Preparation of α,β-Unsaturated γ-Keto Aldehydes and New Tetronic Acid and Pyridazine Derivatives by Oxidative Transformations of Alkoxyallene-Based Dihydrofurans

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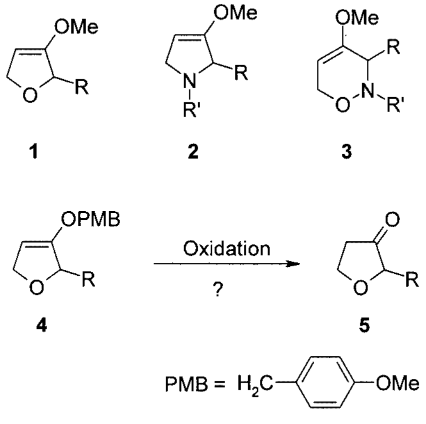
Oxidation of 3-alkoxy-substituted dihydrofuran derivatives **6** and **11** with DDQ unexpectedly provided α,β-unsaturated γ-keto aldehydes **10** and **12**. A mechanism for this new oxidative ring-cleavage is presented. Since α,β-unsaturated γ-keto aldehydes are versatile intermediates, other 3-methoxy-substituted dihydrofuran derivatives **24**, **26**, and **28** were prepared from lithiated methoxyallene and the corresponding aldehydes. Oxidation of dihydrofuran derivatives with DDQ and subsequent treatment with sodium chlorite furnished hydroxy-substituted tetronic acid derivatives, such as **30** and **31**. Condensation of **30** with hydrazine provided the unsaturated pyridazinone derivative **32**. A second route to pyridazine derivatives involves DDQ-mediated oxidation of dihydrofurans and reaction of the products with hydrazine hydrate. This leads to 4-methoxypyridazines **33**, **34**, **35**, and **36** in good overall yields. The oxidative transformations of dihydrofuran derivatives reported here demonstrate new examples of reactivity umpolung; the lithiated alkoxyallenes are equivalents of the unusual synthons **B** and **C**, which represent anions of malondialdehyde or malonaldehydic acid.

Introduction

Lithiated alkoxyallenes are extremely versatile C3 building blocks for the construction of heterocyclic compounds.[1] While their formal [3+2] cyclizations with aldehydes, leading to dihydrofuran derivatives **1**, have been known since the pioneering studies of Brandsma and Arens,[2] the related reactions of lithiated alkoxyallenes with imines and nitrones as electrophiles have only recently been described by us (Scheme 1).[3,4] The new [3+2] cyclization method for the construction of functionalized dihydropyrrole derivatives **2** has been applied to a rather efficient and entirely stereoselective preparation of the uncommon γ-amino acid (−)-detoxinine.[5] The use of nitrones as electrophiles allows an entry into the class of 3,6-dihydro-2*H*-1,2-oxazines **3** by a related [3+3] cyclization process. These heterocycles have turned out to be particularly synthetically valuable.[4] Most experiments in this field so far have been performed with easily available methoxyallene as the precursor, but other substituents at the allene oxygen are also possible; for example, benzyl, (trimethylsilyl)ethyl, or carbohydrate-derived groups.[6] The enol ether group of derivatives **1**−**3** is converted by acidic hydrolysis into the carbonyl group that is often required. Since alternatives would be highly welcome when more complex dihydrofuran, dihydropyrrole, or 1,2-oxazines are involved, we also studied the *para*-methoxybenzyl group, which should allow oxidative cleavage.[7] This method could provide the required heterocycles with a carbonyl group via the corresponding enol forms, for instance, furanone derivatives **5** from dihydrofurans **4** (Scheme 1).[8] Here we describe our results, which were initiated by experiments with compounds of type **4**, and which unexpectedly led to the discovery of new oxidative transformations, opening the way to the synthesis of interesting heterocyclic compounds.



Scheme 1

Results: Oxidations of Dihydrofuran Derivatives

Treatment of 3-*para*-methoxybenzyloxy-substituted dihydrofuran **6** (for its preparation see Scheme 5) with DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) in dichloro-

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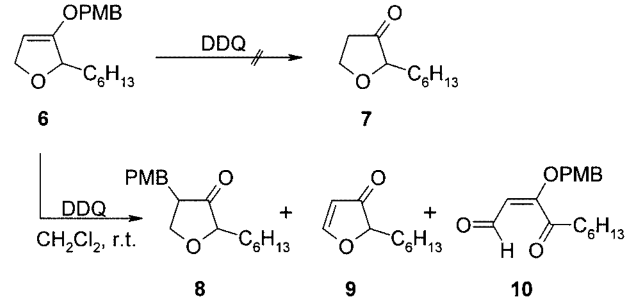
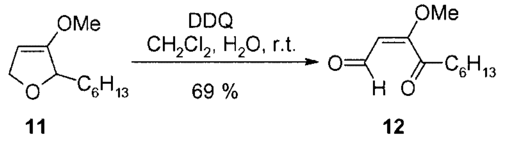
methane did not provide the desired furanone derivative **7**, but a mixture of 4-*para*-methoxybenzyl-3-furanone derivative **8** (two diastereomers) and the unsaturated furanone **9** (Scheme 2). The 1,3-migration of benzyl groups from oxygen to carbon or the formation of oxidation products such as **9** seem generally to be the major pathways in DDQ-mediated oxidations of compounds of type **6**. We will describe the mechanistic details of these reactions in a separate report.[9] If the DDQ-mediated oxidation of **6** was performed in the presence of water, the rearrangement product **8** could not be detected, and **9** was only a minor component. As the major product, we isolated the α,β-unsaturated γ-keto aldehyde **10** in 50% yield.



	8	**9**	**10**
without H_2O	30 % (*trans* : *cis* = 2 : 1)	12 %	–
with H_2O	–	12 %	50 %

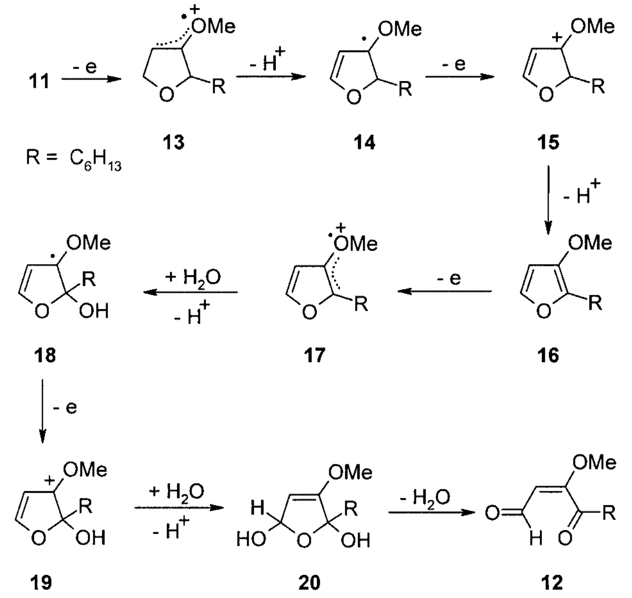
Scheme 2

We immediately recognized that α,β-unsaturated γ-keto aldehydes such as **10** should be very versatile intermediates for the synthesis of heterocycles. In order to avoid complications due to the *para*-methoxybenzyl group, we performed the oxidation of the 3-methoxy-substituted dihydrofuran derivative **11** under these conditions, which smoothly gave the desired compound **12** in 69% yield, without formation of side-products (Scheme 3).



