Anionic Cyclizations of Pentynones and Hexynones: Access to Furan and Pyran Derivatives

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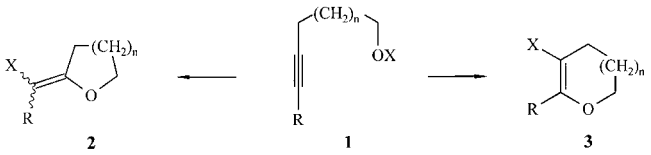
On treatment with base the pentynones **8a−f** undergo anionic addition reactions of the resulting enolate species to the alkyne moiety and afford the 2,5-disubstituted furans **10a−f** in yields ranging from 10−91%. The proposed mechanism involves the 2-methylene-dihydrofurans **11** as intermediates which tautomerize to yield the observed products. In the case of the α-picolyl derivative **8g** both possible enolates **12** and **13** are formed which are subsequently transformed to the products **10g** and **14g**, respectively. Starting with the hexynones **9a−e** an analogous reaction takes place with the formation of the pyran derivatives **15** and **16** in comparable yields. Under the same reaction conditions the *n*-butyl ketone **9f** gives rise to two isomeric compounds, namely the 4*H*-pyran **16f** and the cyclohexenone **17**. This result is explained by assuming initial formation of two isomeric enolates which react either by O- or *C*-attack on the carbon-carbon triple bond.

Introduction

Five- and six-membered oxygen containing heterocycles belong to very important and widespread groups of heterocycles.[1−3] The most common access to such oxacycles include chemical modifications of the preformed ring system (obtained, for instance, from biomass material like sugars[4]), ring transformations,[2] cycloaddition reactions[3,5,6] as well as ionic, radical and metal mediated ring closure of appropriate acyclic precursors.[7] Among the most frequently used synthetic approaches of the latter type, the intramolecular addition of an oxygen functionality to a triple bond has become an increasingly important method.[7−9] As a result of structural features, ring closure gives rise to products containing an exocyclic or endocyclic double bond (schematically represented by **1**→**2/3**). With $n = 1$ the cyclization can take place either by a 5-*exo*-*dig* or 6-*endo*-*dig* mode[10] with the formation of 5- or 6-membered oxacycles; consequently, the next higher homologue of **1** ($n = 2$) should be transformed into 6- or 7-ring products.



Whereas some examples of oxygen-carbon ring closures of enolizable pentynones and hexynones as precursors with acid[11] or transition metal catalysis[12][13] have been described, only a limited number of examples, which involve base-catalyzed nucleophilic enolate cyclization,[14] have been reported.

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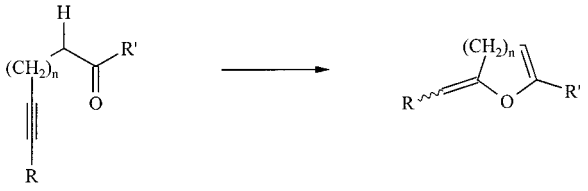
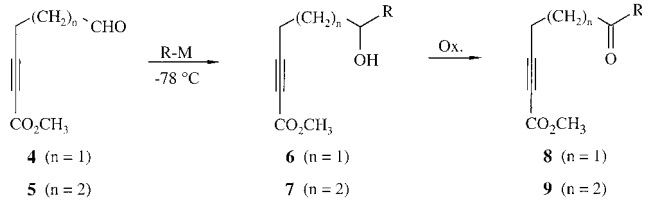
In this paper we report concise details of the base catalyzed cyclization of a series of substituted alkynones of general structure **A** as an alternative route for the preparation of furan and pyran derivatives **B**.[15,19,20]



Results and Discussion

Synthesis and Anionic Cyclization of Pentynones[20]

The synthesis of the required ketones **8** was easily accomplished in two steps from the known pentynal **4**.[21] In



order to introduce the group R at the carbonyl carbon, the use of several organometallic reagents were investigated. Lithium compounds proved to be too reactive and gave rise to a mixture of products resulting from attack at the three electrophilic centers of **4**, whilst when organotitanium reagents were employed,[22] the rate was unacceptable low. As a compromise, organomagnesium derivatives, i.e. Grignard compounds, appeared to be the reagents of choice and gave the secondary alcohols **6** in 56−90% yields (see Table 1).

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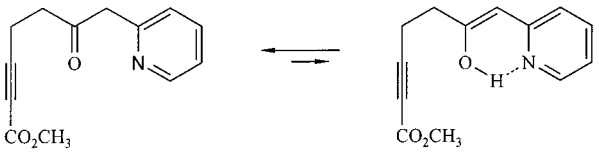
Subsequent transformation into the ketones **8** was carried out preferentially by Swern oxidation, although with derivatives **6d,e,f** higher yields were obtained when MnO_2 was used as the oxidant (see Table 1).

Table 1. Yields of pentynols **6** and pentynones **8**

	R−M	**6** (%)[a]	**8** (%)[a]
a	C_6H_5−MgBr	87	80[b]
b	nC_4H_9−MgBr	90	85[b]
c	2-furyl−MgBr	72	95[b]
d	C_6H_5−C≡C−MgBr	96	90[c]
e	TMS−C≡C−MgBr	91	66[c]
f	THPO−$(CH_2)_3$−C≡C−MgBr	61	70[c]
g	2-pyridyl−CH_2−MgBr	56	46[b]

[a] Isolated yield after chromatography and/or crystallization. − [b] $C_2Cl_2O_2$, DMSO, CH_2Cl_2, −60°C, Et_3N. − [c] MnO_2, CH_2Cl_2, 25°C.

In the case of the α-picolyl derivative **8g** there are two tautomers present in the ratio 5:1 ($CDCl_3$, 25°C), namely the keto and the enol forms **8g/8g′,** respectively, the double bond of the latter being located between the pyridine ring and the CO bond.



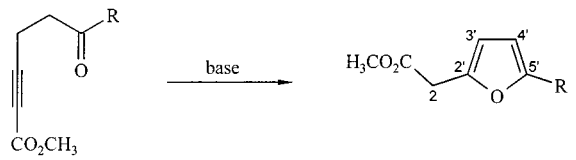
8g **8g'**

Cyclization of the pentynones **8a−f** was investigated under various conditions with different base/solvent systems such as LDA/Et_2O or THF, LDA/THF/DMPU, *t*BuLi/Et_2O or DMSO, NaH/THF or DMF, NaH/DMPU, NaH/THF/DMPU, and NEt_3/Et_2O. In general the best results were obtained with NaH/DMF or NaH/THF/DMPU at 0°C with the formation of the 2,5-disubstituted furans **10a−f** in up to 91% yield (see Table 2).

The importance of additives like DMPU or DMF (when used as solvent) on the cyclization rate is demonstrated by the fact that with NaH/THF as base-solvent pair the transformation of **8a** into **10a** proceeds at a reasonable rate only at higher temperatures (56% yield after 30 min at 40°C, see Table 2).

In order to obtain reproducible results, it is of paramount importance not to exceed the reaction times of approximately 2−5 min; therefore it is advisable to follow the progress of the reaction by TLC, and to isolate the products immediately after quantitative conversion.

After our preliminary communication of this work,[15] analogous results were published with higher substituted pentynones of type **8** with potassium *tert*-butoxide/DMF at 60°C.[16a] However, treatment of **8a** under these conditions gave less than 20% yield of **10a**, compared to 91% under our standard conditions. These results indicate that the nature of the substituents exerts an important influence on the outcome of the reaction. Further anionic cyclization reactions have been observed particularly with pentynones



8 **10**

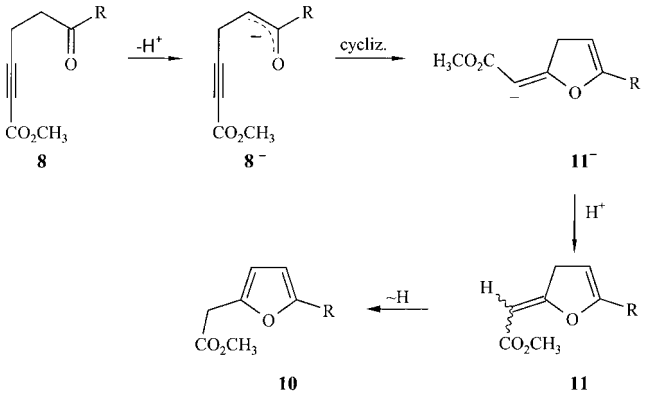
Table 2. Formation of furans **10** by anionic cyclization of pentynones **8**[a]

8	R	Reaction time (min)	Furans **10** (%)[b]
a	C_6H_5−	2	91
a	C_6H_5	30	56[c]
b	nC_4H_9−	10	50
b	nC_4H_9−	2	60[d]
c	2−furyl−	2	67
d	C_6H_5−C≡C−	5	68
d	C_6H_5−C≡C−	2	10
e	TMS−C≡C−	20	64[e]
f	THPO−$(CH_2)_3$−C≡C−	3	67
g	2−pyridyl−CH_2−	5	[f]

[a] 0.05 M solution in DMF, 1.1 eq. NaH, 0°C. − [b] Isolated yield after chromatography and/or crystallization. − [c] 0.05 M solution in THF, 1.1 eq. NaH, 40°C. − [d] 0.03 M solution in THF/DMPU (2:1), 1.1 eq. NaH, 0°C. − [e] 0.05 M solution in NEt_3/CH_2Cl_2 (1:3). − [f] Mixture of **10g** (10%) and (*Z*)/(*E*)-**14g** (66%/12%).

which have electron-withdrawing groups α to the carbonyl group; in these cases zinc carbonate,[14b] tetrabutylammonium fluoride[17] or benzyltrimethylammonium methoxide[18a] can be used as bases.

The formation of the furan derivatives **10** by base treatment of the pentynones **8** is easily explained by a mechanism which involves α-carbonyl deprotonation, addition of the enolate oxygen to the β-position of the α,β-unsaturated alkynoate moiety, proton-quenching, and finally a double bond shift (see sequence **8**→**8**$^-$→**11**$^-$→**11**→**10**).

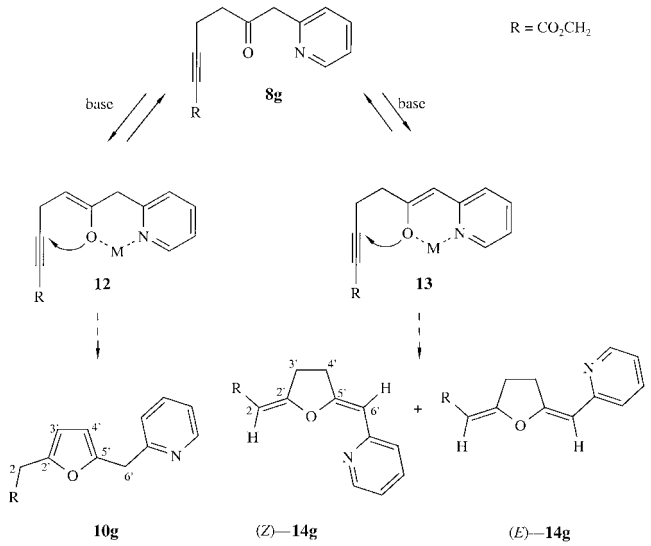


8 **8**$^-$ **11**$^-$ **10** **11**

If the reaction is quenched by D_2O, the resulting furan derivative has quantitatively incorporated two deuteriums at the methylene position of the side chain (^{1}H NMR analysis), which infers that the H-shift during the tautomerization process (e.g. **11**→**10**) does not proceed intramolecularly.[23a,b]

The analytical data of the furan compounds **10** are completely consistent with the assigned structures (see Experimental); the 2,5-disubstitution of the furan ring is clearly indicated by the ^{1}H NMR data, in particular by the ^{1}H chemical shift of the ring protons and their vicinal coupling constant ($J_{3,4}$ = 3−3.4 Hz).

In contrast to the pentynones **8a**−**f**, which are in all instances transformed to only one product **10**, base treatment of the α-picolyl derivative **8g** gave rise to three isomeric compounds, namely the furan **10g** (colorless oil, 10%), and the isomeric bis-exomethylene tetrahydrofurans (*Z*)-**14g** (m.p. 113°C, 66%) and (*E*)-**14g** (m.p. 121°C, 12%), respectively.



Obviously two competing deprotonation processes with the formation of the isomeric enolates **12** and **13** take place, which on *5-exo-dig* cyclization and subsequent reprotonation (and H-shift in case of **10g**) are transformed to the observed products. From an approximate estimate of the acidities of the different α-protons as well as from thermodynamic considerations, the formation of the enolate **13** should be favored over **12** by much more than a factor of 8; this assumption is supported by the presence of the respective tautomer **8g**′ under neutral conditions (see above). Therefore it may be reasonably concluded that the anionic cyclization represents the rate determining step in the reaction sequence. The predominance of the (*Z*)-**14g** compared to (*E*)-**14g** is probably due to the stronger complexation of the metal cation with the delocalized pyridyl-enolate system.

Whereas the structure of **10g** could be unambiguously determined on the basis of the ^{1}H and ^{13}C NMR data, which are closely related to those of **10a**−**f**, detailed NMR studies had to be performed to identify the other two compounds. From the four possible bis-exomethylene tetrahydrofuran isomers, the two diastereomers of **14** with the ester function *trans* to the ring oxygen were derived from NOE experiments, which show, inter alia, the relationship between 4′-H and 6′-H in case of the major compound [(*Z*)-**14g**], and between 2-H and 6′-H for the minor product [(*E*)-**14g**].

Unexpectedly, all attempts to transform **14g** into the furan isomer **10g** have (so far) failed: neither treatment with acid (e.g. PTSA, PPTS) nor with base (e.g. K_2CO_3/CH_3OH) gave the corresponding unsaturated heterocycles.

With the successful conversion of a series of substituted 4-pentynones into 2,5-substituted furans, a promising alternative to other cyclization methods was elaborated and has since found further applications by other research groups;[13,16−18] in some cases the transformations were additionally mediated by transition metals.[13] In contrast to the base-catalyzed transformation of corresponding β-diketones to furans[18a,b] (first examples of this type − albeit in very low-yield − were reported more than 30 years ago),[14] the pentynones **8** are simple, monoactivated systems.

