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Malonylation/Decarbalkoxylation of Furan Derivatives as Key Steps for the Preparation of Nonactic Acid Derivatives. Part I [1]

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Summary. A malonylation/decarbalkoxylation sequence from 2-substituted furans was investigated in view of developing a scalable synthesis of hydrophobic nonactic acid analogues.

Keywords. Heterocycles; Malonylation; Nonactic acid; Natural-like.

Introduction

The antibiotic ionophore nonactin is a natural product produced by a variety of *Streptomyces* species [2]. Structurally, nonactin consists of four nonactic acids (Scheme 1) condensed in a (+) (−) (+) (−) atypical fashion. Nonactin is used as additive in the semi-permeable membranes in ion selective sensors. Its selectivity for ammonium and potassium cations enables one to discriminate in favour of these two cations [3]. The life span of these electrodes is limited due to the loss of nonactin into the aqueous solution. Our goal is to prepare hydrophobic nonactin derivatives [4], to increase the life time of the ionophore in the semi permeable membrane. As part of our studies on the macrocycle nonactin, we plan to develop a new route to generate 2,5-disubstituted furans, precursors of simple analogues of nonactic acid.

In the previous paper, we described an efficient and cheap synthesis of derivatives of nonactic acid, the monomeric precursor of nonactin, from furan using different radical coupling reactions [1]. The yields for the introduction of the second lateral chain in the 5-position of the furan under our conditions was not satisfactory. Thus, we propose alternative, versatile two steps malonylation/decarbalkoxylation sequences. Under these conditions total conversions of **1a**–**1d** into the products **2** and **11**–**21** could be achieved in moderate to good overall yields (Scheme 2). In this paper, which is the first of a series of two publications, we present our results on the first malonylation step.

Results and Discussion

We used as starting material the 2-substituted furans **1a**, **1b**, and **1d** obtained by a radical alkylation strategy and **1c** obtained by a deprotonation alkylation methodology [1]. As large quantities of our model compounds were needed for our studies, it was necessary to achieve total conversion and to develop easy purification procedures. Ce(IV) or Mn(III) can catalyse the creation of electrophilic radical carbons, which are known to react with aromatic rings in good yields [5]. We studied the *Weinstock*'s malonylation procedure using $CeSO_4$ [6]. The transformation of **1a** giving product **2** could be accomplished, however in an unsatisfactory 31% yield (Scheme 3). Sulfuric acid is generated during the reaction. We added a few drops of sulfuric acid right from the beginning without changing the yield. Therefore

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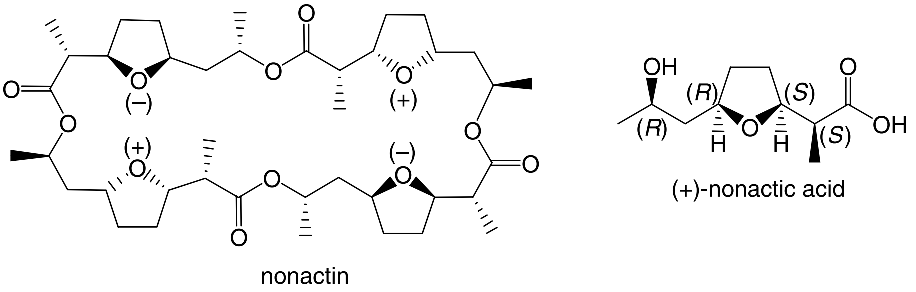
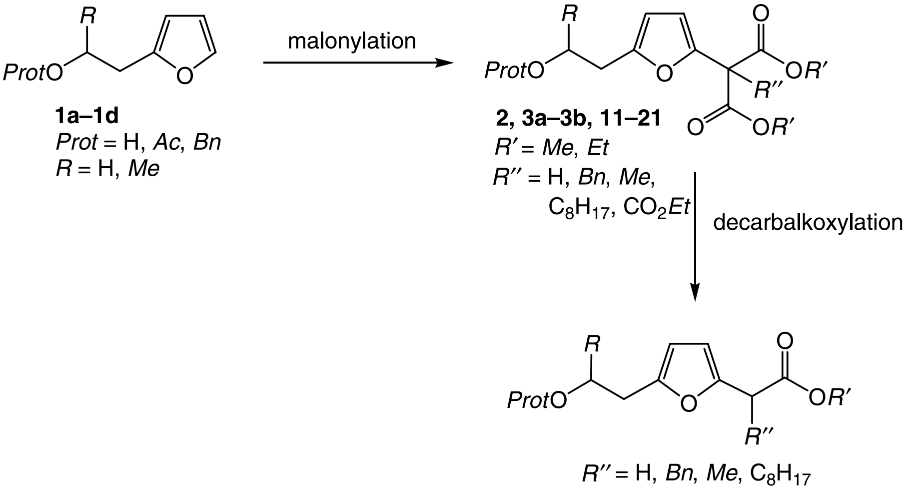
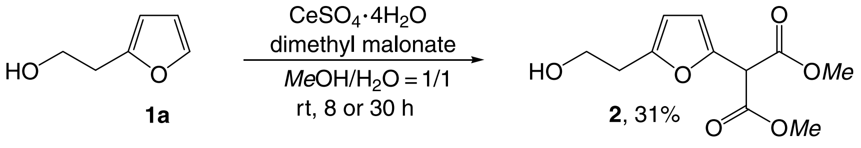