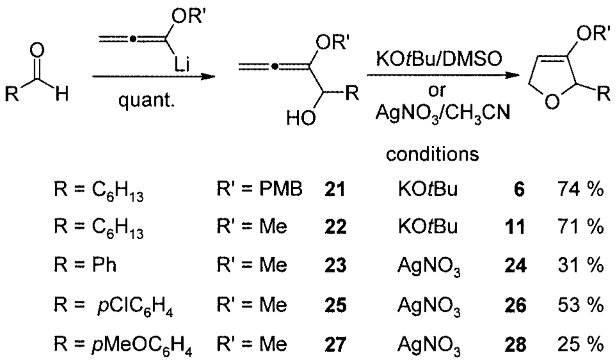
Scheme 3

A suggested mechanism for the oxidative conversion of **11** into **12** is depicted in Scheme 4. It consists of a sequence of electron transfer and deprotonation steps via the radical cation **13**, the radical **14**, and the cation **15**, delivering the 3-methoxy-substituted furan derivative **16** as an intermediate. Oxidative conversions of furans into unsaturated 1,4-dicarbonyl compounds are well known.[10] In our case, the subsequent oxidation of **16** into **12** should be facilitated by the additional methoxy substituent, which stabilizes the intermediate radical cation **17**, the radical **18**, and the cation **19**. The bis-hemiacetal **20** fragments into water and the final product **12**, which is obviously stabilized by the existence of the vinylogous formic ester subunit. Although none of the intermediates were detected or isolated, and alternatives may be conceivable, the overall sequence seems to be highly probable, due to the literature precedent for the individual steps.



Scheme 4

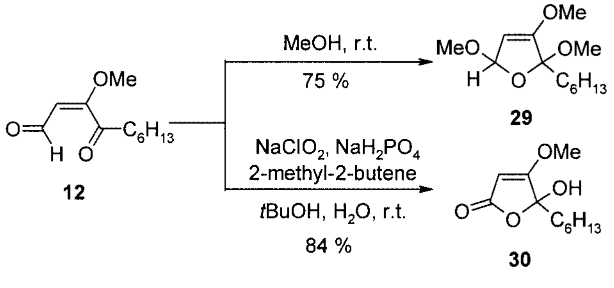
The smooth conversion of **11** into **12** and the obvious synthetic potential of the products motivated us to examine briefly the scope and limitations of this oxidative process. The required dihydrofuran derivatives were prepared by application of the "old" Brandsma method, which, however, revealed some unexpected problems (Scheme 5). While the above-mentioned dihydrofuran derivatives **6** and **11** could easily be prepared via the addition products **21** and **22** of heptanal with lithiated (*para*-methoxybenzyloxy)allene or methoxyallene, respectively, the desired compounds with aryl substituents caused a lot of trouble. Treatment of aromatic aldehydes with an excess of lithiated methoxyallene (and other alkoxyallenes) quantitatively provided the expected addition products **23**, **25**, and **27**. However, we failed to reproducibly perform the cyclization of these compounds under the strongly basic reaction conditions.[9,11] Remarkably, in the seminal papers of Brandsma et al., aromatic aldehydes were not included as electrophiles,[2] and examples reported later have not been cyclized into the corresponding dihydrofuran derivatives.[12] We finally found that under carefully controlled reaction conditions, silver nitrate in acetonitrile gave at least moderate, but reproducible yields of the desired dihydrofuran derivatives **24**, **26**, and **28**.[13] For these cyclizations, a moderately electron-withdrawing substituent such as *para*-chlorophenyl is apparently favourable, whereas an electron-donating group like *para*-methoxyphenyl gave the lowest performance. The reasons for this particular sensitivity of aryl-substituted compounds are so far not clear, but oxidative processes and the formation of radical intermediates which could lead to side reactions may play a role.



Scheme 5

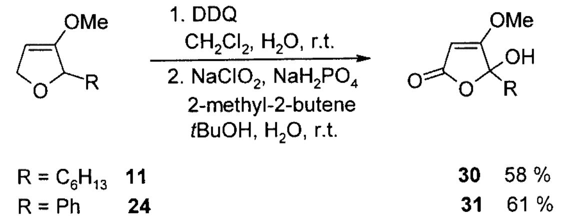
Subsequent Reactions of α,β-Unsaturated γ-Keto Aldehydes

As shown in Scheme 3, we demonstrated the smooth conversion of dihydrofuran **11** into α,β-unsaturated γ-keto aldehyde **12**. Since we observed the addition of methanol as a side-reaction during the condensation of **12** with hydrazine hydrate (Scheme 8), we deliberately treated **12** with methanol, and hence obtained acetal **29** in 75% yield as a mixture of two diastereomers (Scheme 6). A second subsequent reaction of **12** involved its oxidation with sodium chlorite,[14] which selectively converted the aldehyde unit into a carboxylic acid. The intermediate cyclized to furnish the hydroxy-substituted tetronic acid derivative **30** in good yield.



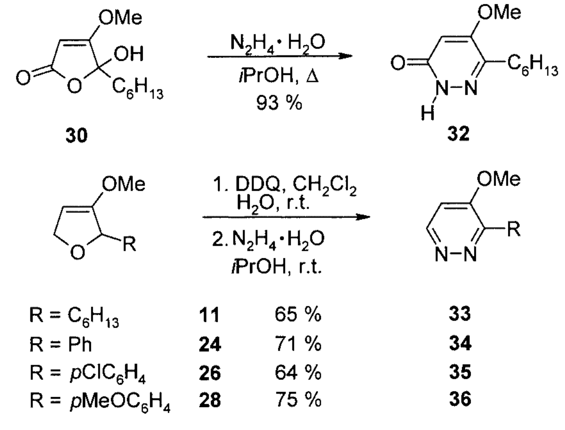
Scheme 6

Formation of the functionalized tetronic acid derivative **30** could be performed efficiently as a one-pot sequence starting from the dihydrofuran **11** (Scheme 7). After DDQ treatment, the crude intermediate **12** was further oxidized, furnishing the desired product **30** in satisfactory overall yield. Analogously, compound **31** was obtained from the phenyl-substituted dihydrofuran derivative **24** in 61% yield (Scheme 7). The structure of compounds **30** and **31** is very close to that of the antibiotic penicillin acid (R = 2-propenyl),[15] and analogues of this compound should be easily available in a flexible manner via our new route to hydroxy-substituted tetronic acid derivatives disclosed here.[16]



Scheme 7

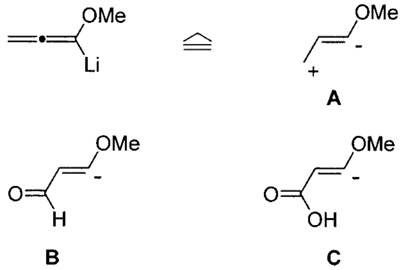
Pyridazines are also important as biologically active compounds,[17] and are frequently synthesized by the condensation of 1,4-dicarbonyl compounds with hydrazine derivatives. It was therefore tempting to use our products as precursors for the synthesis of these heterocycles. Treatment of **30** with hydrazine hydrate afforded the expected unsaturated pyridazinone derivative **32** in excellent yield (Scheme 8). The corresponding aromatic 4-methoxy-substituted pyridazines **33**–**36** could easily be prepared starting from dihydrofurans **11**, **24**, **26**, and **28**, respectively, by oxidation with DDQ, followed by condensation of the intermediate α,β-unsaturated γ-keto aldehydes with hydrazine hydrate and isopropyl alcohol as solvent (when methanol was used, we found that **29** was formed as a side-product, Scheme 6). The overall yields are in the region of 70%, which is, considering the number of steps involved, very satisfactory.



Scheme 8

Conclusion

In this report, we describe our serendipitously discovered DDQ-promoted transformations of 3-methoxy-substituted dihydrofuran derivatives, which led to α,β-unsaturated γ-keto aldehydes. These highly functionalized intermediates could be further transformed into tetronic acid and pyridazine derivatives, thus allowing a very smooth and probably highly flexible entry into these classes of heterocycles, which have known biological activity. Beyond these preparative aspects, our results reveal again the remarkable versatility of metalated alkoxyallenes in organic synthesis.[1] The oxidative processes extend the utility of lithiated methoxyallene from its well established and often exploited use as a 1,3-zwitterionic synthon **A** to being an equivalent for the unusual synthons **B** and **C**. These are equivalent to anions of malondialdehyde or malonaldehydic acid (Scheme 9). All these synthons **A** to **C** involve an umpolung of reactivity[18] at the negatively charged allene carbon next to oxygen, which is responsible for the synthetic value and versatility of metalated alkoxyallenes.