Synthesis and Anionic Cyclization of Hexynones[19]

According to the general method described for the preparation of the pentynones, a number of differently substituted hexynones were synthesized from the known aldehyde **5**[21] as common precursor (Table 3). The introduction of the group R was accomplished in these cases by reaction of **5** with the corresponding organomagnesium compounds, which were prepared either directly from the bromo compound (*R* = Ph) or by transmetalation of the lithium derivatives with $MgBr_2{\cdot}Et_2O$. In order to avoid secondary reactions, the organometallic reagent was added slowly to the aldehyde solution (*i.e.* inverse addition).

Table 3. Yields of hexynols **7** and hexynones **9**

	R−M	**7** (%)[a]	**9** (%)[a]
a	C_6H_5−MgBr	84	64[b]
b	2-furyl−MgBr	87	67[b]
c	C_6H_5−C≡C−MgBr	97	75[c]
d	THPO−$(CH_2)_3$−C≡C−MgBr	91	80[c]
e	THPO−CH_2−C≡CLi	63	63[c]
f	nC$_4$H$_9$−MgBr	83	85[b]

[a] Isolated yield after chromatography. − [b] $C_2Cl_2O_2$, DMSO, CH_2Cl_2, −60°C, Et_3N. − [c] MnO_2, CH_2Cl_2, 25°C.

The cyclization experiments were in general carried out with NaH as base and DMF as solvent (Table 4). In most cases alteration of the conditions with respect to the base (*e.g.* KO*t*Bu), the solvent (e.g. THF) or cosolvent (e.g. DMPU) reduced the overall yield and led to slight changes in the product distribution (see run 1 vs. 2, 3 vs. 4, 5 vs. 6, and 8 vs. 9 in Table 4). Again, the best yields were obtained after very short reaction times at 0°C.

After chromatographic separation of the crude mixture, product analysis of the **a**-**e** series revealed three components in each case, the 4*H*-pyrans **16** as well as the (*E*/*Z*) isomers **15** with an exocyclic double bond in the α-position. All of these substances proved to be quite unstable, especially in

the presence of oxygen, and therefore required to be stored at low temperature under an argon atmosphere.

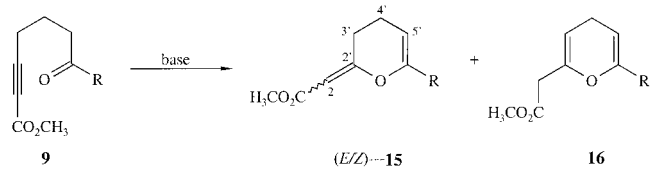


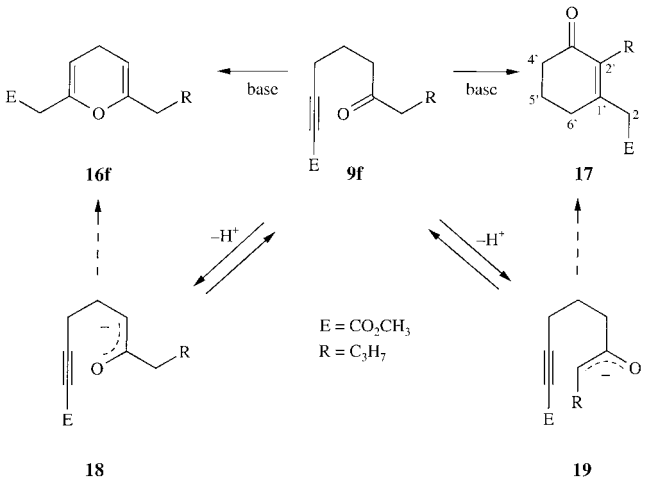
Table 4. Formation of the pyran derivatives **15** and **16** by anionic cyclization of the hexynones **9**

run	**9**	base, solvent	reaction time (min)	products (%)[a] (*E*)-**15**	**16**	(*Z*)-**15**
1	**a**	NaH, DMF	2	16	33	23
2	**a**	NaH, THF/DMPU	4	18	19	33
3	**b**	NaH, DMF	10	18	14	46
4	**b**	KO*t*Bu, DMF	5	2	2	62
5	**c**	NaH, DMF	5	14	12	56
6	**c**	NaH, THF/DMPU	10	13	tr	49
7	**d**	NaH, DMF	10	8	32	23
8	**e**	KO*t*Bu, DMF	1	3	7	28
9	**e**	NaH, DMF	2	8	22	tr
10	**f**	KO*t*Bu, THF/DMF	13	see text		

[a] Isolated yield after chromatography.

The structural identification of the cyclization products was accomplished by careful NMR investigations. Differentiation between (*E*)- and (*Z*)-**15** was based on the fact, that in case of the (*E*)-isomer the absorption of the vinyl proton adjacent to the ester group is shifted to lower field by ca. 0.6 ppm. As documented in other cases, such deshielding effects are due to the influence of the ring oxygen.[20] An estimate of the chemical shift of the respective protons at C-2 using the incremental method[24] resulted in a 0.34 ppm downfield shift for the (*E*)-isomer. In addition, there is a significant deshielding of the 3′-H in the isomers of **15** when the ester group has an (*E*)-configuration ($\Delta\delta \approx 0.7$). The NMR data of **15c** and **16c** collected in Table 5 are representative of other pyran compounds.

In contrast to the results with **9a−e**, treatment of the *n*-butyl derivative **9f** with base afforded two reaction products in approximately equal quantities. The highest overall yield (75−80%) was obtained by treating **9f** with potassium *t*-butoxide in THF/ DMF for 13 min. Structure elucidation of the pure compounds showed that in addition to the expected pyran derivative **16f** (in this case however, there was no evidence for double bond isomers of type **15**) a further product was formed which was subsequently identified as the cyclohexenone **17** from analytical data, especially from that acquired by advanced NMR techniques.



The formation of the two isomers **16f** and **17** is easily explained by assuming deprotonation at both α-carbonyl positions of **16f** with the formation of the distinct enolate anions **18** and **19**. Subsequent anionic cyclization by O- or C-attack of the ambident species on the triple bond occurs in the favorable *6-exo-dig* mode with the eventual formation of the six-membered ring compounds **16f/17**.[25][26]

Compared to the results with the pentynones **8**, the anionic cyclization experiments with the hexynones **9** takes place in an analogous fashion to yield products derived from an initial 6-*exo-dig* cyclization process. However, usually three isomeric compounds are ultimately obtained namely the two exocyclic diastereomers of **15** as well as the γ-pyrans **16**. It could be shown by independent experiments, that the exocyclic derivatives of type **15** are the primary products and these subsequently undergo isomerization into the 4*H*−pyrans. Not unexpectedly, the general stability of the pyran derivatives is rather low, and a certain loss of material is unavoidable during the workup procedures; the pure substances must be stored at low temperature under an inert atmosphere.

Although numerous examples of pyrans and their reduced forms are known,[3] the method described for the synthesis of 4*H*−pyrans **16** by enolate-alkyne cyclization represents a useful alternative approach to such oxacyles substituted in the 2,6-positions, and it also broadens the

Table 5. ^{1}H NMR data of (*E*)-**15c**, (*Z*)-**15c** and **16c** ($CDCl_3$, 400 MHZ)

	δ values						$J_{H,H}$ (Hz)				
	2-H	3′-H	4′-H	5′-H	OCH_3	C_6H_5	2,3′	2,4′	3′,4′	3′,5′	4′,5′
(*E*)-**15c**	5.58	3.20	2.27	5.62	3.69	7.30−7.36 (3 H) 7.47 (2 H)	0.8	−	7.0	−	4.8
(*Z*)-**15c**	5.02	2.51	2.29	5.63	3.72	7.30−7.36 (3 H) 7.47 (2 H)	0.9	−	6.8	−	4.7
16c	3.10	4.71	2.85	5.28	3.73	7.31 (3 H) 7.46 (2 H)	ca. 1	1.1	3.8	1.9	3.8

scope of the anionic alkyne ring forming methodology. It has to be mentioned that, in contrast to the 4*H*−pyran and the γ-pyrone systems, only a limited number of 3,4-dihydropyran-2-ylidenes such as **15** have been described so far in the literature.[28] With respect to the successful isolation of this type of compound, it proved to be quite fortuitous that the isomerization rate to the thermodynamically more stable endocyclic pyrans **16** was relatively slow under the reaction conditions.

One further point deserves consideration, i.e. the formation of both O- and C-alkynylation products (**16f** and **17**, respectively) during base treatment of the butyl-substituted ketone **9f**. There are some other reports on the competitive C/*O*-alkylation with α,ω-bromo enolates; the ratio of the two processes involved in the ring closure seems to depend at least to a certain extent also on the nature of the counter cation.[29]

Experimental Section

General: Melting points are uncorrected. − IR: Perkin−Elmer 257 Infracord. − ^{1}H NMR: Bruker WM 250 (250 MHz) and WM 400 (400 MHz); ^{13}C NMR: Bruker WM 400 (100 MHz); $CDCl_3$ as solvent and TMS as internal standard; δ values marked by an asterisk may be interchangeable. − MS: Finnigan MAT 44 S (70 eV) with Datasystem MAT SS 200. − Elemental analyses: Perkin−Elmer Elemental Analyzer 240. − Products were isolated by flash chromatography on silica gel (Silica 32−36, ICN Biomedicals) or aluminium oxide (Alumina N, Biomedicals). − TLC: SiO_2 60 F-254, O.2 mm (Merck); Al_2O_3 60 F-254, neutral type E, 0.2 mm (Merck).

Methyl 6-Hydroxy-6-phenylhex-2-ynoate (6a): A solution of phenyl magnesium bromide, freshly prepared from bromobenzene (0.74 mL, 7.03 mmol) and magnesium (208 mg, 8.66 mmol) in 10 mL of dry diethyl ether, was added slowly by syringe to a solution of methyl 6-oxohex-2-ynoate (**4**)[21] (0.85g, 8.66 mmol) in 25 mL of dry diethyl ether at −78°C under a nitrogen atmosphere. The suspension was stirred at −78°C for 30 min, warmed to room temp over 1 h, and then treated with 20 mL of satd. aqueous NH_4Cl. After ether extraction the organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate) afforded **6a** as a yellow oil (1.03 g, 87%). − IR (CCl_4): $\tilde{\nu}$ = 3620 cm^{-1} (O−H), 3040, 2960, 2925, 2250 (C≡C), 1720 (C=O), 1495, 1460, 1440, 1325, 1260, 1080, 1060, 1030. − ^{1}H NMR (250 MHz): δ = 7.39−7.28 (m, 5 H, Ph), 4.82 (m, 1 H, 6-H), 3.77 (s, 3H, CO_2Me), 2.59−2.33 (m, 2 H, 4-H), 2.13−1.87 (m, 3 H, 5-H, OH). − MS (EI): *m*/*z* (%) = 218 (2) [M$^+$], 185 (2), 115 (10), 112 (37), 109 (10), 107 (66), 105 (19), 91 (12), 80 (19), 79 (100), 78 (18), 77 (71), 69 (18), 66 (15), 53 (17). − HRMS ($C_{13}H_{14}O_3$): calcd. 218.0943; found 218.0941.

Methyl 6-Hydroxydec-2-ynoate (6b): A solution of 2.0 M *n*-butyllithium/hexane (0.39 mL, 0.78 mmol) in 7 mL of dry diethyl ether was treated dropwise at −65°C with a 2.85 M solution of freshly prepared $MgBr_2$[30] in diethyl ether (0.29 mL, 0.82 mmol). After the suspension had been stirred for 1 h at −45°C, the mixture was cooled to −78°C, treated with a 2.0 M ethereal solution of **4** (1.42 mL, 0.71 mmol), stirred for 30 min, warmed up to 0°C over a 90 min period and then poured into a pH 7 buffer solution (buffer/diethyl ether, 1:1). A solution of 10% HCl was added to dissolve the precipitate, and the reaction mixture was extracted with diethyl ether (3 × 50 mL), washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/diethyl ether, 15:1) of the residue afforded **6b** (127 mg, 90%) as a pale-yellow oil. − IR (CCl_4): $\tilde{\nu}$ = 3630 cm^{-1} (O−H), 2960, 2940, 2245 (C≡C), 1725 (C=O), 1440, 1260, 1120, 1080. − ^{1}H NMR (250 MHz): δ = 3.78−3.64 (m, 1 H, 6-H), 3.75 (s, 3 H, CO_2Me), 2.53−2.45 (m, 2 H, 4-H), 1.84−1.22 (m, 9 H, OH, 5-H, 7-H, 8-H, 9-H), 0.91 (m, 3 H, 10-H). − MS (EI): *m*/*z* (%) = 198 (3) [M$^+$], 167 (15), 141 (22), 112 (73), 109 (100), 101 (15), 97 (16), 81 (24), 80 (22), 79 (23), 69 (36), 69 (20), 59 (16), 57 (21).

Methyl 6-(Furan-2-yl)-6-hydroxyhex-2-ynoate (6c): A 2.0 M solution of *n*-butyllithium in hexane (2.1 mL, 4.10 mmol) was added to a freshly distilled solution of furan (370 mg, 5.45 mmol) in 30 mL of dry diethyl ether. The mixture was stirred for 30 min at −60°C and for 4 h at 5°C, and then a 2.6 M suspension of $MgBr_2$ in diethyl ether (1.73 mL, 4.50 mmol) was added at −60°C. The reaction mixture was stirred for 1 h at −30°C, cooled to −78°C and then slowly treated with a solution of **4** (520 mg, 3.71 mmol) in 10 mL of diethyl ether. After stirring for 1 h, 7.3 mmol of the mixture was warmed to 0°C and poured into pH 7 buffer (buffer/diethyl ether, 1:1). A solution of 10% HCl was added to dissolve the precipitate, the reaction mixture extracted with diethyl ether (3 × 50 mL), washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 15:1, then 10:1) afforded **6c** (553 mg, 72%) as a pale-yellow oil. − IR (CCl_4): $\tilde{\nu}$ = 3600 cm^{-1} (O−H), 2940, 2910, 2230 (C≡C), 1720 (C=O), 1430, 1250, 1070. − ^{1}H NMR (250 MHz): δ = 7.39 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{3',5'}$ = 0.8 Hz, 1 H, 5′-H), 6.34 (dd, $J_{3',4'}$ = 3.3 Hz, $J_{4',5'}$ = 1.8 Hz, 1 H, 4′-H), 6.27 (dd, $J_{3',4'}$ = 3.3 Hz, $J_{4',5'}$ = 0.8 Hz, 1 H, 3′-H), 4.83 (dt, *J* = 6.8 Hz, *J* = 4.7 Hz, 1 H, 6-H), 3.77 (s, 3 H, CO_2Me), 2.39−2.60 (m, 2 H, 4-H), 2.18−2.07 (m, 3 H, 5-H, OH). − MS (EI): *m*/*z* (%) = 208 (3) [M$^+$], 177 (5), 149 (26), 148 (17), 121 (7), 112 (9), 110(8), 97 (100), 95 (16), 81(11), 79 (14), 77(12), 69 (26).