Scheme 1



Scheme 2

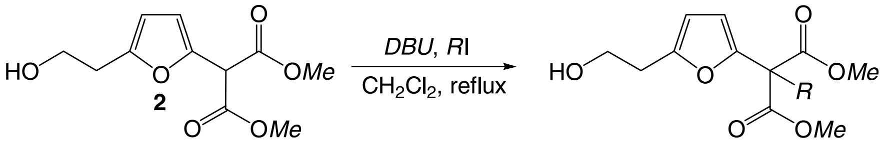


Scheme 3

sulfuric acid is not responsible for the low yield observed. On 0.2 g scale, the total conversion into **1a** was obtained in 8 h, but on 1 g scale, 30 h and 2 equivalents of $CeSO_4$ were necessary to obtain total conversion. In 1 g scale, continuous addition of solvent was necessary to keep the mixture stirrable, as the reaction mixture became more and more viscous. Due to this practical problem the development of a scalable process is difficult.

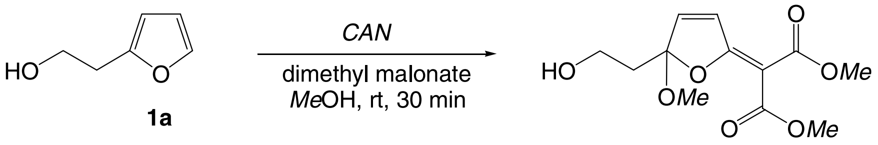
The ease of deprotonation of the malonyl function allows the introduction of a methyl or a more hydrophobic octyl chain. We obtained the best results using *DBU* as a base in CH_2Cl_2 (Scheme 4). The methyl group was introduced in almost quantitative yield within 3 h at rt, whereas the octyl chain required 6.5 h in refluxing CH_2Cl_2 to give a satisfactory 68% yield. Our first attempts to introduce the octyl chain followed the method described by *Van der Gen* using NaH as base in *THF* [7]. In this case, we found that *HMPA* was required as cosolvent to dissolve the corresponding anion of **2**, and the yield in **3b** was only 31% after 18 h under reflux.

With the hope to increase the yield, we studied other reaction conditions for the introduction of the malonyl group into our furans. *Baciocchi* used *CAN* ($Ce(NH_4)(NO_3)_6$) in *Me*OH [5] to perform the malonylation of aromatic compounds. We applied these reaction conditions to our heteroaromatic alcohol **1a**, but only the unexpected product **4** could be isolated in 32% yield (Scheme 5). The formation of **4** can be



3a, $R = Me$, 3 h, rt, 97%
3b, $R = C_8H_{17}$, 6.5 h, reflux, 68%

Scheme 4



1a

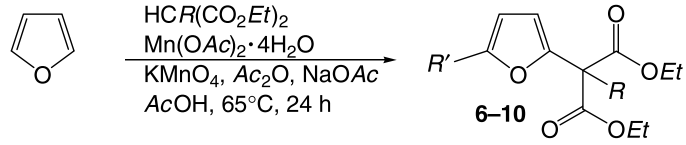
4, 32%

Scheme 5

rationalized by the following sequence: formation of the electrophilic radical, addition of this radical to the heterocycle, oxidation to the stabilized cation followed by rearomatisation, deprotonation of the acidic methin group, addition of methanol to the oxidized heterocyclic ring yielding the dearomatized furan ring. *Baciocchi* used phenyl and naphthyl derivatives as starting materials having higher resonance energies than furans and thereby preventing dearomatization.