Scheme 9

Experimental Section

General Methods: Unless otherwise stated, all reactions were performed under argon in flame-dried flasks, and the reaction components were added via syringe. All solvents were dried using standard procedures. IR spectra were measured with a Perkin−Elmer FT-IR spectrometer Nicolet 5 SXC. ^{1}H- and ^{13}C-NMR spectra were recorded on Bruker instruments (WH 270, AC 250, AC 500) or Jeol Eclipse 500. ^{1}H shifts are reported in ppm relative to TMS ($\delta = 0.00$ ppm) or to $CHCl_3$ ($\delta = 7.26$ ppm). Higher order NMR spectra are approximately interpreted as first-order spectra if possible. ^{13}C chemical shifts are reported relative to $CDCl_3$ ($\delta = 77.0$). Neutral aluminum oxide (activity III, Fluka or Merck) or silica gel (0.040−0.063 mm, Fluka) were used for column chromatography. Nucleosil 50−5 (Macherey−Nagel & Co) was used for HPLC. Melting points are uncorrected. Methoxyallene[19] and *p*-methoxybenzylpropargylic ether[20] were prepared by literature procedures. DMSO was distilled from calcium hydride. All other chemicals were commercially available and used as received.

***p*-(Methoxybenzyloxy)allene:** *p*-(Methoxybenzyl)propargylic ether[20] (3.00 g, 17.0 mmol) was dissolved in absolute toluene (60 mL) under argon, and KO*t*Bu (954 mg, 8.50 mmol) was added. The reaction mixture was heated to 100 °C for 1 h. After cooling to room temperature, water (100 mL) was added. The aqueous phase was extracted with diethyl ether (3 × 40 mL), the combined organic phases were dried (Na_2SO_4) and the solvents were removed. After purification by column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 40:1), the product (1.82 g, 61%) was isolated. Yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.25$, 6.85 (2 d, $J = 8.8$ Hz, 2 H each, Ar), 6.79 (t, $J = 5.9$ Hz, 1 H, 1-H), 5.44 (d, $J = 5.9$ Hz, 2 H, 3-H), 4.51 (s, 2 H, CH_2Ar), 3.73 (s, 3 H, OMe) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): $\delta = 201.3$ (s, C-2), 159.3, 129.2 (2 s, *i*-Ar), 129.4, 121.3, 113.6 (3 d, C-1, 2 Ar), 90.7 (t, C-3), 70.2 (t, CH_2Ar), 49.0 (q, OMe) ppm. IR (neat): $\tilde{\nu} = 3040-2835$ cm^{-1} (C−H), 1955 (C=C=C), 1615 (C=C). MS (80 eV, EI): *m/z* (%) = 176 (11) $[M]^+$, 121 (100) $[M - C_3H_3O]^+$. $C_{11}H_{12}O_2$ (176.2): calcd. C 74.98, H 6.86; found C 75.02, H 6.73.

Oxidation of 3-Alkoxydihydrofurans with DDQ. General Procedure 1: DDQ was added to the solution of the corresponding dihydrofuran in dry dichloromethane or a mixture of dichloromethane and water. After stirring for 40 min at room temperature, $NaHCO_3$ solution (20 mL) was added. The aqueous phase was extracted with dichloromethane (3 × 20 mL), the combined organic phases were washed with brine (20 mL) and dried ($MgSO_4$), and the solvents were removed. The products were purified by column chromatography as described below.

Oxidation of 2-Hexyl-3-(4-methoxybenzyloxy)-2,5-dihydrofuran (6) with DDQ in the Absence of Water: According to general procedure 1, **6** (128 mg, 0.44 mmol) and DDQ (140 mg, 0.62 mmol; added in 35 mg portions every 10 minutes) dissolved in dry dichloromethane (5 mL) gave the two diastereomers *trans*-**8** and *cis*-**8** which were separated by HPLC (silica gel, *n*-hexane/ethyl acetate, 19:1). Yields: *trans*-**8** (26 mg, 20%) and *cis*-**8** (13 mg, 10%). The ^{1}H-NMR spectrum of the crude product showed signals of compound **9** (12%).

***trans*-2-Hexyl-4-[(4-methoxyphenyl)methyl]-4,5-dihydrofuran-3(2*H*)-one (*trans*-8):** Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.06$, 6.82 (2 d, $J = 8.7$ Hz, 2 H each, Ar), 4.30 (ddd, $J = 0.6$, 8.7, 9.3 Hz, 1 H, 5-H_A), 3.78 (s, 3 H, OMe), 3.70 (dd, $J = 9.3$, 9.9 Hz, 1 H, 5-H_B), 3.68 (dd, $J = 4.3$, 7.6 Hz, 1 H, 2-H), 3.10 (dd, $J = 4.3$, 14.2 Hz, 1 H, CH_2Ar), 2.72 (dddd, $J = 4.3$, 8.7, 9.6, 9.9 Hz, 1 H, 4-H), 2.59 (dd, $J = 9.6$, 14.2 Hz, 1 H, CH_2Ar), 1.75 (dddd, $J = 4.3$, 5.8, 10.2, 14.0 Hz, 1 H, 1′-H_A), 1.59 (dddd, $J = 4.9$, 7.6, 10.1, 14.0 Hz, 1 H, 1′-H_B), 1.47−1.22 (m, 8 H, 2′-H, 3′-H, 4′-H, 5′-H), 0.87 (t, $J = 6.9$ Hz, 3 H, 6′-H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 217.1$ (s, C-3), 158.3, 130.6 (2 s, *i*-Ar), 129.5, 114.0 (2 d, Ar), 80.9 (d, C-2), 69.9 (t, C-5), 55.2 (q, OMe), 49.2 (d, C-4), 32.5 (t, CH_2Ar), 31.6, 30.9, 29.0, 25.2, 22.5 (5 t, C-1′, C-2′, C-3′, C-4′, C-5′), 14.0 (q, C-6′) ppm. IR (neat): $\tilde{\nu} = 3100-3000$ cm^{-1} (=C−H), 2955−2855 (C−H), 1740 (C=O). MS (80 eV, EI): *m/z* (%) = 290 (38) $[M]^+$, 169 (100) $[M - C_8H_9O]^+$, 148 (98) $[C_{10}H_{12}O]^+$, 121 (79) $[C_8H_9O]^+$. HRMS (80 eV): calcd. for $C_{18}H_{26}O_3$: 290.18819; found 290.18634.

***cis*-2-Hexyl-4-[(4-methoxyphenyl)methyl]-4,5-dihydrofuran-3(2*H*)-one (*cis*-8):** Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.08$, 6.84 (2 d, $J = 8.8$ Hz, 2 H each, Ar), 4.12 (dd, $J = 7.5$, 9.6 Hz, 1 H, 5-H_A), 3.93 (dd, $J = 5.9$, 9.6 Hz, 1 H, 5-H_B), 3.85 (dd_{br}, $J = 4.1$, 8.0 Hz, 1 H, 2-H), 3.79 (s, 3 H, OMe), 2.99 (dd, $J = 4.3$, 13.9 Hz, 1 H, CH_2Ar), 2.72 (ddddd, $J = 0.9$, 4.3, 5.9, 7.5, 10.2 Hz, 1 H, 4-H), 2.62 (dd, $J = 10.2$, 13.9 Hz, 1 H, CH_2Ar), 1.68−1.61 (m, 1 H, 1′-H_A), 1.52−1.37 (m, 3 H, 1′-H_B, 2′-H), 1.35−1.23 (m, 6 H, 3′-H, 4′-H, 5′-H), 0.88 (t, $J = 7.0$ Hz, 3 H, 6′-H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 217.1$ (s, C-3), 158.4, 130.5 (2 s, *i*-Ar), 129.8, 114.0 (2 d, Ar), 80.5 (d, C-2), 68.8 (t, C-5), 55.2 (q, OMe), 48.8 (d, C-4), 33.5 (t, CH_2Ar), 31.6, 30.3, 29.0, 25.5, 22.5 (5 t, C-1′, C-2′, C-3′, C-4′, C-5′), 14.0 (q, C-6′) ppm. IR (neat): $\tilde{\nu} = 3100-3000$ cm^{-1} (=C−H), 2955−2860 (C−H), 1740 (C=O). MS (80 eV, EI): *m/z* (%) = 290 (49) $[M]^+$, 169 (17) $[M - C_8H_9O]^+$, 148 (100) $[C_{10}H_{12}O]^+$, 121 (77) $[C_8H_9O]^+$. HRMS (80 eV): calcd. for $C_{18}H_{26}O_3$: 290.18819; found 290.18765.