Methyl 6-Hydroxy-8-phenylocta-2,7-diynoate (6d): A solution of phenylethyne (175 mg, 1.72 mmol) in 25 mL of dry diethyl ether at −60°C was treated sequentially with a 2.0 M solution of *n*-butyllithium in hexane (0.79 mL, 1.57 mmol) and a 2.6 M suspension of $MgBr_2$ in diethyl ether (0.7 mL, 1.79 mmol). The reaction mixture was stirred for 1 h at −60°C, warmed to 0°C over 30 min, cooled to −78°C and then treated with a solution of **4** (200 mg, 1.43 mmol) in 3 mL of diethyl ether. After stirring for 1 h the mixture was again warmed to 0°C over 30 min and poured into pH 7 buffer (buffer/diethyl ether, 1:1). A solution of 10% HCl was added to dissolve the precipitate, the reaction mixture extracted with diethyl ether (3 × 30 mL), washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 3:1) gave **6d** (333 mg, 96%) as a pale-yellow oil. − IR (CCl_4): $\tilde{\nu}$ = 3620 cm^{-1} (OH), 3080−2840, 2240 (C≡C), 1720 (br), 1490, 1440, 1430, 1250 (br), 1080, 1060. − ^{1}H NMR (250 MHz): δ = 7.46−7.39 (m, 2 H, *o*-Ph), 7.36−7.28 (m, 3 H, *m*-, *p*-Ph), 4.75 (m_c, 1 H, 6-H), 3.76 (s, 3 H, OCH_3), 2.61 (m_c, 2 H, 4-H), 2.19 (d, *J* = 4.3 Hz, 1 H, OH), 2.12−2.02 (m, 2H, 5-H). − ^{13}C NMR (100 MHz): δ = 154.2 (COO), 131.8 (Ph, C-2), 128.7 (Ph, C-4), 128.4 (Ph, C-3), 122.3 (Ph, C-1), 88.8/88.7 (C-2, C-7), 85.7 (C-8), 73.4 (C-3), 61.4 (C-6), 52.6 (OCH_3), 35.4 (C-5), 14.8 (C-4). − MS (EI): *m*/*z* (%) = 242 (38) [M$^+$], 241 (100), 227 (10), 213 (25), 211 (17), 183 (21), 170 (16), 165 (13), 153 (18), 141 (16), 115 (20), 105 (35), 103 (32), 102 (19), 77 (46).

Methyl 6-Hydroxy-8-trimethylsilylocta-2,7-diynoate (6e): A 2.0 M solution of *n*-butyllithium in hexane (1.18 mL, 2.36 mmol) was added to a freshly distilled solution of trimethylsilylethyne (0.36 mL/252 mg, 2.57 mmol) in 30 mL of dry diethyl ether at −60°C. After

stirring the mixture for 1 h, a 2.6 M suspension of $MgBr_2$ in diethyl ether (1.0 mL, 2.68 mmol) was added at −60°C. The reaction mixture was stirred for 1 h at −30°C, cooled to −78°C and then treated with a solution of **4** (300 mg, 2.14 mmol) in 3 mL of diethyl ether. After stirring for 30 min the mixture was warmed to room temp over 30 min. A 1:1 mixture of saturated NH_4Cl and water was added, the reaction mixture extracted with diethyl ether (3 × 50 mL), washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 10:1) gave **6e** (462 mg, 91%) as a pale-yellow oil. IR (CCl_4): $\tilde{\nu}$ = 3620 cm^{-1} (OH), 2960, 2900, 2240 (C≡C), 2180 (C≡C), 1720 (COO, br) 1440, 1255 (br), 1080 (br). − ^1H NMR (250 MHz): δ = 4.55−4.45 (m, *J* = 4.9 Hz, 1 H, 6-H), 3.76 (s, 3 H, CH_3), 2.65−2.43 (m, 2 H, 4-H), 2.23−2.18 (d, *J* = 4.9 Hz, 1 H, OH), 2.02−1.88 (m, 2 H, 5-H), 0.17 (m_c, 9 H, $Si(CH_3)_3$). − ^{13}C NMR (100 MHz): δ = 154.2 (COO), 105.3/90.6/88.6/73.3 (C≡C), 61.3 (C-6), 52.6 (OCH_3), 35.2 (C-5), 14.7 (C-4), −0.17 [$Si(CH_3)_3$]. − MS (EI): *m*/*z* (%) = 238 (6) [M^+], 237 (11), 223 (33), 207 (24), 179 (9), 163 (14), 112 (30), 111 (14), 99 (26), 91 (14), 89 (100), 83 (10), 79 (11), 73 (68), 69 (10), 59 (28).

Methyl 6-Hydroxy-11-[(tetrahydro-2*H*-pyran-2-yl)-oxy]undeca-2,7-diynoate (6f): A 2.3 M solution of *n*-butyllithium in hexane (18.0 mL, 41.3 mmol) was added to a solution of 5-(tetrahydro-2*H*-pyran-2-yl)pentyne (6.94 g, 41.3 mmol) in 120 mL of dry diethyl ether at −60°C. The mixture was stirred for a further 1 h and a 2.5 M suspension of $MgBr_2$ in diethyl ether (18.0 mL, 45 mmol) was added at −70°C. The reaction mixture was stirred for 1.5 h at −40°C, cooled to −78°C and then treated with a solution of **4** (5.26 g, 37.6 mmol) in 30 mL of diethyl ether. After stirring for 30 min at −70°C the mixture was warmed to 0°C. A solution of 10% HCl was added to dissolve the precipitate, the reaction mixture extracted with diethyl ether (3 × 80 mL), washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 8:1) afforded **6f** (7.06 g, 61%) as a pale yellow oil. − IR (CCl_4): $\tilde{\nu}$ = 3615 cm^{-1} (OH), 2945, 2900, 2870, 2240 (C≡C), 1740 (C=O), 1450, 1440, 1430, 1355, 1255 (C−O), 1200, 1135, 1120, 1075, 1060, 1020. − ^1H NMR (250 MHz): δ = 4.62−4.56 (m, 1 H, 2′-H), 4.53−4.43 (m, 1 H, 6-H), 3.91−3.73 (m, 5 H, 11-H*, OCH_3), 3.56−3.42 (m, 2 H, 6′-H*), 2.57−2.49 (dt, *J* = 7.0 Hz, *J* = 1.5 Hz, 2 H, 4-H), 2.38−2.30 (dt, *J* = 7.0 Hz, *J* = 2.0 Hz, 2 H, 9-H), 2.05 (s, 1 H, OH), 1.98−1.88 (dt, *J* = 7.5 Hz, *J* = 6.2 Hz, 2 H, 5-H), 1.87−1.46 (m, 8 H, 10-H, 3′-H, 4′-H, 5′-H).

Methyl 6-Hydroxy-7-(2-pyridyl)hept-2-ynoate (6g): A 2.3 M solution of *n*-butyllithium in hexane (1.37 mL, 3.15 mmol) was added to a solution of α-picoline (320 mg, 3.44 mmol) in 30 mL of dry diethyl ether at −60°C. The resulting red solution was stirred for 1 h at −60°C and 1 h at −20°C, and then a 2.7 M suspension of $MgBr_2$ in diethyl ether (1.33 mL, 3.58 mmol) was added at −20°C. The reaction mixture was stirred for 1.5 h at −20°C, cooled to −78°C and treated with a solution of **4** (400 mg, 2.86 mmol) in 3 mL of diethyl ether. After stirring for 1 h at −70°C, the mixture was warmed to 0°C over 1 h, and then poured into 30 mL of water. The reaction mixture was extracted with diethyl ether (4 × 30 mL), washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 10:1, 5:1, 2:1) gave a red-brown oil which crystallized from pentane/diethyl ether to yield colorless crystals of **6g** (370 mg, 56%), m.p. 54°C. − IR (CCl_4): $\tilde{\nu}$ = 2400 cm^{-1} (OH, br), 2950, 2920, 2240 (C≡C), 1720 (COO, br), 1595, 1435, 1250 (br), 1075. − ^1H NMR (250 MHz): δ = 8.48 (m_c, 1 H, Py-6-H), 7.68−7.60 (m, 1 H, Py-4-H), 7.21−7.12 (m, 2 H, Py-3/5-H), 4.20−4.09 (m, 1 H, 6-H), 3.75 (s, 3H, CH_3), 3.00−2.80 (m, 2 H, 7-H), 2.61−2.51 (m, 2 H, 4-H), 1.88−1.52 (m, 3 H, 5-H, OH). − ^{13}C NMR (100 MHz): δ = 159.9 (C-2Py), 154.3 (CO), 148.7 (C-6Py), 137.0 (C-4Py), 123.8 (C-3Py), 121.8 (C-5Py), 89.8/73.0 (C≡C), 69.4 (C-6), 52.6 (OCH_3), 42.9/34.9 (C-7, C-5), 15.2 (C-4). − MS (EI): *m*/*z* (%) = 233 (1) [M^+], 202 (9), 136 (34), 122 (45), 120 (15), 94 (24), 93 (100), 92 (12), 79 (6). − $C_{13}H_{15}O_3N$ (233.27): calcd. C 66.94, H 6.48, N 6.00; found C 66.31, H 6.42, N 5.76

Methyl 6-Oxo-6-phenylhex-2-ynoate (8a). General Procedure for the Swern Oxidation of 6: A solution of dry DMSO (2.00 g, 25.4 mmol) in 5 mL of CH_2Cl_2 was added dropwise to a stirred solution of oxalyl chloride (0.72 g, 12.8 mmol) in 30 mL of dry CH_2Cl_2 under nitrogen at −60°C. The mixture was stirred for 5 min, and a solution of **6a** (2.53 g, 11.6 mmol) in 10 mL of CH_2Cl_2 was slowly added (10 min). The reaction mixture was stirred for 1 h at −60°C, then cooled to −78°C and treated dropwise with NEt_3 (8.0 mL, 58 mmol) and then stirred for a further 30 min at −78°C. The mixture was warmed to room temp. over a 30 min period, water (50 mL) and CH_2Cl_2 (50 mL) were added, and the reaction mixture extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phase was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 10:1) and subsequent crystallization from pentane/diethyl ether afforded **8a** as colorless crystals (2.00 g, 80%), m.p. 68°C. − IR (CCl_4): $\tilde{\nu}$ = 3080−2900 cm^{-1}, 2240 (C≡C), 1720 (COO), 1695 (CO), 1600, 1450, 1435, 1360, 1255 (C−O, br) 1210, 1080. − ^1H NMR (250 MHz): δ = 8.00−7.93 (m, 2 H, *o*-Ph), 7.65−7.57 (m, 1 H, *p*-Ph), 7.54−7.44 (m, 2 H, *m*-Ph), 3.77 (s, 3 H, CH_3), 3.36−3.28 (m, 2 H, 5-H), 2.84−2.75 (m, 2 H, 4-H). − ^{13}C NMR (100 MHz): δ = 196.7 (CO), 154.1 (COO), 136.3 (C-*q*Ph), 133.6 (C *p*-Ph), 128.8 (C -*o*Ph), 128.1 (C *m*-Ph), 88.4/73.3 (C≡C), 52.7 (OCH_3), 36.6 (C-5), 13.5 (C-4). − MS (CI; isobutane): *m*/*z* (%): 216 (7) [M^+ + 2], 186 (18) [M^+ + 1], 186 (17), 185 (100) − $C_{13}H_{12}O_3$ (216.24): calcd. C 72.21, H 5.59; found C 71.99, H 5.59

Methyl 6-Oxo-dec-2-ynoate (8b): Swern oxidation of **6b** (1.25 g, 6.3 mmol) by the procedure described above for **6a**, followed by flash chromatography gave **8b** as a pale yellow oil (1.05 g, 85%). − IR (CCl_4): $\tilde{\nu}$ = 2960 cm^{-1}, 2930, 2880, 2220 (C≡C), 1720 (br), 1435, 1255 (br), 1080. − ^1H NMR (250 MHz): δ = 3.77 (s, 3 H, OCH_3), 2.78−2.70 (m, 2 H, 5-H), 2.64−2.56 (m, 2 H, 4-H), 2.45 (t, *J* = 7.3 Hz, 2 H, 7-H), 1.68−1.50 (m, 2 H, 8-H), 1.40−1.26 (m, *J* = 7.5 Hz, 2 H, 9-H), 0.92 (t, 3 H, *J* = 7.5 Hz, 10-H). − ^{13}C NMR (100 MHz): δ = 207.7 (CO), 154.0 (COO), 88.2/73.0 (C≡C), 52.6 (OCH_3), 42.5/40.0 (C-5, C-7), 25.9/22.3 (C-8, C-9), 13.8 (C-4), 13.0 (C-10). − MS (EI): *m*/*z* (%) = 196 (2) [M^+], 165 (27), 154 (14), 139 (22), 123 (19), 111 (29), 96 (12), 95 (23), 85 (86), 79 (23), 66 (18), 57 (100). − HRMS ($C_{11}H_{16}O_3$): calcd. 196.1099; found 196.1099

Methyl 6-(Furan-2-yl)-6-oxohex-2-ynoate (8c): Swern oxidation of **6c** (520 mg, 2.50 mmol) by the procedure described above for **6a**, followed by flash chromatography and subsequent crystallization gave **8c** as colorless crystals (488 mg, 95%), m.p. 59°C (pentane/diethyl ether). − IR (CCl_4): $\tilde{\nu}$ = 2940 cm^{-1}, 2240 (C≡C), 1740 (COO), 1670 (CO), 1470, 1430, 1360, 1250 (br), 1155, 1080, 1050. − ^1H NMR (250 MHz): δ = 7.62 (dd, $J_{4',5'}$ = 1.8 Hz, $J_{3',5'}$ = 0.8 Hz, 1 H, 5′-H), 7.23 (dd, $J_{3',4'}$ = 3.7 Hz, $J_{3',5'}$ = 0.8 Hz, 1 H, 3′-H), 6.57 (dd, $J_{3',4'}$ = 3.7 Hz, $J_{4',5'}$ = 1.8 Hz, 1 H, 4′-H), 3.77 (s, 3 H, OCH_3), 3.21−3.13 (m, 2 H, 5-H), 2.80−2.73 (m, 2 H, 4-H). − ^{13}C NMR (100 MHz): δ = 185.9 (C-6), 154.0 (C-1), 152.2 (C-2′), 146.7 (C-5′), 117.4/112.4 (C-3′/C-4′), 88.0/73.2 (C-2/C-3), 52.6 (OCH_3), 36.2, 13.1. − MS (EI): *m*/*z* (%) = 175 (20) [M^+], 148 (17), 119 (14), 95 (100), 91 (22), 79 (25). − $C_{11}H_{10}O_4$ (206.20): calcd. C 64.08, H 4.89; found C 63.88, H 4.83.

