν_{max}: 2946, 1758, 1617, 1410, 1355, 1217, 1162, 1111, 993, 854 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 8.3 Hz, 2H), 4.20 (s, 3H), 3.61 (s, 3H), 2.11 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.7, 163.9, 141.1, 136.7, 135.4, 131.1 (q, J_{C-F} = 32.8 Hz, 1C), 128.9 (2C), 125.4 (q, J_{C-F} = 3.7 Hz, 2C), 123.8 (q, J_{C-F} = 272.5 Hz, 1C), 101.26, 60.8, 59.7, 8.9 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{13}F_3O_4Na$, 337.0658; found, 337.0661.

*(Z)-5-((4-Chlorophenyl)(methoxy)methylene)-4-methoxy-3-methylfuran-2(5H)-one (**Z-1n**) and (E)-5-((4-Chlorophenyl)-(methoxy)methylene)-4-methoxy-3-methylfuran-2(5H)-one (**E-1n**).* Following the general method A, the reaction of the thionoester **16n** (187 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), ***Z*-1n** and ***E*-1n** (233 mg, yield: 83%, Z/E = 1:1.3) as a white solid. ***Z*-1n**: mp: 145−146 °C; IR (film) ν_{max}: 2943, 1754, 1625, 1456, 1273, 1211, 1149, 1076, 981, 842 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.36 (d, J = 8.5 Hz, 2H), 7.32 (d, J = 8.5 Hz, 2H), 3.74 (s, 3H), 3.71 (s, 3H), 2.03 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.6, 163.1, 141.3, 135.8, 131.4 (2C), 130.1, 129.9, 128.1 (2C), 99.7, 59.1, 58.9, 8.9 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{14}H_{13}ClO_4Na$, 303.0395; found, 303.0397. ***E*-1n**: mp: 124−125 °C; IR (film) ν_{max}: 2946, 1759, 1619, 1449, 1356, 1211, 1162, 1012, 992, 841 cm^{-1}; ^1H NMR (850 MHz, $CDCl_3$): δ 7.67 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 4.21 (s, 3H), 3.62 (s, 3H), 2.12 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (212.5 MHz, $CDCl_3$): δ 170.0, 164.0, 141.9, 135.8, 135.5, 130.3, 130.0 (2C), 128.8 (2C), 101.1, 60.8, 59.8, 9.0 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{14}H_{13}ClO_4Na$, 303.0395; found, 303.0397.

*(Z)-5-(Isopropoxy(phenyl)methylene)-4-methoxy-3-methylfuran-2(5H)-one (**Z-1o**) and (E)-5-(Isopropoxy(phenyl)methylene)-4-methoxy-3-methylfuran-2(5H)-one (**E-1o**).* Following the general method C, the reaction of the thionoester **16o** (180 mg, 1 mmol) with **12c** (3.3 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), ***Z*-1o** and ***E*-1o** (238 mg, yield: 87%, Z/E = 3.7:1) as a white solid. ***Z*-1o**: mp: 120−121 °C; IR (film) ν_{max}: 2964, 1747, 1620, 1391, 1361, 1217, 1171, 1060, 1023, 995 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.43−7.34 (m, 5H), 4.19 (dq, J = 18.4, 6.2 Hz, 1H), 3.67 (s, 3H), 2.01 (s, 3H), 1.23 (d, J = 6.2 Hz, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.2, 163.4, 141.0, 131.9, 131.5, 130.0 (2C), 129.6, 127.7 (2C), 100.4, 72.8, 58.8, 22.3 (2C), 8.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{16}H_{18}O_4Na$, 297.1097; found, 291.1102. ***E*-1o**: pale yellow oil; IR (film) ν_{max}: 2926, 1748, 1621, 1614, 1394, 1362, 1167, 1106, 1065, 984 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.63−7.60 (m, 2H), 7.43−7.33 (m, 3H), 4.17 (s, 3H), 4.08 (dq, J = 18.4, 6.1 Hz, 1H), 2.10 (s, 3H), 1.23 (d, J = 6.1 Hz, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.4, 164.3, 141.6, 135.3, 132.3, 129.5, 129.0 (2C), 128.3 (2C), 100.9, 73.7, 59.4, 21.9 (2C), 8.9 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{16}H_{18}O_4Na$, 297.1097; found, 297.1100.

*4-Methoxy-5-(1-methoxy-2-phenylethylidene)-3-methylfuran-2(5H)-one (**1p**) and 4-Methoxy-5-(1-methoxy-2-phenylvinyl)-3-methylfuran-2(5H)-one (**1p′**).* Following the general method A, the reaction of the thionoester **16p** (166 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:3), **1p** and **1p′** (206 mg, yield: 79%, **1p**/**1p′** = 2.2:1) as a colorless oil. **1p** and **1p′**: IR (film) ν_{max}: 2923, 2851, 1747, 1621, 1454, 1392, 1351, 1271, 1155, 1067, 1031, 993, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, data of two geometric isomers, ratio **1p**/**1p′** = 1.2:1): δ 7.36−7.28 (m, 3H), 7.25−7.21 (m, 2H), 6.07 (s, 0.4H), 5.46 (s, 0.4H), 4.13 (s, 1.6H), 3.95 (s, 1.4H), 3.88 (s, 1.0H), 3.86 (s, 1.6H), 3.67 (s, 1.4H), 2.09 (s, 1.6H), 1.92 (s, 1.4H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, data of two geometric isomers, ratio **1p**/**1p′** = 1.2:1): δ 174.8, 171.0, 169.6, 163.8, 150.8, 143.4, 137.4, 134.9, 129.0 (2C), 128.5 (2C), 128.4 (2C), 128.3 (2C), 126.7, 126.6, 107.2, 99.3, 97.7, 77.2, 74.1, 59.4, 59.3, 58.4, 55.4, 35.0, 9.1, 7.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}O_4Na$, 283.0941; found, 283.0948.