2-Hexylfuran-3-one (9): Characteristic data: ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 8.20$ (d, $J = 2.9$ Hz, 1 H, 5-H), 5.70 (d, $J = 2.9$ Hz, 1 H, 4-H) ppm. For further characterization see ref.[9]

Oxidation of 2-Hexyl-3-(4-methoxybenzyloxy)-2,5-dihydrofuran (6) with DDQ in the Presence of Water: According to general procedure 1, **6** (145 mg, 0.50 mmol) and DDQ (227 mg, 1.00 mmol) dissolved in dichloromethane and water (5 mL/0.25 mL) gave, after column chromatography on silica gel (*n*-hexane/ethyl acetate, 4:1), **10** (76 mg, 50%). The ^{1}H NMR spectrum of the crude product showed compound **9** (12%).

(*E*)-3-(4-Methoxybenzyloxy)-4-oxodec-2-enal (10): Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.92 (d, *J* = 7.1 Hz, 1 H, 1-H), 7.31, 6.94 (2 d, *J* = 8.8 Hz, 2 H each, Ar), 5.61 (d, *J* = 7.1 Hz, 1 H, 2-H), 4.87 (s, 2 H, C*H*$_2$Ar), 3.84 (s, 3 H, OMe), 2.74 (t, *J* = 7.3 Hz, 2 H, 5-H), 1.72−1.55, 1.37−1.20 (2 m, 8 H, 6-H, 7-H, 8-H, 9-H), 0.87 (t, *J* = 6.7 Hz, 3 H, 10-H) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 198.7 (s, C-4), 191.4 (d, C-1), 167.3 (s, C-3), 160.1, 126.1 (2 s, *i*-Ar), 129.7, 114.3 (2 d, Ar), 109.0 (d, C-2), 71.3 (t, *C*H$_2$Ar), 55.3 (q, OMe), 40.0, 31.5, 28.7, 23.2, 22.4 (5 t, C-5, C-6, C-7, C-8, C-9), 14.0 (q, C-10) ppm. IR (neat): ṽ = 3100−3000 cm^{-1} (=C−H), 2955−2860 (C−H), 1710, 1665 (C=O), 1600 (C=C). MS (80 eV, EI): *m*/*z* (%) = 304 (2) [M]$^+$, 276 (1) [M − CO]$^+$, 191 (3) [M − $C_7H_{13}O$]$^+$, 137 (2) [$C_8H_9O_2$]$^+$, 121 (100) [$C_8H_{10}O$]$^+$. HRMS (80 eV): calcd. for $C_{18}H_{24}O_4$: 304.16746; found 304.16922.

Oxidation of 2-Hexyl-3-methoxy-2,5-dihydrofuran (11) with DDQ in the Presence of Water: According to general procedure 1, **11** (92 mg, 0.50 mmol) and DDQ (227 mg, 1.00 mmol) dissolved in dichloromethane and water (5 mL/0.25 mL) provided, after column chromatography on silica gel (*n*-hexane/ethyl acetate, 4:1), **12** (68 mg, 69%) as a colorless oil.

(*E*)-3-Methoxy-4-oxodec-2-enal (12): ^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.94, 5.50 (2 d, *J* = 6.8 Hz, 1 H each, 1-H, 2-H), 3.78 (s, 3 H, OMe), 2.74 (t, *J* = 7.3 Hz, 2 H, 5-H), 1.70−1.56, 1.40−1.22 (2 m, 8 H, 6-H, 7-H, 8-H, 9-H), 0.89 (t, *J* = 6.6 Hz, 3 H, 10-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 198.6 (s, C-4), 191.4 (d, C-1), 168.0 (s, C-3), 108.3 (d, C-2), 56.3 (q, OMe), 39.9, 31.5, 28.7, 23.1, 22.4 (5 t, C-5, C-6, C-7, C-8, C-9), 14.0 (q, C-10) ppm. IR (neat): ṽ = 2955−2860 cm^{-1} (C−H), 1760, 1715, 1665 (C=O), 1600 (C=C). MS (80 eV, EI): *m*/*z* (%) = 198 (48) [M]$^+$, 127 (91) [M − C_5H_{11}]$^+$, 113 (25) [M − C_6H_{13}]$^+$, 43 (100) [C_3H_7]$^+$. HRMS (80 eV): calcd. for $C_{11}H_{18}O_3$: 198.12559; found 198.12754.

Addition of Lithiated Alkoxyallenes to Aldehydes. General Procedure 2: *n*BuLi (1.3−2 equiv.) was added to a solution of alkoxyallene (1.7−2.5 equiv.) in dry THF (2 mL/1 mmol) at −40 °C. After stirring for 15 min at −50 °C to −40 °C, the solution was cooled to −78 °C, and the corresponding aldehyde (1 equiv.), dissolved in dry THF (1.6 mL/1 mmol), was added. After stirring for 1.5 h at this temperature, water (10 mL/1 mmol) was added. The aqueous phase was extracted with ethyl acetate (3 × 10 mL/1 mmol), the combined organic phases were dried ($MgSO_4$), and the solvents were removed under reduced pressure. The crude product was used without purification in the next step.

Cyclization with KO*t*Bu. General Procedure 3: KO*t*Bu (0.5 equiv.) was added to a solution of the allene adduct (1 equiv.) in dry DMSO (5 mL/1 mmol). After stirring at 50 °C for 2 h, $NaHCO_3$ solution and water (7 mL each/1 mmol) were added. The aqueous phase was extracted with ethyl acetate (3 × 7 mL/1 mmol), the combined organic phases were washed with $NaHCO_3$ solution (2 × 7 mL/1 mmol), dried ($MgSO_4$), and the solvents were evaporated at reduced pressure. The products were purified by column chromatography as described below.

Cyclization with Silver Nitrate in Acetonitrile. General Procedure 4: The allene adduct (1 equiv.) was dissolved in dry acetonitrile (5 mL/1 mmol), silver nitrate (0.2 equiv.) was added, and the resulting mixture was stirred under an argon atmosphere with the exclusion of light at room temperature. The mixture was filtered through Celite, washing with ethyl acetate, and the filtrate was concentrated. The products were purified by column chromatography as described below.

3-(4-Methoxybenzyloxy)deca-1,2-dien-4-ol (21): According to general procedure 2, heptanal (0.42 mL, 344 mg, 3.02 mmol), *p*-(methoxybenzyloxy)allene (0.88 g, 5.00 mmol) and *n*-butyllithium (1.60 mL, 2.5 M in *n*-hexane, 4.00 mmol) afforded a mixture of **21** and (*p*-methoxybenzyloxy)allene (1.15 g) as brownish oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.21, 6.82 (2 d, *J* = 8.5 Hz, 2 H each, Ar), 5.46 (br. s, 2 H, 1-H), 4.48 (s, 2 H, C*H*$_2$Ar), 4.17−4.05 (m, 1 H, 4-H), 3.69 (s, 3 H, OMe), 2.65 (d, *J* = 5.9 Hz, 1 H, OH), 1.75−1.18 (m, 10 H, 5-H, 6-H, 7-H, 8-H, 9-H), 0.91−0.82 (m, 3 H, 10-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 197.2 (s, C-2), 159.0, 134.5, 121.2 (3 s, C-3, 2 *i*-Ar), 134.5, 113.4 (2 d, Ar), 91.2 (t, C-1), 70.7, 70.0 (d, t, C-4, *C*H$_2$Ar), 54.7 (q, OMe), 34.2, 31.5, 28.8, 25.1, 22.3 (5 t, C-5, C-6, C-7, C-8, C-9), 13.7 (q, C-10) ppm.