Methyl 6-Oxo-8-phenylocta-2,7-diynoate (8d). General Procedure for the MnO_2 Oxidation of 6: A ca. 50-fold excess of activated

MnO_2 was added to a stirred solution of **6d** (280 mg, 1.16 mmol) in 50 mL of CH_2Cl_2 at room temp. After 1 h the reaction mixture was filtered through a column packed with sea sand/kieselguhr/sea sand, using 300 mL of ethyl acetate as the final eluent. The combined solutions were concentrated and the residue purified by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 15:1, 10:1) to afford 250 mg (90%) of **8d** as light-brown crystals; m.p. 29°C (pentane/diethyl ether). Oxidation of **6d** by the Swern method gave **8d** in 82% yield. − IR (CCl_4): $\tilde{\nu}$ = 3100−2910 cm^{-1}, 2250 (C≡C), 2210 (C≡C), 1725 (COO), 1680 (CO), 1490, 1450, 1140, 1360, 1260 (br), 1110, 1080. − ^1H NMR (250 MHz): δ = 7.64−7.56 (m, 2 H, *o*-Ph), 7.54−7.33 (m, 3 H, *m*-Ph, *p*-Ph), 3.76 (s, 3 H, OCH_3), 3.05−2.96 (m, 2 H, 5-H), 2.78−2.69 (m, 2 H, 4-H). − ^{13}C NMR (100 MHz): δ = 184.1 (CO), 154.0 (COO), 133.2 (C *o*-Ph), 131.1 (C *m*-Ph), 128.8 (C *p*-Ph), 119.7 (C-*q*Ph), 92.3/87.2/87.2/73.5 (C≡C), 52.7 (OCH_3), 42.9 (C-5), 13.4 (C-4). − MS (EI): *m*/*z* (%) = 240 (21) [M^+], 239 (60), 225 (9), 211 (27), 209 (20), 181 (6), 153 (16), 129 (100), 77 (7). − HRMS ($C_{15}H_{12}O_3$): calcd. 240.0786; found 240.0786.

Methyl 6-Oxo-8-trimethylsilylocta-2,7-diynoate (8e): Oxidation of **6e** (100 mg, 0.42 mmol) with MnO_2 as described above for **6d**, followed by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 40:1) gave **8e** (66 mg, 66%). − IR (CCl_4): $\tilde{\nu}$ = 2960 cm^{-1}, 2250 (C≡C), 2160 (C≡C), 1725 (COO), 1685 (CO), 1440, 1255 (br), 1120, 1080. − ^1H NMR (250 MHz): δ = 3.75 (s, 3H, OCH_3), 2.93−2.85 (m, 2 H, 5-H), 2.69−2.62 (m, 2 H, 4-H), 0.25 (s, 9 H, $Si(CH_3)_3$). − MS (EI): *m*/*z* (%) = 236 (7) [M^+] 221 (61), 206 (42), 205 (23), 191 (16), 177 (16), 163 (25), 133 (14), 125 (100), 111 (28), 97 (56), 89 (39), 79 (25). − HRMS ($C_{12}H_{16}O_3Si$): calcd. 236.0869; found 236.0869.

Methyl 6-Oxo-11-[(tetrahydro-2*H*-pyran-2-yl)oxy]undeca-2,7-diynoate (8f): Oxidation of **6f** (5.3g, 17.1 mmol) with MnO_2 as described for **6d**, followed by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 10:1) gave **8f** as a brown oil (3.7 g, 70%). − IR (CCl_4): $\tilde{\nu}$ = 2940 cm^{-1}, 2860, 2240 (C≡C), 2210 (C≡C), 1715 (C=O), 1680 (C=O), 1450, 1440, 1430, 1350, 1250, 1160, 1135, 1120, 1075. − ^1H NMR (250 MHz): δ = 4.60 (m, 1 H, 2′-H), 3.91−3.77 (m, 2 H, 11-H*), 3.76 (s, 3 H, OCH_3), 3.57−3.43 (m, 2 H, 6′-H*), 2.89−2.83 (m, 2 H, 4-H), 2.70−2.63 (m, 2 H, 5-H), 3.05−2.48 (m, 2 H, 9-H), 1.93−1.48 (m, 8 H, 10-H, 3′-H, 4′-H, 5′-H). − MS [CI; NH_3]: *m*/*z* (%) = 325 (22) [(M + 1) + NH_4]$^+$, 324 (100) [M + NH_4]$^+$, 240 (63), 225 (7), 223 (18), 207 (13), 102 (13).

Methyl 6-Oxo-7-(2-pyridyl)hept-2-ynoate (8g): Swern oxidation of **6g** (440 mg, 1.90 mmol) as described above for **6a**, gave a crude material which was purified by repeated flash chromatography (firstly with SiO_2, cyclohexane/ ethyl acetate, 3:1, 1:1; and then SiO_2, cyclohexane/ethyl acetate, 2:3) to afford **8g** (203 mg, 46%) as a keto-enol mixture (5:1, pale yellow oil). IR (CCl_4): $\tilde{\nu}$ = 2970 cm^{-1}, 2940, 2860 (br), 2240 (C≡C), 1740 (br), 1645 (br), 1590 (br), 1470, 1430, 1250 (br). − ^1H NMR (250 MHz); **8g** (keto isomer): δ = 8.56 (m_c, 1 H, Py-6-H), 7.69−7.63 (m, 1 H, Py-4-H), 7.25−7.17 (m, 2 H, Py-3-/5-H), 3.92 (m, 2 H, 7-H), 3.74 (s, 3 H, CH_3), 2.88−2.82 (m, 2 H, 5-H), 2.62−2.57 (m, 2 H, 4-H); **8g′** (enol isomer): δ = 15.02 (broad s, 1 H, OH), 8.17 (m_c, 1 H, Py-6-H), 7.56−7.53 (m, 1 H, Py-4-H), 6.94−6.89 (m, 2 H, Py-3-/5-H), 5.36 (s, 1 H, 7-H), 3.74 (s, 3 H, CH_3), 2.71−2.67 (m, 2 H, 5-H), 2.57−2.52 (m, 2 H, 4-H). − MS (EI): *m*/*z* (%) = 231 (6) [M^+], 230 (21), 200 (10), 173 (13), 172 (12), 144 (12), 94 (13), 93 (100), 92 (31), 83 (11), 79 (9), 66 (13).

Methyl (5-Phenyl-furan-2-yl)acetate (10a). General Procedure for the Anionic Cyclization of 8: A solution of **8a** (130 mg, 0.60 mmol) in DMF (2 mL) was rapidly added to a stirred solution of 27 mg of a 60% mineral oil dispersion of NaH (0.68 mmol) in 10 mL of dry DMF at 0°C (prepared under nitrogen in a flame-dried round bottom flask). After complete reaction (2 min, TLC), 1 mL of satd. aqueous NH_4Cl, 20 mL of water and 50 mL of diethyl ether were added to the dark mixture. The organic layer was separated, and the aqueous phase extracted with diethyl ether (3 × 40 mL). The combined organic phases were washed with water (10 mL) and brine (5 mL), and then dried ($MgSO_4$). After concentration in vacuo, purification by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 20:1) afforded **10a** as an oil (118 mg, 91%)− IR (CCl_4): $\tilde{\nu}$ = 3080 cm^{-1}, 3055, 3020, 2950, 2840, 1750 (COO), 1595, 1485, 1450, 1435, 1340, 1210, 1140. − ^1H NMR (400 MHz): δ = 7.66−7.62 (m, 2 H, *o*-Ph), 7.39−7.32 (m, 2 H, *m*-Ph), 7.25−7.21 (m, 1 H, *p*-Ph), 6.59 (d, $J_{3',4'}$ = 3.2 Hz, 1 H, 4′-H), 6.31 (d, $J_{3',4'}$ = 3.2 Hz, 1 H, 3′-H), 3.75 (s, 2 H, 2-H), 3.73 (s, 3 H, CH_3). − ^{13}C NMR (100 MHz): δ = 169.8 (C-1), 153.6 (C-5′), 147.3 (C-2′), 130.9 (C-*q*Ph), 128.7 (C *m*-Ph), 127.3 (C *p*-Ph), 123.7 (C *o*-Ph), 110.2/106.0 (C-3′/4′) 52.3 (OCH_3), 34.2 (C-2). − MS (EI): *m*/*z* (%) = 216 (27) [M^+], 158 (11), 157 (100), 128 (18), 108 (7), 89 (7), 77 (23). − HRMS ($C_{13}H_{12}O_3$): calcd. 216.0786; found 216.0789.

Methyl (5-Butyl-furan-2-yl)acetate (10b): Anionic cyclization of **8b** (100 mg, 0.51 mmol; reaction time 10 min) as described above for **10a**, followed by flash chromatography (SiO_2, cyclohexane/ ethyl acetate, 20:1) gave **10b** as an oil (50 mg, 50%). When the solvent was changed from DMF to THF/DMPU (2:1), the yield of **10b** was increased to about 60%. − IR (CCl_4): $\tilde{\nu}$ = 2960 cm^{-1}, 2940, 2880, 2865, 1750 (COO), 1440, 1270, 1230, 1170. − ^1H NMR (250 MHz): δ = 6.09 (d, $J_{3',4'=3}$.0 Hz, 1 H, 3′-H*), 5.91 (d, $J_{3',4'}$ = 3.0 Hz, 1 H, 4′-H*), 3.72 (s, 3 H, OCH_3), 3.64 (s, 2 H, 2-H), 2.59 (t, *J* = 7.6 Hz, 2 H, 6′-H), 1.67−1.54 (m, 2 H, 7′-H), 1.44−1.28 (m, 2 H, 8′-H). 0.93 (t, *J* = 7.3 Hz, 3 H, 9′-H). − ^{13}C NMR (100 MHz): δ = 170.2 (C-1), 156.3/145.6 (C-2′/5′), 108.5/105.6 (C-3′/C-4′), 52.2 (OCH_3), 34.1 (C-2), 30.2 (C-6′), 27.8 (C-7′), 22.3 (C-8′), 13.9 (C-9′). − MS (EI): *m*/*z* (%) = 196 (28) [M^+], 167 (15), 153 (42), 137 (100), 111 (34), 95 (18), 94 (15), 79 (7). − HRMS ($C_{11}H_{16}O_3$): calcd. 196.1099; found 196.1100.

Methyl (2′,5-Bifuranyl-2-yl)acetate (10c): Anionic cyclization of **8c** (120 mg, 0.58 mmol; reaction time 2 min) as described for **10a**, followed by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 20:1) gave **10c** as an oil (80 mg, 67%). − IR (CCl_4): $\tilde{\nu}$ = 2950 cm^{-1}, 1750 (COO), 1460, 1435, 1270, 1210, 1160, 1145, 1085, 1010. − ^1H NMR (400 MHz): δ = 7.39 (dd, $J_{4'',5''}$ = 1.8 Hz, $J_{3'',5''}$ = 0.8 Hz, 1 H, 5′′-H), 6.51 (dd, $J_{3'',4''}$ = 3.2 Hz, $J_{3'',5''}$ = 0.8 Hz, 1 H, 3′′-H), 6.49 (d, $J_{3',4'}$ = 3.3 Hz, 1 H, 4′-H), 6.43 (dd, $J_{3'',4''}$ = 3.2 Hz, $J_{4'',5''}$ = 1.8 Hz, 1 H, 4′′-H), 6.29 (m, $J_{3',4'}$ = 3.3 Hz, 1 H, 3′-H), 3.72 (m, 5 H, 2-H, OCH_3). − ^{13}C NMR (100 MHz): δ = 169.6 (C-1), 147.1 (C-5′), 146.5/146.2 (C-2′/C-2′′-Fu), 141.7 (C-5′′), 111.4/110.0/106.1/105.1 (C-3′-/4′-/3′′-/4′), 52.3 (OCH_3), 34.0 (C-2). − MS (EI): *m*/*z* (%) = 206 (29) [M^+], 147 (100), 95 (5), 91 (18). − HRMS ($C_{11}H_{10}O_4$): calcd. 206.0579; found 206.0579.

Methyl (5-Phenylethynylfuran-2-yl)acetate (10d): Anionic cyclization of **8d** (120 mg, 0.50 mmol; reaction time 5 min) as described for **10a**, followed by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 25:1) gave **10d** as an oil (82 mg, 68%). − IR (CCl_4): $\tilde{\nu}$ = 3080−3000 cm^{-1}, 2950, 2210, (C≡C), 1750 (COO), 1600, 1485, 1445, 1440, 1330, 1270, 1205, 1155, 1140, 1020. − ^1H NMR (250 MHz): δ = 7.55−7.47 (m, 2 H, *o*-Ph), 7.38−7.31 (m, 3 H, *m*/*p*-Ph), 6.61 (d, $J_{3',4'}$ = 3.4 Hz, 1 H, 4′-H), 6.28 (dt, $J_{3',4'}$ = 3.4 Hz, $J_{2,3'}$ = 0.8 Hz, 1 H, 3′-H), 3.74 (s, 3 H, OCH_3), 3.72 (m, 2 H, 2-H). − MS (EI): *m*/*z* (%) = 241 (11) [M^++1], 240 (68) [M^+], 182 (14), 181 (100), 152 (16). − HRMS ($C_{11}H_{16}O_3$): calcd. 240.0786; found 240.0783.