Citterio et al. [8] reported the utilisation of Mn(III) acetate to introduce the malonyl group into aromatic rings. *Cho* and *Muchowski* [9] prepared Mn(III) salt *in situ* [10] from potassium permanganate and Mn(II) acetate. This is a cheaper alternative to achieve the malonylation of aromatic substrates. So we combined these two methodologies to prepare a set of mono- and disubstituted products, first from furan and triethyl methanetricarboxylate and from substituted malonates as well (Table 1). As expected from the proposed mechanism, the reaction is regioselective for positions 2 and 5 of the furan ring. The use of dimethyloctyl malonate doesn't affect the overall yields of **8** and **9** if compared with the results obtained for **6** and **7**. We can therefore successfully introduce the malonyl unit together with the octyl chain (Table 1). The formation of the mixture of mono- and disubstituted products can be avoided using tri(ethoxycarbonyl)methane. The product **10**

Table 1. Introduction of substituted malonyl groups and of triethyl methanetricarboxylate group to furan



6–10

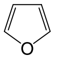
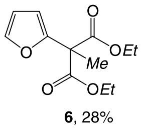
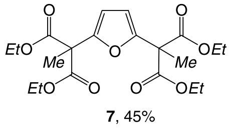
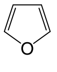
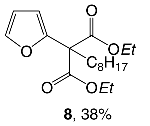
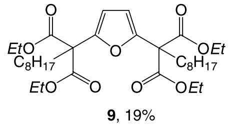
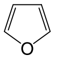
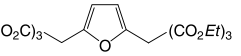
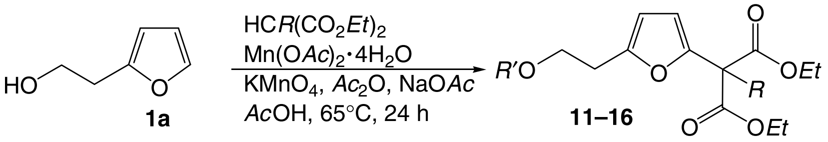
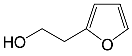
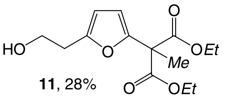
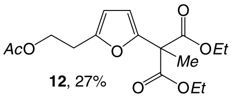
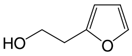
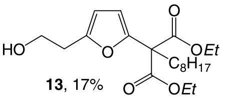
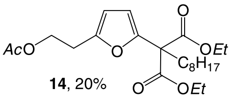
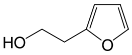
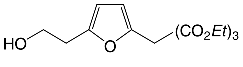
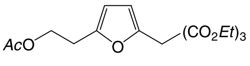
Furan	Substituent	Products and yields
	$MeCH(CO_2Et)_2$	 **6**, 28%  **7**, 45%
	$H_{17}C_8CH(CO_2Et)_2$	 **8**, 38%  **9**, 19%
	$HC(CO_2Et)_3$	 **10**, 73%

Table 2. Introduction of substituted malonyl groups and of triethyl methanetricarboxylate group to 2-(furan-2-yl)ethanol (**1a**)



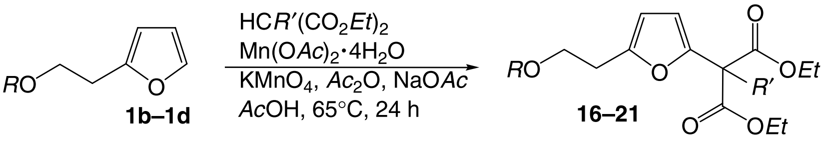
Furan	Substituent	Products and yields
 **1a**	$Me\text{CH}(\text{CO}_2Et)_2$	 **11**, 28%  **12**, 27%
 **1a**	$\text{H}_{17}\text{C}_8\text{CH}(\text{CO}_2Et)_2$	 **13**, 17%  **14**, 20%
 **1a**	$\text{HC}(\text{CO}_2Et)_3$	 **15**, 20%  **16**, 36%