2-Hexyl-3-(4-methoxybenzyloxy)-2,5-dihydrofuran (6): According to general procedure 3, crude **21** (1.15 g, max. 3.02 mmol) and KO*t*Bu (168 mg, 1.50 mmol) in dry DMSO (15 mL) furnished, after column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 30:1), **6** (637 mg, 74%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.25, 6.87 (2 d, *J* = 8.5 Hz, 2 H each, Ar), 4.74 (s, 2 H, C*H*$_2$Ar), 4.64 (m$_c$, 1 H, 4-H), 4.60 (m$_c$, 3 H, 2-H, 5-H), 3.75 (s, 3 H, OMe), 1.84−1.20 (m, 10 H, 1′-H, 2′-H, 3′-H, 4′-H, 5′-H), 0.87 (t, *J* = 6.6 Hz, 3 H, 6′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 159.3, 156.8, 128.3 (3 s, C-3, *i*-Ar), 129.0, 113.6 (2 d, Ar), 90.5 (d, C-4), 81.3 (d, C-2), 72.5 (t, C-5), 71.6 (*C*H$_2$Ar), 54.9 (q, OMe), 33.7, 31.7, 29.2, 24.3, 22.4 (5 t, C-1′, C-2′, C-3′, C-4′, C-5′), 13.9 (q, C-6′) ppm. IR (neat): ṽ = 3100−3000 cm^{-1} (=C−H), 2955−2855 (C−H), 1660 (C=C). MS (80 eV, EI): *m*/*z* (%) = 290 (3) [M]$^+$, 288 (2) [M − 2 H]$^+$, 205 (1) [M − C_6H_{13}]$^+$, 121 (100) [C_8H_9O]$^+$. HRMS (80 eV): calcd. for $C_{18}H_{26}O_3$: 290.18819; found 290.18554.

3-Methoxydeca-1,2-dien-4-ol (22): According to general procedure 2, heptanal (1.26 mL, 1.03 g, 9.03 mmol), methoxyallene (1.89 mL, 1.59 g, 22.7 mmol) and *n*-butyllithium (7.20 mL, 2.5 M in *n*-hexane, 18.0 mmol) provided **22** (1.60 g, purity > 90%) as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.52 (s, 2 H, 1-H), 4.20−4.05 (m, 1 H, 4-H), 3.44 (s, 3 H, OMe), 2.63 (br. s, 1 H, OH), 1.73−1.20 (m, 10 H, 5-H, 6-H, 7-H, 8-H, 9-H), 0.96−0.82 (m, 3 H, 10-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 196.9 (s, C-2), 135.9 (s, C-3), 91.5 (t, C-1), 70.8 (d, C-4), 55.9 (q, OMe), 34.2, 31.5, 28.9, 25.2, 22.3 (5 t, C-5, C-6, C-7, C-8, C-9), 13.7 (q, C-10) ppm.

2-Hexyl-3-methoxy-2,5-dihydrofuran (11): According to general procedure 3, crude **22** (1.60 g, max. 9.03 mmol) and KO*t*Bu (504 mg, 4.50 mmol) in dry DMSO (60 mL) furnished, after column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 30:1), **11** (1.18 g, 71%) as a colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.65−4.55 (m, 4 H, 2-H, 4-H, 5-H), 3.66 (s, 3 H, OMe), 1.73−1.22 (m, 10 H, 1′-H, 2′-H, 3′-H, 4′-H, 5′-H), 0.88 (t, *J* = 6.6 Hz, 3 H, 6′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 158.3 (s, C-3), 89.5 (d, C-4), 81.0 (d, C-2), 72.4 (t, C-5), 57.0 (q, OMe), 33.7, 31.7, 29.2, 24.3, 22.4 (5 t, C-1′, C-2′, C-3′, C-4′, C-5′), 13.8 (q, C-6′) ppm. IR (neat): ṽ = 2955−2860 cm^{-1} (C−H), 1665 (C=C). MS (80 eV, EI): *m*/*z* (%) = 184 (3) [M]$^+$, 153 (6) [M − OCH_3]$^+$, 99 (100) [M − C_6H_{13}]$^+$. HRMS (80 eV): calcd. for $C_{11}H_{20}O_2$: 184.1463; found 184.1460.

2-Methoxy-1-phenylbuta-2,3-dien-1-ol (23): According to general procedure 2, benzaldehyde (0.20 mL, 209 mg, 1.97 mmol), methoxyallene (0.42 mL, 353 mg, 5.04 mmol) and *n*-butyllithium (1.60 mL, 2.5 M in *n*-hexane, 4.00 mmol) afforded **23** (378 mg, purity > 90%) as a yellow oil. The spectroscopic data of **23** are identical with those reported earlier (ref. 12d).

3-Methoxy-2-phenyl-2,5-dihydrofuran (24): According to general procedure 4, crude **23** (378 mg, max. 1.97 mmol) and silver nitrate (68 mg, 0.40 mmol) in dry acetonitrile (10 mL) afforded, after column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 8:1), **24** (107 mg, 31%) as a colorless oil, which rapidly decomposed. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 7.43−7.28 (m, 5 H, Ph), 5.56−5.50 (m, 1 H, 2-H), 4.94−4.87 (m, 1 H, 5-H$_A$), 4.84−4.75 (m, 2 H, 4-H, 5-H$_B$), 3.61 (s, 3 H, OMe) ppm. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 157.6, 140.6 (2 s, C-3, *i*-Ar), 128.1, 127.8, 126.6 (3 d, Ar), 90.2 (d, C-4), 83.3 (d, C-2), 73.2 (t, C-5), 57.5 (q, OMe) ppm. IR (neat): ṽ = 3090−3030 cm^{-1} (=C−H), 2935−2840 (C−H), 1665 (C=C). MS (80 eV, EI): *m*/*z* (%) = 176 (100) [M]$^+$, 174 (19) [M − 2 H]$^+$, 145 (34) [M − OCH$_3$]$^+$, 105 (46) [M − C$_6$H$_5$]$^+$, 77 (35) [C$_6$H$_5$]$^+$. HRMS (80 eV): calcd. for C$_{11}$H$_{12}$O$_2$: 176.08373; found 176.08444.

1-(4-Chlorophenyl)-2-methoxybuta-2,3-dien-1-ol (25): According to general procedure 2, *p*-chlorobenzaldehyde (281 mg, 2.00 mmol), methoxyallene (0.42 mL, 353 mg, 5.04 mmol) and *n*-butyllithium (1.60 mL, 2.5 M in *n*-hexane, 4.00 mmol) furnished **25** (391 mg, purity >90%) as a yellow oil. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 7.33−7.20 (m, 5 H, Ph), 5.48 (d, *J* = 1.9 Hz, 2 H, 4-H), 5.15 (td, *J* = 1.9, 5.3 Hz, 1 H, 1-H), 3.37 (s, 3 H, OMe), 3.21 (d, *J* = 5.3 Hz, 1 H, OH) ppm. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 196.7 (s, C-3), 139.3, 135.4, 133.1 (3 s, C-2, 2 *i*-Ar), 128.0, 127.8 (2 d, Ar), 92.8 (t, C-4), 72.1 (d, C-1), 56.3 (q, OMe) ppm.