Methyl (5-Trimethylsilylethynylfuran-2-yl)acetate (10e): A solution of **8e** (250 mg, 1.05 mmol) in dry CH_2Cl_2 (15 mL) and dry NEt_3 (6 mL) was stirred for 30 min at 0°C under nitrogen. The black reaction mixture was concentrated in vacuo (0−10°C) and the residue purified by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 10:1) to afford **10e** (158 mg, 64%) as a pale-yellow oil. When the cyclization reaction was performed under conditions as described for **10a** only about 10% yield of the furan derivative was obtained. − IR (CCl_4): $\tilde{\nu}$ = 2950 cm^{-1}, 2900, 2160 (C≡C), 1750 (br), 1440, 1250, 1205 (br). − ^1H NMR (400 MHz): δ = 6.55 (d, *J* = 3.4 Hz, 1 H, 4′-H), 6.21 (dt, *J* = 0.8 Hz, *J* = 3.4 Hz, 1 H, 3′-H), 3.72 (s, 3 H, CH_3), 3.67 (2 H, C-2), 0.24 [m_c, 9 H, $Si(CH_3)_3$]. − ^{13}C NMR (100 MHz): δ = 169.2 (C-1), 148.9 (C-2′), 136.7 (C-5′), 116.9/109.4 (C-3′-/4′), 99.7/94.3 (C-6′/7′), 52.4 (OCH_3), 34.2 (C-2), 0.2 [$Si(CH_3)_3$]. − MS (EI): *m*/*z* (%) = 237 (19) [M^++1], 236 (100) [M^+], 222 (15), 221 (91), 177 (73), 162 (11), 119 (16), 99 (8), 89 (10), 73 (8).

Methyl {5-[5-(Tetrahydropyran-2-yloxy)-pent-1-ynyl]furan-2-yl}acetate (10f): Anionic cyclization of **8f** (140 mg, 0.46 mmol; reaction time 3 min) as described for **10a**, followed by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 20:1) gave **10f** as an oil (93 mg, 67%). − IR (CCl_4): $\tilde{\nu}$ = 2950 cm^{-1}, 2880, 2220 (C≡C), 1750 (br), 1440, 1200, 1140, 1120, 1080, 1060, 1035. − ^1H NMR (250 MHz): δ = 6.41 (d, $J_{3',4'}$ = 3.4 Hz, 1 H, 4′-H), 6.20 (dt, $J_{3',4'}$ = 3.4 Hz, $J_{2,3'}$ = 0.8 Hz, 1 H, 3′-H), 4.61 (m_c, 1 H, 2′′-H), 3.94−3.80 (m, 2 H, 10′-H*), 3.72 (s, 3 H, OCH_3), 3.67 (m, 2 H, 2-H), 3.57−3.45 (m, 2 H, 6′′-H*), 2.56 (t, 2 H, *J* = 6.8 Hz, 8′-H) 1.94−1.44 (m, 8 H, 4-H, 9′-H/3′′-H/4′′-H/5′′-H). − MS (EI): *m*/*z* (%) = 307(12) [M^+ + 1], 306 (63) [M^+], 247 (28), 222 (37), 205 (10), 204 (19), 163 (59), 145 (49), 131 (13), 118 (12), 85 (100), 67 (19), 57 (27) − HRMS ($C_{17}H_{22}O_5$): calcd. 306.1467; found 306.1467.

Anionic Cyclisation of 8g: Anionic cyclization of **8g** (185 mg, 0.80 mmol; reaction time 5 min) as described for **10a**, gave a reaction mixture which was separated by flash chromatography (SiO_2, cyclohexane/diethyl ether, 1:1) to give three isomeric products: methyl [5-(pyridin-2-yl-methyl)-furan-2-yl]acetate (**10g**) (18 mg, 10%), methyl [5-(*Z*)-pyridin-2-yl-methylen)-3,4-dihydro-furan-2-yliden]acetate [(*Z*)-**14g**] (22 mg, 12%), and the corresponding *trans*-isomer (*E*)-**14g** (122 mg, 66%). − **10g** (oil): IR (CCl_4): $\tilde{\nu}$ = 3010 cm^{-1}, 2950, 2920, 1750 (br), 1595, 1480, 1440, 1275, 1225, 1180, 1140, 1120. − ^1H NMR (250 MHz): δ = 8.54 (m_c, 1 H, Py-6-H), 7.66−7.58 (m, 1 H, Py-4-H), 7.20−7.11 (m, 2 H, Py-3-H, Py-5-H), 6.15 (d, *J* = 3.1 Hz, 1 H, 4′-H*), 6.05 (d, *J* = 3.1 Hz, 1 H, 3′-H*), 4.15 (s, 2 H, 6′-H), 3.71 (s, 3 H, OCH_3), 3.65 (s, 2H, 2-H). − MS (EI): *m*/*z* (%) = 232 (15) [M^+ + 1], 231(80) [M^+], 173 (27), 172 (100), 144 (24), 130 (11), 117 (6), 94 (9), 93 (11), 79 (8), 65 (11), 59 (7). − [(*E*)-**14g**]: m.p. 113°C (pentane/diethyl ether). − IR (CCl_4): $\tilde{\nu}$ = 3000 cm^{-1}, 2950, 2850, 1715 (br), 1640 (br), 1585, 1475, 1435, 1360, 1120 (br), 1090. − ^1H NMR (400 MHz): δ = 8.53 (m_c, 1 H, Py-6-H), 7.59−7.54 (m, 1 H, Py-4-H), 7.09−7.06 (m, 1 H, Py-3-H), 7.03−6.99 (m, 1 H, Py-5-H), 6.22 (t, *J* = 1.8 Hz, 1 H, 6′-H), 5.55 (t, *J* = 1.8 Hz, 1 H, 2-H), 3.71 (s, 3H, OCH_3), 3.36−3.25 (m, 4 H, 3′-H, 4′-H). − MS (EI): *m*/*z* (%) = 231 (34) [M^+], 216 (71), 200 (12), 198 (100), 172 (27), 170 (35), 144 (40), 143 (62), 130 (89), 117 (28), 103 (12), 99 (13), 92 (27), 79 (30). − $C_{13}H_{13}NO_3$ (231.26): calcd. C 67.52, H 5.67, N 6.06; found C 67.05, H 5.66, N 6.01. − [(*Z*)-**14g**]: m.p. 121°C (pentane/diethyl ether). − IR (CCl_4): $\tilde{\nu}$ = 3060 cm^{-1}, 3000, 2950, 2840, 1720 (br), 1645 (br), 1585, 1465, 1435, 1370, 1330 (br), 1305, 1290, 1190, 1115 (br), 1090, 1035. − ^1H NMR (400 MHz): δ = 8.52 (m_c, 1 H, Py-6-H), 7.90−7.84 (m, 1 H, Py-3-H), 7.70−7.62 (m, 1 H, Py-4-H), 7.11−7.03 (m, 1 H, Py-5-H), 5.80 (t, *J* = 1.8 Hz, 1 H, 6′-H), 5.69 (t, *J* = 1.8 Hz, 1 H, 2-H), 3.72 (s, 3 H, OCH_3), 3.30−3.18 (m, 2 H, 4′-H), 3.02−2.92 (m, 2 H, 3′-H). − ^{13}C NMR (100 MHz): δ = 173.9 (C-2*), 168.0 (C-1), 156.4 (C-5*), 154.2 (C-2-Py), 149.2 (C-6-Py), 136.2 (C-4-Py), 123.0/120.8 (C-5-/3-Py), 103.8/93.7 (C-2, C-6′), 51.2 (OCH_3), 27.9/ 27.3 (C-3′, C-4′). − MS (EI): *m*/*z* (%) = 231 (58) [M^+], 216 (83), 200 (14), 198 (100), 172 (24), 170 (27), 144 (34), 143 (48), 130 (66), 117 (18), 92 (17), 91 (15), 79 (16), 59 (12). HRMS ($C_{13}H_{13}NO_3$): calcd. 231.0895; found 231.0895.

Methyl 7-Hydroxy-7-phenylhept-2-ynoate (7a): A Grignard solution, freshly prepared under nitrogen from Mg turnings (0.615g, 25.30 mmol) and bromobenzene (3.180 g, 20.25 mmol) in diethyl ether (15 mL), was cooled to −50°C and then transferred under nitrogen to a solution of **5**[21] (2.250 g, 14.59 mmol) in THF (100 mL) at −78°C. The suspension was stirred at −78°C for 2.5 h, warmed to room temp over 30 min and treated with 50 mL of a 1:1 mixture of saturated NH_4Cl and water. After extraction with diethyl ether (3 × 100 mL), the organic layer was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 5:1) afforded **7a** (2.854 g, 84%) as a yellow oil. − IR (CCl_4): $\tilde{\nu}$ = 3610 cm^{-1}, 2970, 2240, 1720, 1430, 1250, 1075, 905. − ^1H NMR (250 MHz): δ = 7.39−7.23 (m, 5 H, Ar−H), 4.71 (m, 1 H, 7-H), 3.75 (s, 3 H, OCH_3), 2.38 (t, *J* = 7.0 Hz, 2 H, 4-H), 2.03−1.52 (m, 5 H, OH, 5-H, 6-H). − ^{13}C NMR (100 MHz): δ = 154.3 (C-1), 144.4 (C-1′), 128.7 (Ar-C), 127.8 (Ar−C), 125.9 (Ar−C), 89.4 (C-2), 74.1 (C-7), 73.3 (C-3), 52.6 (OCH_3), 38.0 (C-6), 23.9 (C-5), 18.7 (C-4). − MS (EI): *m*/*z* (%) = 232 (1) [M^+], 155 (13), 133 (24), 127 (12), 126 (33), 123 (20), 107 (85), 105 (27), 98 (100), 79 (56), 77 (32), 66 (15). − HRMS ($C_{14}H_{16}O_3$): calcd. 232.1099; found 232.1099.

Methyl 7-Furan-2-yl-7-hydroxyhept-2-ynoate (7b). Preparation of $MgBr_2$·OEt_2. General Procedure:[30] A suspension of Mg turnings (0.316 g, 13.0 mmol) in 10 mL of diethyl ether under N_2 was treated dropwise with 1,2-dibromoethane (1.879 g, 10.0 mmol) with constant maintenance of gas evolution. After completion of addition, the mixture was heated to reflux for 45 min. The Grignard solutions were always freshly prepared before use, and then transferred by means of a syringe. − **Preparation of 7b:** A solution of *n*-butyllithium in hexane (3.8 mL, 2.2 N, 8.4 mmol) was added to a solution of furan (0.64 g, 9.4 mmol) in diethyl ether (40 mL) under N_2 at −70°C. After stirring for 4 h at 0°C, a solution of $MgBr_2$·OEt_2 (10.2 mmol, see above) was added at −60°C. The mixture was warmed to −30°C (1 h), then cooled to −70°C and added to a precooled solution (−78°C) of **5** (1.021 g, 6.62 mmol) in 40 mL of diethyl ether . The reaction mixture was stirred for 1 h at −78°C, warmed to 0°C and then hydrolyzed by the addition of 25 mL of buffer (pH 7) and 2N HCl. After separation of the ethereal solution, the aqueous solution was extracted with diethyl ether (2 × 50 mL), the combined organic phases were washed with 25 mL of satd. $NaHCO_3$ and 25 mL of brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 5:1) afforded **7b** (1.272 g, 86%) as a pale yellow oil. − IR (CCl_4): $\tilde{\nu}$ = 3650 cm^{-1}, 3000, 2800, 2270, 1740, 1455, 1270, 1100, 1025. − ^1H NMR (250 MHz): δ = 7.37 (dd, *J* = 1.8 Hz, *J* = 0.9 Hz, 1 H, 5′-H), 6.36 (dd, *J* = 3.3 Hz, *J* = 1.8 Hz, 1 H, 4′-H), 6.25 (m, 1 H, 3′-H), 4.70 (t, *J* = 6.5 Hz, 1 H, 7-H), 3.78 (s, 3 H, OCH_3), 2.40 (m, 3 H, 4-H, OH), 2.00−1.57 (m, 4 H, 5-H, 6-H). − ^{13}C NMR (100 MHz): δ = 156.4 (C-5′), 154.3 (C-1), 142.1 (C-4′), 110.3 (C-2′/3′), 106.1 (C-2′/3′), 89.2 (C-2), 73.3 (C-3), 67.3 (C-7), 52.6 (OCH_3), 34.5 (C-6), 23.7 (C-5), 18.5 (C-4). − MS (EI):*m*/*z* (%) = 222 (1) [M^+], 162 (30), 123 (66), 98 (85), 97 (100), 79 (35), 69 (31), 66 (35), 55 (33). − HRMS ($C_{12}H_{14}O_4$): calcd. 222.0892; found 222.0891.

Methyl 7-Hydroxy-9-phenylnona-2,8-diynoate (7c): A solution of *n*-butyllithium in hexane (3.3 mL, 2.2 N, 7.3 mmol) was added to

a solution of phenylethyne (0.799 g, 7.82 mmol) in diethyl ether (25 mL) under N_2 at −70°C. After stirring for 1 h at −70°C, an ethereal solution of $MgBr_2{\cdot}OEt_2$ (10.1 mmol, see above) was added. The mixture was stirred at −60°C for 45 min, then cooled to −78°C and added to a precooled solution (−78°C) of **5** (1.029 g, 6.67 mmol) in 50 mL of diethyl ether . The suspension was stirred for 1 h at − 78°C, warmed to 0°C and then hydrolyzed by the addition of 25 mL of buffer (pH 7) and 2N HCl. After separation of the ethereal solution, the aqueous solution was extracted with diethyl ether (2 × 50 mL), the combined organic phases washed with 25 mL of satd. $NaHCO_3$ and 25 mL of brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 5:1) afforded **7c** (1.667 g, 97%) as a yellow oil. − IR (CCl_4): $\tilde{\nu}$ = 3620 cm^{-1}, 2950, 2240, 1720, 1435, 1255, 1075. − ^1H NMR (250 MHz): δ = 7.42 (m, 2 H, 2′-H), 7.37−7.28 (m, 3 H, 3′-H, 4′-H), 4.63 (m, 1 H, 7-H), 3.76 (s, 3 H, OCH_3), 2.43 (t, *J* = 6.7 Hz, 2 H, 4-H), 2.20 (m, br, 1 H, OH), 1.98−1.75 (m, 4 H, 5-H, 6-H). − ^{13}C NMR (100 MHz): δ = 154.3 (C-1), 131.8 (Ar−C), 128.6 (Ar−C), 128.4 (Ar−C), 122.5 (C-1′), 89.6 (C-9), 89.2 (C-2), 85.4 (C-8), 73.4 (C-3), 62.4 (C-7), 52.6 (OCH_3), 36.7 (C-6), 23.4 (C-5), 18.5 (C-4). − MS (EI): *m*/*z* (%) = 256 (19) [M^+], 255 (64), 237 (39), 167 (36), 141 (40) 131 (100), 129 (38), 115 (37), 105 (47), 103 (62). − HRMS ($C_{16}H_{16}O_3$) [M^+ − 1]: calcd. 255.1021; found 255.1022.