*(Z)-4-Methoxy-5-(1-methoxyhexadecylidene)-3-methylfuran-2(5H)-one (**Z-1q**) and (E)-4-Methoxy-5-(1-methoxyhexadecylidene)-3-methylfuran-2(5H)-one (**E-1q**).* Following the general method A, the reaction of the thionoester **16q** (286 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:6), ***Z*-1q** and ***E*-1q** (190 mg, yield: 50%, Z/E = 3.7:1) as a colorless oil. ***Z*-1q**: IR (film) ν_{max}: 2923, 2854, 1748, 1627, 1457, 1376, 453 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.10 (s, 3H), 3.91 (s, 3H), 2.46 (t, J = 7.7 Hz, 2H), 2.04 (s, 3H), 1.51−1.44 (m, 2H), 1.28−1.22 (m, 24H), 0.85 (t, J = 6.9 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 Hz, $CDCl_3$): δ 169.8, 164.2, 146.3, 127.7, 97.2, 59.3, 59.1, 31.8, 29.62 (3C), 29.60 (3C), 29.5, 29.3 (2C), 29.1, 29.0, 27.9, 22.6, 14.0, 9.0 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{23}H_{40}O_4Na$, 403.2819; found, 403.2834. ***E*-1q**: IR (film) ν_{max}: 2924, 2853, 1748, 1621, 1456, 1366, 1017, 801, 435 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.11 (s, 3H), 3.67 (s, 3H), 2.48 (t, J = 7.7 Hz, 2H), 2.04 (s, 3H), 1.55−1.48 (m, 2H), 1.32−1.23 (m, 24H), 0.87 (t, J = 6.8 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.4, 163.3, 148.2, 132.8, 100.3, 59.5, 57.6, 31.9, 29.68 (2C), 29.65, 29.64 (2C), 29.60, 29.5, 29.4, 29.34, 29.27, 27.3, 27.1, 22.7, 14.1, 8.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{23}H_{40}O_4Na$, 403.2819; found, 403.2829.

*(Z)-5-(1-(Hexadecyloxy)hexadecylidene)-4-methoxy-3-methylfuran-2(5H)-one (**Z-1r**) and (E)-5-(1-(Hexadecyloxy)-hexadecylidene)-4-methoxy-3-methylfuran-2(5H)-one (**E-1r**).* Following the general method A, the reaction of the thionoester **16r** (497 mg, 1 mmol) with **12c** (1.1 mmol) gave, after FC (eluent: EtOAc/*n*-hexane = 1:10), ***Z*-1r** and ***E*-1r** (307 mg, yield: 52%, Z/E = 2:1) as a white solid. ***Z*-1r**: mp: 58−59 °C; IR (film) ν_{max}: 2954, 2849, 1725, 1607, 1467, 1398, 1361, 1158, 435 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.17 (t, J = 6.6 Hz, 2H), 4.10 (s, 3H), 2.48 (t, J = 7.5 Hz, 2H), 2.05 (s, 3H), 1.68−1.58 (m, 2H), 1.53−1.46 (m, 2H), 1.38−

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1.23 (m, 50H), 0.86 (m, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.9, 164.4, 146.0, 127.6, 97.2, 72.0, 59.1, 31.9 (2C), 30.0, 29.7 (11C), 29.6 (3C), 29.5 (2C), 29.32 (3C), 29.30, 29.1, 27.9, 25.8, 22.6 (2C), 14.0 (2C), 9.0 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{38}H_{70}O_4Na$, 613.5166; found, 613.5181. ***E*-1r**: mp: 55−56 °C; IR (film) ν_{max}: 2915, 2849, 1731, 1621, 1470, 1399, 1201, 1165, 431 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.09 (s, 3H), 3.82 (t, J = 6.4 Hz, 2H), 2.47 (t, J = 7.6 Hz, 2H), 2.04 (s, 3H), 1.69−1.63 (m, 2H), 1.55−1.47 (m, 2H), 1.42−1.24 (m, 50H), 0.87 (m, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.4, 163.4, 147.6, 133.2, 100.1, 70.3, 59.3, 31.9 (2C), 29.8, 29.7 (6C), 29.65 (5C), 29.61 (3C), 29.5, 29.4, 29.39, 29.34 (3C), 27.6, 27.1, 25.8, 22.7 (2C), 14.1 (2C), 8.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{38}H_{70}O_4Na$, 613.5166; found, 613.5185.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02502.

Comparison of NMR data and copies of NMR spectra; comparison of $^{13}C\{^1H\}$ NMR data for deducing stereochemistry; and NOESY spectra of ***Z*-1a**, ***Z*-1b**, ***Z*-1d**, ***Z*-1e**, ***Z*-1g**, and ***Z*-1r** (PDF)

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Notes

The authors declare no competing financial interest.

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