2-(4-Chlorophenyl)-3-methoxy-2,5-dihydrofuran (26): According to general procedure 4, crude **25** (391 mg, max. 2.00 mmol) and silver nitrate (68 mg, 0.40 mmol) in dry acetonitrile (10 mL) provided, after column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 8:1), **26** (223 mg, 53%) as a colorless oil. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 7.33−7.25 (m, 4 H, Ar), 5.47−5.40 (m, 1 H, 2-H), 4.87−4.81 (m, 1 H, 5-H$_A$), 4.77−4.70 (m, 2 H, 4-H, 5-H$_B$), 3.57 (s, 3 H, OMe) ppm. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 157.3, 139.3, 133.6 (3 s, C-3, 2 *i*-Ar), 128.3, 128.0 (2 d, Ar), 90.4 (d, C-4), 82.6 (d, C-2), 73.4 (t, C-5), 57.6 (q, OMe) ppm. IR (neat): ṽ = 3095−3005 cm^{-1} (=C−H), 2960−2850 (C−H), 1665 (C=C). MS (80 eV, EI): *m*/*z* (%) = 210 (100) [M]$^+$, 179 (47) [M − OCH$_3$]$^+$, 175 (44) [M − Cl]$^+$, 139 (35) [M − C$_2$H$_5$O$_2$]$^+$. HRMS (80 eV): calcd. for C$_{11}$H$_{11}$ClO$_2$: 210.04476; found 210.04537.

2-Methoxy-1-(4-methoxyphenyl)buta-2,3-dien-1-ol (27): According to general procedure 2, *p*-methoxybenzaldehyde (0.96 mL, 1.08 g, 7.91 mmol), methoxyallene (1.68 mL, 1.41 g, 20.2 mmol) and *n*-butyllithium (6.40 mL, 2.5 M in *n*-hexane, 16.0 mmol) afforded **27** (1.50 g, purity >90%) as a yellow oil. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 7.31, 6.83 (2 d, *J* = 8.8 Hz, 2 H each, Ar), 5.52 (d, *J* = 1.9 Hz, 2 H, 4-H), 5.16 (td, *J* = 1.9, 5.2 Hz, 1 H, 1-H), 3.74, 3.40 (2 s, 3 H each, 2 OMe), 3.03 (d, *J* = 5.2 Hz, 1 H, OH) ppm. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 196.9 (s, C-3), 158.9, 135.9, 133.1 (3 s, C-2, 2 *i*-Ar), 127.6, 113.2 (2 d, Ar), 92.4 (t, C-4), 72.2 (d, C-1), 56.2, 54.8 (2 q, 2 OMe) ppm.

3-Methoxy-2-(4-methoxyphenyl)-2,5-dihydrofuran (28): According to general procedure 4, crude **27** (376 mg, max. 1.98 mmol) and silver nitrate (68 mg, 0.40 mmol) dissolved in dry acetonitrile (10 mL) provided, after column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 8:1) **28** (104 mg, 25%) as a colorless oil, which rapidly decomposed. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.32, 6.93 (2 d, *J* = 8.8 Hz, 2 H each, Ar), 5.48 (ddd, *J* = 1.6, 3.1, 5.1 Hz, 1 H, 2-H), 4.87 (ddd, *J* = 1.6, 5.1, 10.4 Hz, 1 H, 5-H$_A$), 4.80 (q, *J* = 1.6 Hz, 1 H, 4-H), 4.77 (ddd, *J* = 1.6, 3.1, 10.4 Hz, 1 H, 5-H$_B$), 3.80, 3.64 (2 s, 3 H each, 2 OMe) ppm. ^{13}C NMR (125.8 MHz, CDCl$_3$): δ = 159.4, 157.7, 132.7 (3 s, C-3, *i*-Ar), 128.0, 113.6 (2 d, Ar), 90.3 (d, C-4), 83.0 (d, C-2), 72.9 (t, C-5), 57.5, 55.0 (2 q, 2 OMe) ppm. IR (neat): ṽ = 3100−3005 cm^{-1} (=C−H), 2960−2840 (C−H), 1665 (C=C). MS (80 eV, EI): *m*/*z* (%) = 206 (100) [M]$^+$, 175 (84) [M − OCH$_3$]$^+$, 135 (46) [M − C$_2$H$_5$O$_2$]$^+$, 77 (24) [C$_6$H$_5$]$^+$. HRMS (80 eV): calcd. for C$_{12}$H$_{14}$O$_2$: 206.09429; found 206.09534.

2-Hexyl-2,3,5-trimethoxy-2,5-dihydrofuran (29): Crude **12** (max. 0.5 mmol) was dissolved in methanol (5 mL). After 16 h at room temperature, the solvent was evaporated. Column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 4:1) provided **29** as a yellowish oil (91 mg, 75%, purity 90%, 2 diastereomers, ratio 2:1, signals of minor diastereomer are marked*). ^{1}H NMR (500 MHz, C$_6$D$_6$): δ = 5.59*, 5.36, 4.62, 4.57* (4 d, *J* = 1.3, *J** = 1.1 Hz, 1 H each, 4-H, 5-H), 3.41, 3.37, 3.36*, 3.13*, 3.11, 3.10* (6 s, 18 H, 6 OMe), 2.18−2.00, 1.89−1.79, 1.65−1.54, 1.49−1.10, 0.90−0.78 (5 m, 26 H, 1′-H, 2′-H, 3′-H, 4′-H, 5′-H) ppm. ^{13}C NMR (125.8 MHz, C$_6$D$_6$): δ = 159.6*, 159.3 (2 s, C-3), 110.6*, 109.8 (2 s, C-2), 105.9*, 104.7, 96.4, 96.3* (4 d, C-4, C-5), 57.1*, 57.1, 55.3, 54.7*, 50.2, 49.5* (6 q, 6 OMe), 37.7*, 37.6, 32.2, 32.2*, 29.9*, 29.7, 23.8, 23.7*, 22.9*, 22.8 (10 t, C-1′, C-2′, C-3′, C-4′, C-5′), 14.2*, 14.2 (2 q, C-6′) ppm. IR (neat): ṽ = 2955−2860 cm^{-1} (C-H), 1670 (C=C). MS (80 eV, EI): *m*/*z* (%) = 244 (1) [M]$^+$, 243 (2) [M − H]$^+$, 213 (24) [M − OCH$_3$]$^+$, 181 (2) [M − 2 OCH$_3$]$^+$, 159 (100) [M − C$_6$H$_{13}$]$^+$, 85 (16) [C$_6$H$_{13}$]$^+$. HRMS (80 eV): calcd. for C$_{13}$H$_{24}$O$_4$: 244.16746; found 244.16563.

Oxidation of α,β-Unsaturated γ-Keto Aldehydes Using Sodium Chlorite. General Procedure 5: The α,β-unsaturated γ-keto aldehyde was dissolved in *tert*-butyl alcohol, and 2-methyl-2-butene was added. A mixture of sodium chlorite and sodium dihydrogen phosphate in water was added to this solution. After stirring for 2 h, sodium sulfite was added with cooling by a water-bath. The reaction mixture was stirred for 10 min, and then water (20 mL) was added. The aqueous phase was extracted with ethyl acetate (3 × 20 mL), the combined organic phases were dried (MgSO$_4$) and the solvents were removed. The products were purified by column chromatography as described below.

Oxidation of Purified 12 with Sodium Chlorite: According to general procedure 5, **12** (65 mg, 0.33 mmol) and 2-methyl-2-butene (2.0 mL) dissolved in *tert*-butyl alcohol (8 mL), sodium chlorite (298 mg, 3.30 mmol) and sodium dihydrogen phosphate (364 mg, 2.64 mmol) dissolved in water (5 mL) furnished, after addition of sodium sulfite (832 mg, 6.60 mmol) and purification by column chromatography on silica gel (*n*-hexane/ethyl acetate, 1:1), **30** (62 mg, 84%, 55% with respect to **11**, 2 steps).