Methyl 12-[(Tetrahydro-2*H*-pyran-2-yl)-oxy]-7-hydroxydodeca-2,8-diynoate (7d): A solution of *n*-butyllithium in hexane (4.2 mL, 2.35 N, 9.86 mmol) was added to a solution of 5-[(tetrahydro-2*H*-pyran-2-yl)oxy]-1-pentyne (1.65 g, 9.86 mmol) in diethyl ether (30 mL) under N_2 at −60°C. After stirring for 1 h at −60°C, an ethereal solution of $MgBr_2{\cdot}OEt_2$ (10.75 mmol, see above) was added at −70°C. The reaction mixture was stirred at −40°C for 1.5 h, then cooled to −78°C and treated with the solution of **5** (1.38 g, 8.96 mmol) in 10 mL of diethyl ether . The suspension was stirred for 1 h at − 70°C, warmed to 0°C (30 min) and then hydrolyzed by the addition of pH 7 buffer and 10% HCl. After phase separation the aqueous solution was extracted with diethyl ether (3 × 50 mL), the combined organic phases were washed with 30 mL of brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 5:1) gave **7d** (2.62 g, 91%) as a bright yellow oil. − IR (CCl_4): $\tilde{\nu}$ = 3620 cm^{-1} (O−H), 2950, 2870, 2240 (C≡C), 1720 (br), 1455, 1435, 1355, 1255 (br), 1140, 1120, 1080. − ^1H NMR (250 MHz): δ = 4.63 (*t*, *J* = 3.0 Hz, 1 H, 2′-H), 4.40 (m, 1 H, 7-H), 3.94−3.73 (m, 5 H, 12-H*, OCH_3), 3.60−3.40 (m, 2 H, 6′-H*), 2.48−2.28 (m, 4 H, 10-H, 4-H), 2.18 (s, 1 H, OH), 1.94−1.44 (m, 12 H, 5-H/6-H/11-H/3′-H/4′-H/5′-H). − MS (CI, NH_3), *m*/*z* (%) = 341 (28%), 340 (100) [M^+ + NH_4], 339 (7), 257 (5), 256 (27), 239 (3), 222 (4), 221(26), 172 (3), 102 (13).

Methyl 7-Hydroxy-9-[(tetrahydro-2*H*-pyran-2-yl)oxy]nona-2,8-diynoate (7e): A solution of butyllithium in hexane (2.0 mL, 2.3 N, 4.6 mmol) was added to a solution of 2-propynyloxytetrahydropyran (0.711 g, 5.07 mmol) in THF (20 mL) under N_2 at −78°C. After stirring for 2 h at −78°C, the mixture was added dropwise to a precooled solution (−78°C) of **5** (0.602 g, 3.90 mmol) in 50 mL of THF. The solution was stirred for 40 min at − 78°C, warmed to 0°C (25 min) and then hydrolyzed by the addition of 50 mL of an aqueous solution of a 1:1 mixture of NH_4Cl and water. After separation of the ethereal solution, the aqueous solution was extracted with diethyl ether (2 × 70 mL), and the combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 40:1/20:1/10:1) afforded **7e** (0.724 g, 63%) as a yellow oil. − IR (CCl_4): $\tilde{\nu}$ = 3620 cm^{-1}, 2940, 2870, 2240, 1700, 1435, 1250, 1120, 1080, 1040, 905. − ^1H NMR (250 MHz): δ = 4.81 (t, *J* = 3.7 Hz, 1 H, 2′-H), 4.45 (m, 1 H, 7-H), 4.34 (dd, *J* = 15.6 Hz, *J* = 1.5 Hz, 1 H, 10-H), 4.25 (dd, *J* = 15.6 Hz, *J* = 1.5 Hz, 1 H, 10-H), 3.85 (m, 1 H, 6′-H), 3.76 (s, 3 H, OCH_3), 3.53 (m, 1 H, 6′-H), 2.85 (m, br, 1 H, OH), 2.41 (t, *J* = 7.0 Hz, 2 H, 4-H), 1.92−1.45 (m, 10 H, 5-H, 6-H, 3′-H, 4′-H, 5′-H). − ^{13}C NMR (100 MHz): δ = 154.2 (C-1), 97.0 (C-2′), 89.1 (C-2), 86.6 (C-8/9), 81.3 (C-8/9), 73.3 (C-3), 63.8 (C-7), 62.1 (C-6′), 54.3 (C-10), 52.6 (OCH_3), 36.5 (C-6), 30.3 (C-3′), 25.4 (C-5′), 23.3 (C-5), 19.0 (C-4′), 18.4 (C-4). − MS (CI, isobutane): *m*/*z* (%) = 295 (8) [M^+ + 1], 212 (14), 211 (100), 193 (35), 175 (11), 147 (21), 85 (20).

Methyl 7-Hydroxy-undec-2-ynoate (7f): A stirred hexane solution of *n*-butyllithium (8.5 mL, 2.4 N, 20.4 mmol) in diethyl ether (20 mL) was treated at −30°C under N_2 with a suspension of freshly prepared $MgBr_2$ (see above) in diethyl ether (26.8 mmol). The mixture was stirred for 1 h at −30°C and then added to a precooled solution (−78°C) of **5** (2.591 g, 5.22 mmol) in diethyl ether (100 mL). The suspension was stirred at −78°C for 1 h, warmed to 0°C and then treated with 40 mL of saturated NH_4Cl/water. After extraction with diethyl ether (3 × 50 mL) the organic layer was washed with 25 mL of satd. NaCl, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, cyclohexane/ethyl acetate, 5:1) afforded **7f** (2.947 g, 83%) as a colorless oil. − IR (CCl_4): $\tilde{\nu}$ = 3630 cm^{-1}, 2950, 2930, 2880, 2250, 1720, 1435, 1255, 1075. − ^1H NMR (250 MHz): δ = 3.78 (s, 3 H, OCH_3), 3.62 (m, 1 H, 7-H), 2.40 (t, *J* = 6.7 Hz, 2 H, 4-H), 1.89−1.22 (m, 11 H, 5-H, 6-H, 8-H, 9-H, 10-H, OH), 0.92 (m, 3 H, 11-H). − ^{13}C NMR (100 MHz): δ = 154.3 (C-1), 89.6 (C-2), 73.2 (C-3), 71.4 (C-7), 52.6 (OCH_3), 37.4 (C-6/8), 36.4 (C-6/8), 27.9 (C-9/10), 23.9 (C-5), 22.8 (C-9/10), 18.8 (C-4), 14.1 (C-11). − MS (CI, isobutane): *m*/*z* (%) = 213 (62), 212 (1) [M^+], 196 (14), 195 (100), 181 (30), 163 (30), 155 (86), 139 (12), 123 (38).

Methyl 7-Oxo-7-phenylhept-2-ynoate (9a): Swern oxidation of **7a** (2.96 g, 12.73 mmol) by the procedure described above for **6a**, gave a crude material which was purified by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 10:1) to yield **9a** (1.88 g, 64%) as a colorless solid; m.p. 38°C (diethyl ether/pentane). − IR (CCl_4): $\tilde{\nu}$ = 2950 cm^{-1}, 2230, 1720, 1690, 1435, 1255, 1075. − ^1H NMR (250 MHz): δ = 8.03−7.97 (m, 2 H, 2′-H), 7.63−7.44 (m, 3 H, 3′-H, 4′-H), 3.77 (s, 3 H, OCH_3), 3.16 (t, *J* = 7.0 Hz, 2 H, 6-H), 2.50 (t, *J* = 7.0 Hz, 2 H, 4-H), 2.06 (quin, *J* = 7.0 Hz, 2 H, 5-H). − ^{13}C NMR (100 MHz): δ = 199.0 (C-7), 154.2 (C-1), 136.9 (C-1′), 129.6 (Ar−C), 128.7 (Ar−C), 128.1 (Ar−C), 88.9 (C-2), 73.7 (C-3), 52.6 (OCH_3), 36.9 (C-6), 21.9 (C-5), 18.2 (C-4). − MS (EI):*m*/*z* (%) = 230 (4) [M^+], 200 (22), 199 (30), 198 (53), 170 (23), 120 (57), 106 (23), 105 (100), 79 (16), 78 (14), 77 (70). − $C_{14}H_{16}O_3$ (230.3): calcd. C 73.03, H 6.13; found C 73.05, H 6.03.

Methyl 7-Furan-2-yl-7-oxohept-2-ynoate (9b): Swern oxidation of **7b** (0.470 g, 2.11 mmol) by the procedure described above for **6a**, gave a crude material which was purified by flash chromatography (SiO_2, dichloromethane) to afford **9b** (0.312 g, 67%) as a colorless solid; m.p. 34°C (diethyl ether/pentane). − IR (CCl_4): $\tilde{\nu}$ = 2950 cm^{-1}, 2240, 1720, 1685, 1550, 1470, 1435, 1255, 1080, 1010. − ^1H NMR (250 MHz): δ = 7.60 (dd, *J* = 1.8 Hz, *J* = 0.9 Hz, 1 H, 5′-H), 7.21 (dd, *J* = 3.6 Hz, *J* = 0.9 Hz, 1 H, 3′-H), 6.54 (dd, *J* = 3.6 Hz, *J* = 1.8 Hz, 1 H, 4′-H), 3.77 (s, 3 H, OCH_3), 2.99 (t, *J* = 7.0 Hz, 2 H, 6-H), 2.48 (t, *J* = 7.0 Hz, 2 H, 4-H), 2.01 (m, *J* = 7.0 Hz, 2 H, 5-H). − ^{13}C NMR (100 MHz): δ = 188.2 (C-7), 154.1 (C-1), 152.6 (C-2′), 146.4 (C-5′), 117.1 (C-3′/4′), 112.3 (C-3′/4′), 88.6 (C-2), 73.6 (C-3), 52.6 (OCH_3), 36.7 (C-6), 21.7 (C-5), 18.2 (C-4). − MS (CI, isobutane): *m*/*z* (%) = 222 (14), 221 (100), 220 (1) [M^+], 190 (5), 189 (39), 188 (5), 161 (3), 155 (5), 110 (3). −

$C_{12}H_{12}O_4$ (220.2): calcd. C 65.45, H 5.43; found: C 65.32, H 5.53.

Methyl 7-Oxo-9-phenylnona-2,8-diynoate (9c): Oxidation of **7c** (1.325 g, 5.17 mmol; reaction time 4 h) with MnO_2 by the procedure described above for **6d**, followed by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 20:1) gave **9c** (0.985 g, 75%) as a colorless solid; m.p. 34°C (diethyl ether/pentane). − IR (CCl_4): $\tilde{\nu}$ = 2950 cm^{-1}, 2235, 2200, 1720, 1670, 1430, 1250, 1095, 1075. − ^1H NMR (250 MHz): δ = 7.58 (m, 2 H, 2′-H), 7.52−7.35 (m, 3 H, 3′-H, 4′-H), 3.76 (s, 3 H, OCH_3), 2.84 (t, *J* = 7.0 Hz, 2 H, 6-H), 2.46 (t, *J* = 7.0 Hz, 2 H, 4-H), 2.00 (m, *J* = 7.0 Hz, 2 H, 5-H). − ^{13}C NMR (100 MHz): δ = 186.4 (C-7), 154.1 (C-1), 133.2 (Ar−C), 130.9 (Ar−C), 128.7 (Ar−C), 119.9 (C-1′), 91.3 (C-8/9), 88.3 (C-2), 87.8 (C-8/9), 73.8 (C-3), 52.7 (OCH_3), 43.9 (C-6), 21.9 (C-5), 18.0 (C-4). − MS (CI, isobutane): *m/z* (%) = 257 (10), 255 (6) [M^+], 241 (6), 240 (19), 239 (100), 213 (12), 211 (41), 209 (8), 195 (17), 181 (8), 179 (8), 155 (30), 135 (11), 123 (8), 105 (7). − $C_{16}H_{14}O_3$ (254.3): calcd. C 75.58, H 5.55; found C 75.57, H 5.58.

Methyl 12-[(Tetrahydro-2*H*-pyran-2-yl)oxy]-7-oxododeca-2,8-diynoate (9d): Oxidation of **7d** (3.90 g, 12.11 mmol; reaction time 24 h) with MnO_2 by the procedure described above for **6d**, followed by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 5:1) gave **9d** (3.10 g, 80%) as a colorless oil. − IR (CCl_4): $\tilde{\nu}$ = 2950 cm^{-1}, 2880, 2250 (C≡C), 2220 (C≡C), 1725 (C=O), 1680 (C=O), 1740, 1260 (br),1140, 1130, 1080, 1040. − ^1H NMR (250 MHz): δ = 4.60 (t, *J* = 3.5 Hz, 1 H, 2′-H), 3.91−3.74 (m, 5 H, 12-H*, OCH_3), 3.57−3.42 (m, 2 H, 6′-H*), 2.70 (t, *J* = 7.4 Hz, 2 H, 4-H), 2.53 (t, *J* = 7.4 Hz, 2 H, 6-H*), 2.41 (t, *J* = 7.4 Hz, 2 H, 10-H*), 1.98−1.48 (m, 10 H, 5-H/11-H/3′-H/4′-H/5′-H). − MS (CI, NH_3): *m/z* = 338 (100) [$M^+ + NH_4$], 337 (5), 254 (14), 238 (4), 237 (29), 102 (4).

Methyl 7-Oxo-9-(tetrahydro-pyran-2-yloxy)nona-2,8-diynoate (9e): Oxidation of **7e** (1.335 g, 4.54 mmol; reaction time 2 h) with MnO_2 by the procedure described above for **6d** (see above), followed by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 40:1/20:1/10:1/5:1) gave **9e** (0.834 g, 63%) as a colorless oil. − IR (CCl_4): $\tilde{\nu}$ = 2950 cm^{-1}, 2240, 1680, 1435, 1255, 1145, 1125, 1080, 1035, 905. − ^1H NMR (250 MHz): δ = 4.80 (t, *J* = 3.0 Hz, 1 H, 2′-H), 4.43 (s, 2 H, 10-H), 3.83 (m, 1 H, 6′-H), 3.76 (s, 3 H, OCH_3), 3.55 (m, 1 H, 6′-H), 2.74 (t, *J* = 7.0 Hz, 2 H, 6-H), 2.41 (t, *J* = 7.0 Hz, 2 H, 4-H), 1.93 (m, *J* = 7.0 Hz, 2 H, 5-H), 1.87−1.48 (m, 6 H, 3′-H, 4′-H, 5′-H). − ^{13}C NMR (100 MHz): δ = 185.8 (C-7), 154.0 (C-1), 97.3 (C-2′), 88.7 (C-2), 88.1 (C-8/9), 84.6 (C-8/9), 73.7 (C-3), 62.1 (C-6′), 53.9 (C-10), 52.6 (OCH_3), 43.7 (C-6), 30.1 (C-3′), 26.9 (C-5′), 21.5 (C-5), 18.9 (C-4′), 17.9 (C-4). MS (CI, isobutane): *m/z* (%) = 293 (1) [$M^+ + 1$], 210 (16), 209 (100), 191 (4), 85 (62).

Methyl 7-Oxoundec-2-ynoate (9f): Swern oxidation of **7f** (2.947 g, 13.95 mmol) by the procedure described above for **6a**, gave a crude material which was purified by flash chromatography (SiO_2, cyclohexane/ethyl acetate, 10:1) to afford **9f** (2.487 g, 85%) as a colorless liquid. − IR (CCl_4): $\tilde{\nu}$ = 2960 cm^{-1}, 2930, 2870, 2240, 1720, 1435, 1255, 1080. − ^1H NMR (250 MHz): δ = 3.78 (s, 3 H, OCH_3), 2.57 (t, *J* = 7.0 Hz, 2 H, 4-H), 2.40 (m, 4 H, 6-H, 8-H), 1.85 (m, *J* = 7.0 Hz, 2 H, 5-H), 1.57 (m, 2 H, 9-H), 1.30 (m, *J* = 7.5 Hz, 2 H, 10-H), 0.91 (t, *J* = 7 Hz, 3 H, 11-H). − ^{13}C NMR (100 MHz): δ = 210.1 (C-7), 154.2 (C-1), 88.8 (C-2), 73.6 (C-3), 52.6 (OCH_3), 42.8 (C-6/8), 40.9 (C-6/8), 26.0 (C-9/10), 22.4 (C-9/10), 21.4 (C-5), 18.1 (C-4), 13.9 (C-11). − MS (CI, isobutane): *m/z* (%) = 213 (62), 211 (1) [M^++1], 196 (14), 195 (100), 181 (30), 163 (30), 155 (86), 139 (12), 135 (97), 123 (38).

Anionic Cyclization of 9a: The general procedure described above for the reactions of **8** was used except that pH 7 buffer solution was employed for the hydrolytic work up instead of aqueous NH_4Cl. Following this protocol, the reaction of **9a** (100 mg, 0.43 mmol, reaction time 2 min) afforded after careful flash chromatography (SiO_2, cyclohexane/ethyl acetate, 40:1) three oily products, methyl (*E*)-2-(6-phenyl-3,4-dihydropyran-2-ylidene)acetate [(*E*)-**15a**] (16 mg, 16%), the corresponding isomer (*Z*)-**15a** (33 mg, 33%), and methyl 2-(6-phenyl-4*H*-pyran-2-yl)acetate (**16a**) (23 mg, 23%). With THF/ DMPU (2:1) as solvent the yields after chromatography were: 18%, 19% and 33%, respectively.

(*E*)-**15:** IR (CCl_4): $\tilde{\nu}$ = 3060 cm^{-1}, 3020, 2950, 2850, 1695, 1655, 1645, 1430, 1370, 1195, 1275, 1170, 1075. − ^1H NMR (250 MHz): δ = 7.56 (m, 2 H, 2′′-H), 7.34 (m, 3 H, 3′′-H, 4′′-H), 5.67 (t, *J* = 4.6 Hz, 1 H, 5′-H), 5.65 (s, 1 H, 2-H), 3.71 (s, 3 H, OCH_3), 3.23 (t, *J* = 7.0 Hz, 2 H, 3′-H), 2.32 (dt, *J* = 7.0 Hz, *J* = 4.6 Hz, 2 H, 4′-H). − ^{13}C NMR (100 MHz): δ = 168.4 (C-1/2′), 168.1 (C-1/2′), 149.4 (C-1′′), 133.8 (C-6′), 128.5 (Ar−C), 128.4 (Ar−C), 124.4 (Ar−C), 99.9 (C-2/5′), 97.8 (C-2/5′), 51.0 (OCH_3), 22.3 (C-3′), 18.6 (C-4′). − MS (EI): *m/z* (%) = 230 (100) [M^+], 171 (77), 170 (53), 115 (42), 105 (87), 77 (45). − HRMS ($C_{12}H_{12}O_4$): calcd. 230.0943; found 230.0945.

(*Z*)-**15:** IR (CCl_4): $\tilde{\nu}$ = 3060 cm^{-1}, 2950, 2850, 1700, 1670, 1650, 1435, 1345, 1285, 1205, 1150, 1080. − ^1H NMR (250 MHz): δ = 7.77 (m, 2 H, 2′′-H), 7.36 (m, 3 H, 3′′-H, 4′′-H), 5.68 (t, *J* = 4.6 Hz, 1 H, 5′-H), 5.07 (m, 1 H, 2-H), 3.75 (s, 3 H, OCH_3), 2.55 (t, *J* = 7.0 Hz, 2 H, 3′-H), 2.35 (dt, *J* = 7.0 Hz, *J* = 4.6 Hz, 2 H, 4′-H). − ^{13}C NMR (100 MHz): δ = 168.4 (C-1/2′), 168.1 (C-1/2′), 149.4 (C-1′′), 133.8 (C-6′), 128.5 (Ar−C), 128.4 (Ar−C), 124.4 (Ar−C), 99.9 (C-2/5′), 97.8 (C-2/5′), 51.1 (OCH_3), 22.3 (C-3′), 18.6 (C-4′). − MS (EI): *m/z* (%) = 230 (100) [M^+], 171 (79), 170 (54), 115 (46), 105 (88), 77 (48). − HRMS ($C_{12}H_{12}O_4$): calcd. 230.0943; found 230.0943.

16a: IR (CCl_4): $\tilde{\nu}$ = 3060 cm^{-1}, 2950, 2830, 1745, 1650, 1450, 1435, 1285, 1125, 1070. − ^1H NMR (250 MHz): δ = 7.65−7.22 (m, 5 H, Ar−H), 5.31 (dt, *J* = 3.4 Hz, *J* = 1.8 Hz, 1 H, 5′-H), 4.79 (m, 1 H, 3′-H), 3.74 (s, 3H, OCH_3), 3.17 (m, 2 H, 2-H), 2.91 (t, *J* = 3.4 Hz, 2 H, 4′-H). MS (EI): *m/z* (%) = 230 (100) [M^+], 171 (63), 157 (56), 105 (62), 77 (44). − HRMS ($C_{12}H_{12}O_4$): calcd. 230.0943; found 230.0945.

Anionic Cyclization of 9b: Reaction of **9b** (110 mg, 0.50 mmol, reaction time 10 min) by the same procedure described above for **9a**, gave after flash chromatography methyl (*E*)-2-(6-furan-2-yl-3,4-dihydropyran-2-ylidene)acetate [(*E*)-**15b**] (20 mg, 18%), (*Z*)-**15b** (15 mg, 14%), and methyl 2-(6-furan-2-yl-4*H*-pyran-2-yl)acetate (**16b**) (51 mg, 46%). The reaction of **9b** in DMF with potassium *tert*-butoxide as base yielded after chromatography (SiO_2, cyclohexane/ethyl acetate, 40:1) the same products in 2%, 2% and 62% yields, respectively.

(*E*)-**15b:** IR (CCl_4): $\tilde{\nu}$ = 2950 cm^{-1}, 2930, 2850, 1715, 1650, 1370, 1195, 1125, 1080. − ^1H NMR (250 MHz): δ = 7.37 (m, 1 H, 5′′-H), 6.46 (d, *J* = 3.3 Hz, 1 H, 3′′-H), 6.41 (dd, *J* = 3.3 Hz, *J* = 1.8 Hz, 1 H, 4′′-H), 5.63 (t, *J* = 4.6 Hz, 1 H, 5′-H), 5.61 (t, *J* = 0.9 Hz, 1 H, 2-H), 3.71 (s, 3 H, OCH_3), 3.22 (t, *J* = 6.9 Hz, 2 H, 3′-H), 2.31 (dt, *J* = 6.9 Hz, *J* = 4.6 Hz, 2 H, 4′-H). − ^{13}C NMR (100 MHz): δ = 167.9 (C-1/2′), 167.7 (C-1/2′), 148.1 (C-2′′), 142.5 (C-6′), 142.4 (C-5′′), 111.1 (C-3′′/4′′), 106.1 (C-3′′/4′′), 98.7 (C-2/5′), 98.2 (C-2/5′), 51.0 (OCH_3), 22.3 (C-3′), 18.0 (C-4′). − MS (EI): *m/z* (%) = 221 (13), 220 (100) [M^+], 205 (12), 161 (34), 160 (17), 95 (27). − HRMS ($C_{12}H_{12}O_4$) calcd. 220.0736; found 220.0736.

(*Z*)-**15b:** IR (CCl_4): $\tilde{\nu}$ = 2960 cm^{-1}, 2850, 1700, 1685, 1655, 1490, 1435, 1205, 1150, 1085, 905. − ^1H NMR (250 MHz): δ = 7.37 (m, 1 H, 5′′-H), 6.68 (d, *J* = 3.4 Hz, 1 H, 3′′-H), 6.43 (dd, *J* = 3.4 Hz, *J* = 1.8 Hz, 1 H, 4′′-H), 5.61 (t, *J* = 4.6 Hz, 1 H, 5′-H), 5.05 (t, *J* = 0.9 Hz, 1 H, 2-H), 3.73 (s, 3 H, OCH_3), 2.55 (dt, *J* = 6.7 Hz,

0.9 Hz, 2 H, 3′-H), 2.33 (m, 2 H, 4′-H). − ^{13}C NMR (100 MHz): δ = 165.4 (C-1/2′), 162.5 (C-1/2′), 148.3 (C-2′′), 142.8 (C-6′), 142.6 (C-5′′), 111.4 (C-3′′/4′′), 107.1 (C-3′′/4′′), 97.4 (C-2/5′), 96.9 (C-2/5′), 51.0 (OCH_3), 27.2 (C-3′), 18.7 (C-4′). − MS (EI): *m/z* (%) = 220 (100) [M^+], 161 (78), 160 (47), 132 (25), 105 (25), 95 (70). − HRMS ($C_{12}H_{12}O_4$) calcd. 220.0736; found 220.0738.

16b: IR (CCl_4): ṽ = 2940 cm^{-1}, 2830, 1745, 1710, 1490, 1435, 1295, 1220, 1155, 1085. − ^{1}H NMR (250 MHz): δ = 7.34 (m, 1 H, 5′′-H), 6.37 (m, 2 H, 3′′-H, 4′′-H), 5.32 (dt, *J* = 3.6 Hz, *J* = 1.8 Hz, 1 H, 5′-H), 4.77 (m, 1 H, 3′-H), 3.73 (s, 3 H, OCH_3), 3.14 (m, 2 H, 2-H), 2.88 (m, 2 H, 4′-H). − ^{13}C NMR (100 MHz): δ = 170.2 (C-1), 148.8 (C-2′′), 142.5 (C-6′), 142.1 (C-5′′), 131.6 (C-2′), 111.0 (C-3′′/4′′), 105.8 (C-3′′/4′′), 99.4 (C-3′/5′), 95.5 (C-3′/5′), 52.2 (OCH_3), 39.4 (C-2), 20.7 (C-4′). − MS (70 eV, EI): *m/z* (%) = 221 (14), 220 (100) [M^+], 219 (44), 191 (32), 161 (28), 160 (11), 147 (19), 95 (28). − HRMS ($C_{12}H_{12}O_4$): calcd. 220.0736; found 220.0736.

Anionic Cyclization of 9c: Reaction of **9c** (100 mg, 0.39 mmol, reaction time 5 min) by the same procedure described above for **9a**, gave after flash chromatography (SiO_2, cyclohexane/ethyl acetate, 40:1) methyl (*E*)-2-(6-phenylethynyl-3,4-dihydropyran-2-ylidene)acetate [(*E*)-**15c**] (14 mg, 14%), the *cis*-isomer (*Z*)-**15c** (12 mg, 12%) and methyl-2-(6-phenylethynyl-4*H*-pyran-2-yl)acetate (**16c**) (56 mg, 56%). The reaction of **9c** in a 2:1 mixture of THF/DMPU as solvent yielded after chromatography the same products in 13%, traces, and 49% yield, respectively.

(*E*)-**15c:** IR (CCl_4): ṽ = 2940 cm^{-1}, 2220, 1710, 1655, 1435, 1370, 1120, 1060. − ^{1}H NMR (400 MHz): δ = 7.47 (m, 2 H, 2′′-H), 7.36−7.30 (m, 3 H, 3′′-H, 4′′-H), 5.62 (t, *J* = 4.8 Hz, 1 H, 5′-H), 5.58 (t, *J* = 0.8 Hz, 1 H, 2-H), 3.69 (s, 3 H, OCH_3), 3.20 (t, *J* = 7.0 Hz, 2 H, 3′-H), 2.27 (dt, *J* = 7.0 Hz, *J* = 4.8 Hz, 2 H, 4′-H). − ^{13}C NMR (100 MHz): δ = 167.9 (C-1/2′), 167.3 (C-1/2′), 135.2 (C-6′), 131.8 (Ar−C), 129.1 (Ar−C), 128.5 (Ar−C), 121.9 (C-1′′), 111.3 (C-5′), 98.4 (C-2), 88.9 (C-7′/8′), 82.8 (C-7′/8′), 51.1 (OCH_3), 21.7 (C-3′), 19.0 (C-4′). − MS (EI): *m/z* (%) = 255 (16), 254 (100) [M^+], 195 (14), 194 (11), 167 (11), 166 (11), 165 (28), 152 (20), 129 (13). − HRMS ($C_{16}H_{14}O_3$): calcd. 254.0943; found 254.0943.