5-Hexyl-5-hydroxy-4-methoxy-5*H*-furan-2-one (30): Colorless solid; m.p. 47−53 °C. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 5.38 (br. s, 1 H, OH), 5.05 (s, 1 H, 3-H), 3.92 (s, 3 H, OMe), 2.08−1.77, 1.43−1.16, 0.92−0.83 (3 m, 13 H, 1′-H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H) ppm. ^{13}C NMR (62.9 MHz, CDCl$_3$): δ = 179.9, 171.3, 104.0 (3 s, C-2, C-4, C-5), 88.9 (d, C-3), 59.7 (q, OMe), 35.5, 31.5, 28.9, 22.7, 22.4 (5 t, C-1′, C-2′, C-3′, C-4′, C-5′), 13.9 (q, C-6′) ppm. IR (KBr): ṽ = 3330 cm^{-1} (O−H), 2980−2855 (C−H), 1755, 1725 (C=O), 1645, 1635 (C=C). MS (80 eV, EI): *m*/*z* (%) = 214 (1) [M]$^+$, 196 (1) [M − H$_2$O]$^+$, 186 (1) [M − CO]$^+$, 129 (100) [M − C$_6$H$_{13}$]$^+$, 85 (7) [C$_6$H$_{13}$]$^+$. C$_{11}$H$_{18}$O$_4$ (214.3): calcd. C 61.66, H 8.47; found C 61.59, H 8.21.

Conversion of 11 into 30: According to general procedure 1, **11** (92 mg, 0.50 mmol) and DDQ (227 mg, 1.00 mmol) dissolved in dichloromethane and water (5 mL/0.25 mL) gave, after evaporation of the solvents, crude **12** (97 mg). According to general procedure 5, crude **12** (97 mg, max. 0.50 mmol) and 2-methyl-2-butene (3.0 mL) dissolved in *tert*-butyl alcohol (12 mL), sodium chlorite (452 mg, 5.00 mmol) and sodium dihydrogen phosphate (552 mg, 4.00 mmol) dissolved in water (5 mL) furnished, after addition of sodium sulfite (1.26 g, 10.0 mmol) and purification by column chromatography on silica gel (*n*-hexane/ethyl acetate, 1:1), **30** (62 mg, 58% with respect to **11**).

5-Hydroxy-4-methoxy-5-phenyl-5*H*-furan-2-one (31): According to general procedure 1, **24** (88 mg, 0.50 mmol) and DDQ (227 mg, 1.00 mmol) dissolved in dichloromethane and water (5 mL/0.25 mL) gave, after evaporation of the solvents, crude (*E*)-3-methoxy-4-oxo-4-phenylbut-2-enal (99 mg) as a yellow oil. ^1H NMR (250 MHz, $CDCl_3$): δ = 9.45 (d, *J* = 7.6 Hz, 1 H, 1-H), 7.88−7.78, 7.62−7.51, 7.48−7.37 (3 m, 5 H, Ph), 5.68 (d, *J* = 7.6 Hz, 1 H, 2-H), 3.80 (s, 3 H, OMe) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 189.3, 172.2 (s, d, C-1, C-4), 134.7, 129.8, 128.8 (3 d, Ph), 134.4 (s, *i*-Ph), 107.4 (d, C-2), 56.8 (q, OMe) ppm, C-3-signal was not detected.

According to general procedure 5, the crude product (99 mg, max. 0.50 mmol) and 2-methyl-2-butene (3.0 mL) dissolved in *tert*-butyl alcohol (12 mL), sodium chlorite (452 mg, 5.00 mmol) and sodium dihydrogen phosphate (552 mg, 4.00 mmol) dissolved in water (5 mL) furnished, after addition of sodium sulfite (1.26 g, 10.0 mmol) and purification by column chromatography on silica gel (*n*-hexane/ethyl acetate, 1:1), **31** (63 mg, 61% with respect to **24**) as a colorless solid; m.p. 139−142 °C. ^1H NMR (250 MHz, $[D_6]$acetone): δ = 7.60−7.52, 7.45−7.38 (2 m, 5 H, Ph), 7.15 (br. s, 1 H, OH), 5.30 (s, 1 H, 3-H), 3.87 (s, 3 H, OMe) ppm. ^{13}C NMR (62.9 MHz, $[D_6]$acetone): δ = 179.9, 169.1, 136.8 (3 s, C-2, C-4, *i*-Ph), 128.6, 127.7, 125.3 (3 d, Ph), 101.3 (s, C-5), 87.5 (d, C-3), 58.9 (q, OMe) ppm. IR (KBr): $\tilde{\nu}$ = 3240 cm^{-1} (O−H), 3070−3000 (=C−H), 2995−2855 (C−H), 1745 (C=O), 1645 (C=C). MS (80 eV, EI): *m*/*z* (%) = 206 (27) $[M]^+$, 129 (8) $[M - C_6H_5]^+$, 84 (45) $[M - C_7H_6O_2]^+$, 69 (100) $[M - C_8H_9O_2]^+$, 18 (62) $[H_2O]^+$. $C_{11}H_{10}O_4$ (206.2): calcd. C 64.08, H 4.89; found C 63.75, H 4.66.

6-Hexyl-5-methoxypyridazine-3(2*H*)-one (32): 30 (94 mg, 0.44 mmol) was dissolved in isopropyl alcohol (5 mL), and hydrazine monohydrate (0.10 mL, 103 mg, 2.06 mmol) was added. After heating to reflux for 4 h, water (20 mL) was added. The aqueous phase was extracted with ethyl acetate (3 × 20 mL), the combined organic phases were dried ($MgSO_4$) and the solvents were removed. **32** (86 mg, 93%) was isolated as a colorless solid; m.p. 163−165 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 11.12 (br. s, 1 H, NH), 6.11 (s, 1 H, 4-H), 3.82 (s, 3 H, OMe), 2.57 (m_c, 2 H, 1′-H), 1.66−1.53, 1.40−1.22 (2 m, 8 H, 2′-H, 3′-H, 4′-H, 5′-H), 0.92−0.83 (m, 3 H, 6′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 164.1, 160.8, 144.6 (3 s, C-3, C-5, C-6), 102.6 (d, C-4), 55.6 (q, OMe), 31.5, 29.9, 28.9, 26.8, 22.5 (5 t, C-1′, C-2′, C-3′, C-4′, C-5′), 14.0 (q, C-6′) ppm. IR (KBr): $\tilde{\nu}$ = 3290, 3200 cm^{-1} (N−H), 3135−3000 (=C−H), 2950−2855 (C−H), 1670 (C=O). MS (80 eV, EI): *m*/*z* (%) = 210 (33) $[M]^+$, 195 (2) $[M - CH_3]^+$, 179 (5) $[M - OCH_3]^+$, 167 (8) $[M - C_3H_7]^+$, 153 (23) $[M - C_4H_9]^+$, 140 (100) $[M - C_2H_2N_2O]^+$. HRMS (80 eV): calcd. for $C_{11}H_{18}N_2O_2$: 210.13683; found 210.13671. $C_{11}H_{18}N_2O_2$ (210.3): calcd. C 62.83, H 8.63, N 13.32; found C 62.83, H 8.26, N 13.16.

Reaction of α,β-Unsaturated γ-Keto Aldehydes with Hydrazine Monohydrate. General Procedure 6: The α,β-unsaturated γ-keto aldehyde was dissolved in isopropyl alcohol, and hydrazine monohydrate was added. After stirring for 16 h at room temperature, water (20 mL) was added. The aqueous phase was extracted with diethyl ether (3 × 20 mL), the combined organic phases were dried ($MgSO_4$) and the solvents were removed. The products were purified by column chromatography as described below.

3-Hexyl-4-methoxypyridazine (33): According to general procedure 1, **11** (92 mg, 0.50 mmol) and DDQ (227 mg, 1.00 mmol) dissolved in dichloromethane and water (5 mL/0.25 mL), gave crude **12** (98 mg).