(*Z*)-**15c:** IR (CCl_4): ṽ = 2940 cm^{-1}, 1990, 1730, 1705, 1665, 1430, 1340, 1205, 1120, 1060. −^{1}H NMR (250 MHz): δ = 7.50 (m, 2 H, 2′′-H), 7.33 (m, 3 H, 3′′-H, 4′′-H), 5.63 (t, *J* = 4.7 Hz, 1 H, 5′-H), 5.02 (t, *J* = 0.9 Hz, 1 H, 2-H), 3.72 (s, 3 H, OCH_3), 2.51 (dt, *J* = 6.8 Hz, *J* = 0.9 Hz, 2 H, 3′-H), 2.29 (m, 2 H, 4′-H). − ^{13}C NMR (100 MHz): δ = 165.2 (C-1/2′), 162.1 C-1/2′), 135.6 (C-6′), 131.9 (Ar−C), 128.9 (Ar−C), 128.4 (Ar−C), 122.1 (C-1′′), 110.5 (C-2), 97.2 (C-5′), 89.1 (C-7′/8′), 82.8 (C-7′/8′), 54.1 (OCH_3), 26.8 (C-3′), 16.7 (C-4′). − MS (EI): *m/z* (%) = 255 (20), 254 (100) [M^+], 195 (20), 194 (15), 167 (20), 166 (16), 165 (40), 153 (15), 152 (26), 139 (17), 129 (57). − HRMS ($C_{16}H_{14}O_3$): calcd. 254.0943; found 254.0940.

16c: IR (CCl_4): ṽ = 2960 cm^{-1}, 2840, 2210, 1750, 1710, 1490, 1440, 1355, 1305, 1275, 1125, 1050, 910. − ^{1}H NMR (400 MHz): δ = 7.46 (m, 2 H, 2′′-H), 7.31 (m, 3 H, 3′′-H, 4′′-H), 5.28 (dt, *J* = 3.8 Hz, *J* = 1.9 Hz, 1 H, 5′-H), 4.71 (m, 1 H, 3′-H), 3.73 (s, 3 H, OCH_3), 3.10 (m, 2 H, 2-H), 2.85 (tt, *J* = 3.8 Hz, *J* = 1.1 Hz, 2 H, 4′-H). − ^{13}C NMR (100 MHz): δ = 170.1 (C-1), 145.4 (C-6′), 135.1 (C-2′), 131.8 (Ar−C), 128.8 (Ar−C), 128.4 (Ar−C), 122.3 (C-1′′), 107.9 (C-5′), 98.6 (C-3′), 88.4 (C-7′/8′), 83.4 (C-7′/8′), 52.2 (OCH_3), 39.2 (C-2), 21.7 (C-4′). − MS (EI): *m/z* (%) = 255 (16), 254 (100) [M^+], 253 (54), 195 (19), 181 (13), 165 (15), 152 (14), 126 (10). − HRMS ($C_{16}H_{14}O_3$): calcd. 254.0943; found 254.0943.

Anionic Cyclization of 9d: Reaction of **9d** (300 mg, 0.94 mmol, reaction time 10 min) by the procedure described for **9a**, gave after flash chromatography (SiO_2, cyclohexane/ethyl acetate, 60:1) methyl (*E*)-2-{6-[5-(tetrahydro-pyran-2-yloxy)pent-1-ynyl]3,4-dihydropyran-2-ylidene}acetate [(*E*)-**15d**] (25 mg, 8%), the *cis*-isomer (*Z*)-**15d** (95 mg, 32%) and methyl 2-{6-[5-(tetrahydro-pyran-2-yloxy)pent-1-ynyl]4*H*-pyran-2-yl}-acetate (**16d**) (68 mg, 23%).

(*E*)-**15d:** IR (CCl_4): ṽ = 2945 cm^{-1}, 2870, 2850, 2240 (C≡C), 1715, 1660, 1645, 1435, 1370, 1285, 1195, 1160, 1120, 1070. − ^{1}H NMR (250 MHz): δ = 5.52 (s, 1 H, 2-H), 5.43 (t, $J_{5,4}$ = 4.7 Hz, 1 H, 5′-H), 4.65−4.56 (m, 1 H, 2′′-H), 3.93−3.76 (m, 2 H, 11′-H*), 3.68 (s, 3 H, OCH_3), 3.57−3.41 (m, 2 H, 6′′-H*), 3.14 (t, $J_{4',3'}$ = 7.0 Hz, 2 H, 3′-H), 2.47 (t, $J_{9',10'}$ = 7.1 Hz, 2 H, 9′-H), 2.24−2.13 (dt, $J_{4',3'}$ = 7.0 Hz, $J_{4,5}$ = 4.7 Hz, 2 H, 4′-H), 1.92−1.45 (m, 8 H, 10′-H/3′′-H/ 4′′-H/5′′-H). − MS (EI): *m/z* (%) = 289 (3) [M^+ − OCH_3], 261 (48), 243 (14), 236 (34), 217 (22), 204 (48), 201 (27), 187 (29), 177 (100), 159 (54), 149 (56). − HRMS ($C_{18}H_{21}O_3$ − CO_2CH_3 = $C_{16}H_{21}O_3$): calcd. 261.1491; found 261.1491.

(*Z*)-**15d:** IR (CCl_4): ṽ = 2945 cm^{-1}, 2870, 2850, 2235 (C≡C), 1730, 1710, 1670, 1450, 1440, 1435, 1345, 1275, 1205, 1150, 1120, 1065. − ^{1}H NMR (250 MHz): δ = 5.41 (t, $J_{5',4'}$ = 4.7 Hz, 1 H, 5′-H), 4.96 (s, 1 H, 2-H), 4.65−4.56 (m, 1 H, 2′′-H), 3.92−3.77 (m, 2 H, 11′-H*), 3.70 (s, 3 H, OCH_3), 3.57−3.40 (m, 2 H, 6′′-H*), 2.52−2.40 (m, $J_{9',10'}$ = 6.7 Hz, $J_{3',4'}$ = 7.0 Hz, 4 H, 3′-H, 9′-H), 2.26−2.15 (dt, $J_{4',3'}$ = 7.0 Hz, $J_{4',5'}$ = 4.7 Hz, 2 H, 4′-H), 1.91−1.45 (m, $J_{9',10'}$ = 6.7 Hz, 8 H, 10′-H/3′′-H/4′′-H/5′′-H). − MS (CI, isobutane): *m/z* (%) = 321 (6%) [M^+ + 1], 289 (5) [M^+ − OCH_3], 237 (100), 235 (6) [M^+ − THP], 205 (39), 177 (5).

16d: IR (CCl_4): ṽ = 2940 cm^{-1}, 2870, 2230 (C≡C), 1750, 1695, 1645, 1575, 1440, 1285, 1120. − ^{1}H NMR (250 MHz): δ = 5.12−5.04 (m, 1 H, 5′-H), 4.69−4.64 (m, 1 H, 3′-H), 4.64−4.55 (m, 1 H, 2′′-H), 3.92−3.62 (m, 2 H, 11′-H*), 3.72 (s, 3 H, OCH_3), 3.60−3.41 (m, 2 H, 6′′-H*), 3.07−3.04 (m, 2 H, 2-H), 2.81−2.75 (m, 2 H, 4′-H), 2.48−2.40 (m, 2 H, 9′-H), 1.97−1.44 (m, 8 H, 10′-H, 3′′-H, 4′′-H, 5′′-H).

Anionic Cyclization of 9e: Reaction of **9e** (100 mg, 0.34 mmol, reaction time ca. 1 min) by the procedure described for **9a** with DMF as solvent and potassium *tert*-butoxide as base gave after flash chromatography (SiO_2, cyclohexane/ethyl acetate, 40:1) methyl (*E*)-2-[6-(tetrahydro-pyran-2-yloxyethynyl)-3,4-dihydropyran-2-ylidene]acetate [(*E*)-**15e**] (3 mg, 3%), the *cis*-isomer (*Z*)-**15e** (7 mg, 7%), and methyl 2-[6-(tetrahydro-pyran-2-yloxyethynyl)4*H*-pyran-2-yl]acetate (**16e**) (28 mg, 28%). The reaction of **9e** under the standard conditions, *i.e.* in DMF as solvent and with sodium hydride as base (ca. 2 min), yielded after chromatography the same products, albeit in a different ratio: (*E*)-**15e** (8%), (*Z*)-**15e** (22%), and only traces of **16e**, respectively.

(*E*)-**15e:** IR (CCl_4): ṽ = 2940 cm^{-1}, 2220, 1710, 1655, 1435, 1370, 1120, 1060. − ^{1}H NMR (250 MHz): δ = 5.56 (t, *J* = 4.9 Hz, 1 H, 5′-H), 5.53 (m, 1 H, 2-H), 4.82 (t, *J* = 3.0 Hz, 1 H, 2′′-H), 4.44 (d, *J* = 16.1 Hz, 1 H, 9′-H), 4.36 (d, *J* = 16.1 Hz, 1 H, 9′-H), 3.84 (m, 1 H, 6′′-H), 3.69 (d, *J* = 0.6 Hz, 3 H, OCH_3), 3.55 (m, 1 H, 6′′-H), 3.15 (t, *J* = 7.0 Hz, 2 H, 3′-H), 2.21 (dt, *J* = 7.0 Hz, J = 4.9 Hz, 2 H, 4′-H), 1.90−1.45 (m, 6H, 3′′-H, 4′′-H, 5′′-H). − MS (EI): *m/z* (%) = 292 (23) [M^+], 204 (30), 192 (22), 191 (43), 159 (25), 132 (24), 131 (45), 103 (24), 101 (41), 85 (100). − HRMS ($C_{16}H_{20}O_5$): calcd. 292.1311; found 292.1312.

(*Z*)-**15e:** IR (CCl_4): ṽ = 2960 cm^{-1}, 2230, 1655, 1340, 1200, 1125, 1065, 1030, 900. − ^{1}H NMR (250 MHz): δ = 5.55 (t, *J* = 4.7 Hz, 1 H, 5′-H), 4.98 (m, 1 H, 2-H), 4.82 (t, *J* = 3.0 Hz, 1 H, 2′′-H), 4.44 (d, *J* = 16.1 Hz, 1 H, 9′-H), 4.36 (d, *J* = 16.1 Hz, 1 H, 9′-H), 3.80 (m, 1 H, 6′′-H), 3.70 (d, *J* = 0.6 Hz, 3 H, OCH_3), 3.55 (m, 1 H, 6′′-H), 2.46 (t, *J* = 6.7 Hz, 2 H, 3′-H), 2.24 (m, 2 H, 4′-H),

1.93−1.43 (m, 6 H, 3′′-H, 4′′-H, 5′′-H). − MS (EI):*m/z* (%) = 292 (19) [M$^+$], 192 (25), 191 (55), 133 (25), 131 (38), 101 (32), 85 (100). − HRMS ($C_{16}H_{20}O_5$): calcd. 292.1311; found 292.1315.

16e: IR (CCl_4): $\tilde{\nu}$ = 2960 cm^{-1}, 2230, 1655, 1340, 1200, 1125, 1065, 1030, 900. − ^{1}H NMR (250 MHz): δ = 5.55 (t, *J* = 4.7 Hz, 1 H, 5′-H), 4.98 (m, 1 H, 2-H), 4.82 (t, *J* = 3.0 Hz, 1 H, 2′′-H), 4.44 (d, *J* = 16.1 Hz, 1 H, 9′-H), 4.36 (d, *J* = 16.1 Hz, 1 H, 9′-H), 3.80 (m, 1 H, 6′′-H), 3.70 (d, *J* = 0.6 Hz, 3 H, OCH_3), 3.55 (m, 1H, 6′′-H), 2.46 (t, *J* = 6.7 Hz, 2 H, 3′-H), 2.24 (m, 2 H, 4′-H), 1.93−1.43 (m, 6 H, 3′′-H, 4′′-H, 5′′-H). − MS (EI): *m/z* (%) = 292 (19) [M$^+$], 192 (25), 191 (55), 133 (25), 131 (38), 101 (32), 85 (100). − HRMS ($C_{16}H_{20}O_5$): calcd. 292.1311; found 292.1312.

Anionic Cyclization of 9f: Reaction of **9f** (100 mg, 0.48 mmol, reaction time 13 min) by the procedure described for **9a** with THF/DMF (2:1) as solvent and potassium *tert*-butoxide as base gave after flash chromatography (SiO_2, cyclohexane/ethyl acetate, 40:1) methyl 2-(6-butyl-4*H*-pyran-2-yl)acetate (**16f**) (36 mg, 36%) and methyl 3-oxo-2-propyl-cyclohex-1-enyl)acetate (**17**) (42 mg, 42%). Compound **16f** was isolated as a very unstable brown oil which could only be characterized by ^{1}H NMR spectroscopy.

16f: ^{1}H NMR (250 MHz): δ = 4.66 (m, 1 H, 5′-H), 4.47 (m, 1 H, 3′-H), 3.72 (s, 3 H, OCH_3), 3.04 (d, *J* = 0.9 Hz, 2 H, 2-H), 2.70 (m, 2 H, 4′-H), 2.08 (m, 2 H, 7′-H), 1.40−1.30 (m, 4 H, 8′-H, 9′-H), 0.93 (m, 3 H, 10′-H).

17: IR (CCl_4): $\tilde{\nu}$ = 2960 cm^{-1}, 2870, 1745, 1675, 1435, 1320, 1195, 1175. − ^{1}H NMR (400 MHz): δ = 3.72 (s, 3 H, OCH_3), 3.31 (s, 2 H, 2-H), 2.42 (m, 4 H, 4′-H, 6′-H), 2.26 (t, *J* = 8.0 Hz, 2 H, 1′′-H), 1.96 (m, *J* = 6.2 Hz, 2 H, 5′-H), 1.31 (m, 2 H, 2′′-H), 0.90 (t, *J* = 7.2 Hz, 3 H, 3′′-H). − ^{13}C NMR (100 MHz): δ = 198.8 (C-3′), 170.5 (C-1), 149.5 (C-1′), 138.3 (C-2′), 52.2 (OCH_3), 40.0 (C-2/4′), 38.0 (C-2/4′), 31.3 (C-6′/1′′), 27.5 (C-6′/1′′), 22.5 (C-5′/2′′), 22.3 (C-5′/2′′), 14.2 (C-3′′). − MS (EI): *m/z* (%) = 210 (100) [M$^+$], 139 (99), 137 (83), 136 (53), 121 (87), 108 (63), 98 (50), 96 (70), 81 (70). − HRMS ($C_{12}H_{18}O_3$): calcd. 210.1256; found 210.1257.

Acknowledgments

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