According to general procedure 6, crude **12** (98 mg, max. 0.50 mmol) and hydrazine monohydrate (0.10 mL, 103 mg, 2.06 mmol) dissolved in isopropyl alcohol (5 mL) afforded, after column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 1:1), **33** (63 mg, 65% with respect to **11**) as a pale yellow oil. ^1H NMR (250 MHz, $CDCl_3$): δ = 8.85, 6.79 (2 d, *J* = 5.9 Hz, 1 H each, 5-H, 6-H), 3.90 (s, 3 H, OMe), 2.96 (m_c, 2 H, 1′-H), 1.81−1.67, 1.47−1.24, 0.94−0.83 (3 m, 11 H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 156.5, 156.4 (2 s, C-3, C-4), 150.3 (d, C-6), 105.8 (d, C-5), 55.0 (q, OMe), 31.5, 30.8, 29.1, 27.7, 22.4 (5 t, C-1′, C-2′, C-3′, C-4′, C-5′), 13.9 (q, C-6′) ppm. IR (neat): $\tilde{\nu}$ = 3050−3000 cm^{-1} (=C−H), 2955−2860 (C−H). MS (80 eV, EI): *m*/*z* (%) = 194 (3) $[M]^+$, 179 (3) $[M - CH_3]^+$, 165 (4) $[M - C_2H_5]^+$, 163 (6) $[M - OCH_3]^+$, 151 (13) $[M - C_3H_7]^+$, 137 (30) $[M - C_4H_9]^+$, 124 (100) $[M - C_4H_6O]^+$. HRMS (80 eV): calcd. for $C_{11}H_{18}N_2O$: 194.14191; found 194.14433. $C_{11}H_{18}N_2O$ (194.3): calcd. C 68.01, H 9.34, N 14.42; found C 68.25, H 9.38, N 14.22.

4-Methoxy-3-phenylpyridazine (34): According to general procedure 1, **24** (88 mg, 0.50 mmol) and DDQ (227 mg, 1.00 mmol) dissolved in dichloromethane and water (5 mL/0.25 mL), gave crude (*E*)-3-methoxy-4-oxo-4-phenylbut-2-enal (98 mg).

According to general procedure 6, the crude aldehyde (98 mg, max. 0.50 mmol) and hydrazine monohydrate (0.10 mL, 103 mg, 2.06 mmol) dissolved in isopropyl alcohol (5 mL) afforded, after column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 1:1), **34** (66 mg, 71% with respect to **24**) as a colorless solid; m.p. 107−108 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 8.89 (d, *J* = 5.9 Hz, 1 H, 6-H), 7.94−7.85, 7.49−7.40 (2 m, 5 H, Ph), 6.92 (d, *J* = 5.9 Hz, 1 H, 5-H), 3.85 (s, 3 H, OMe) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 156.1, 152.9, 134.2 (3 s, C-3, C-4, *i*-Ph), 150.6 (d, C-6), 129.3, 129.1, 127.9 (3 d, Ph), 107.2 (d, C-5), 55.1 (q, OMe) ppm. IR (KBr): $\tilde{\nu}$ = 3050−3000 cm^{-1} (=C−H), 2985−2850 (C−H). MS (80 eV, EI): *m*/*z* (%) = 186 (11) $[M]^+$, 185 (15) $[M - H]^+$, 156 (100) $[M - CH_2O]^+$. $C_{11}H_{10}N_2O$ (186.2): calcd. C 70.95, H 5.41, N 15.04; found C 70.86, H 5.32, N 15.02.

3-(4-Chlorophenyl)-4-methoxypyridazine (35): According to general procedure 1, **26** (105 mg, 0.50 mmol) and DDQ (227 mg, 1.00 mmol) dissolved in dichloromethane and water (5 mL/0.25 mL) furnished crude (*E*)-4-(4-chlorophenyl)-3-methoxy-4-oxobut-2-enal (119 mg) as a colorless solid. ^1H NMR (250 MHz, $CDCl_3$): δ = 9.47 (d, *J* = 7.3 Hz, 1 H, 1-H), 7.77, 7.40 (2 d, *J* = 8.8 Hz, 2 H each, Ar), 5.69 (d, *J* = 7.3 Hz, 1 H, 2-H), 3.82 (s, 3 H, OMe) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 189.2, 188.1, 171.4, 141.3, 132.7 (4 s, d, C-1, C-3, C-4, 2 *i*-Ar), 131.1, 129.2 (2 d, Ar), 107.7 (d, C-2), 56.9 (q, OMe) ppm. According to general procedure 6, the crude aldehyde (119 mg, max. 0.50 mmol) and hydrazine monohydrate (0.10 mL, 103 mg, 2.06 mmol) dissolved in isopropyl alcohol (5 mL) furnished, after column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 1:2), **34** (82 mg, 75% with respect to **26**) as a colorless solid; m.p. 123−125 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 8.90 (d, *J* = 5.9 Hz, 1 H, 6-H), 7.87, 7.39 (2 d, *J* = 8.6 Hz, 2 H each, Ar), 6.93 (d, *J* = 5.9 Hz, 1 H, 5-H), 3.88 (s, 3 H, OMe) ppm. ^{13}C NMR (62.9 MHz, CDCl$_3$): $\delta = 156.1$, 151.8,* 135.3, 132.7 (4 s, C-3, C-4, 2 *i*-Ar), 150.8 (d, C-6), 130.7, 128.2 (2 d, Ar), 107.3 (d, C-5), 55.2 (q, OMe) ppm, * signal with low intensity. IR (KBr): $\tilde{\nu} = 3050-3000$ cm^{-1} (=C−H), 2955−2855 (C−H). $C_{11}H_9ClN_2O$ (220.7): calcd. C 59.88, H 4.11, N 12.70; found C 59.82, H 3.80, N 12.50.

4-Methoxy-3-(4-methoxyphenyl)pyridazine (36): According to general procedure 1, **28** (103 mg, 0.50 mmol) and DDQ (227 mg, 1.00 mmol) dissolved in dichloromethane and water (5 mL/0.25 mL) furnished crude (*E*)-3-methoxy-4-(4-methoxyphenyl)-4-oxobut-2-enal (93 mg) as a yellow solid. ^{1}H NMR (250 MHz, CDCl$_3$): $\delta = 9.49$ (d, $J = 7.8$ Hz, 1 H, 1-H), 7.86, 6.94 (2 d, $J = 8.9$ Hz, 2 H each, Ar), 5.68 (d, $J = 7.8$ Hz, 2 H, 2-H), 3.85 (s, 6 H, 2 OMe) ppm. ^{13}C NMR (62.9 MHz, CDCl$_3$): $\delta = 189.6$, 187.6, 173.0, 164.9, 127.4 (4 s, d, C-1, C-3, C-4, 2 *i*-Ar), 132.4, 114.2 (2 d, Ar), 107.0 (d, C-2), 56.8, 55.6 (2 q, OMe) ppm.

According to general procedure 6, the crude aldehyde (93 mg, max. 0.50 mmol) and hydrazine monohydrate (0.10 mL, 103 mg, 2.06 mmol) dissolved in isopropyl alcohol (5 mL) furnished, after column chromatography on aluminum oxide (*n*-hexane/ethyl acetate, 1:2), **36** (69 mg, 64% with respect to **28**) as a colorless solid; m.p. 72−73 °C. ^{1}H NMR (250 MHz, CDCl$_3$): $\delta = 8.88$ (d, $J = 5.9$ Hz, 1 H, 6-H), 7.92, 6.98 (2 d, $J = 8.8$ Hz, 2 H each, Ar), 6.90 (d, $J = 5.9$ Hz, 1 H, 5-H), 3.89, 3.84 (2 s, 3 H each, 2 OMe) ppm. ^{13}C NMR (62.9 MHz, CDCl$_3$): $\delta = 160.5$, 156.1, 152.6,* 126.7 (4 s, C-3, C-4, 2 *i*-Ar), 150.2 (d, C-6), 130.9, 113.5 (2 d, Ar), 107.1 (d, C-5), 55.2, 55.2 (2 q, OMe) ppm, * signal with low intensity. IR (neat): $\tilde{\nu} = 3075-3000$ cm^{-1} (=C−H), 2975−2840 (C−H). MS (80 eV, EI): *m*/*z* (%) = 216 (93) [M]$^+$, 215 (100) [M − H]$^+$, 201 (9) [M − CH$_3$]$^+$, 187 (16) [M − CH$_2$O]$^+$. HRMS (80 eV): calcd. for $C_{12}H_{12}N_2O_2$: 216.08988; found 216.08869.

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