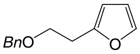
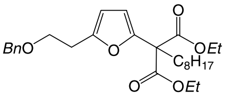
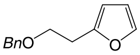
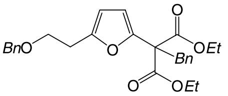
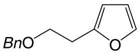
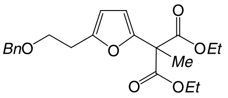
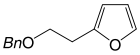
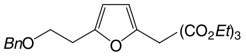
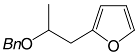
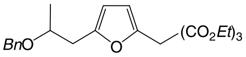
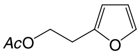
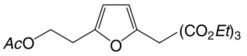
was obtained using two equivalents of triethyl methanetricarboxylate.

Based on these preliminary studies the method was applied to 2-(furan-2-yl)ethanol (**1a**). Promising yields could be obtained (Table 2). However, we could observe the O-acetylation of roughly half of the product under the reaction conditions.

O-Protected 2-(furan-2-yl)ethanol derivatives reported in our previous paper [1] were then investigated. The best yields and the easiest purifications

Table 3. Introduction of substituted malonyl groups and of triethyl methanetricarboxylate group to the O-protected furans **1b**–**1d**



Furan	Substituent	Product and yield
 **1b**	$\text{H}_{17}\text{C}_8\text{CH}(\text{CO}_2Et)_2$	 **17**, 61%
 **1b**	$Bn\text{CH}(\text{CO}_2Et)_2$	 **18**, 77%
 **1b**	$Me\text{CH}(\text{CO}_2Et)_2$	 **19**, 81%
 **1b**	$\text{HC}(\text{CO}_2Et)_3$	 **20**, 80–89%[a]
 **1c**	$\text{HC}(\text{CO}_2Et)_3$	 **21**, 55%
 **1d**	$\text{HC}(\text{CO}_2Et)_3$	 **16**, 75%

[a] This reaction was performed many times in this reproducible range of yields

were observed for the O-benzyl derivatives **1b** and **1c**. The O-acetylated compound **1d** gave also satisfactory results (Table 3). Purification by chromatography can be avoided despite the presence of some impurities in small quantities. Chromatography was necessary to fully characterise the new products synthesized in 55–89% yields. The diastereotopic protons of the CH_2-group of the ethyl esters resonated at different chemical shifts in the products **6**, **8**, **9**, **14**, **17**, and **18** (see Experimental).

Conclusions

2,5-Disubstituted furans were prepared avoiding purification by chromatography as much as possible. In many cases the products could be obtained in good overall yields without any chromatography and in some cases, only one purification by chromatography was necessary. The best results were obtained for the synthesis of **19** and **20**. On a 15 g scale **19** was obtained in 81% yield; the compound **20** was obtained in 89% yield on a 19 g scale. This efficient and scalable strategy allowed us to prepare these compounds in sufficient quantities for our further synthesis studies. The development of an efficient decarbalkoxylation methodology leading to our target molecules will be reported in the subsequent publication.

Experimental

All moisture-sensitive reactions were carried out under Ar and N_2 using oven-dried glassware. All reagents were of commercial quality if not specifically mentioned. Solvents were freshly distilled prior to use. Flash chromatography (FC): Brunschwig silica gel 60, 0.032–0.063 mm, under positive pressure. TLC: Merck precoated silica gel thin-layer sheets 60 F 254, detection by UV and treatment with basic $KMnO_4$ sol. Mp: Gallenkamp MFB-595. IR spectra: Perkin Elmer Spectrum One FT-IR, in cm^{-1}. NMR spectra: Bruker Avance-400 (400 MHz (^{1}H) and 100 MHz (^{13}C)), at rt, chemical shifts δ in ppm rel. to $CDCl_3$ (^{1}H: 7.264 ppm, ^{13}C: 77.0 ppm) as internal reference, coupling constants J in Hz. ESI-MS: Finnigan LCQ. Elemental analyses or HR-ESI-MS of novel compounds agreed favourably with calculated values.

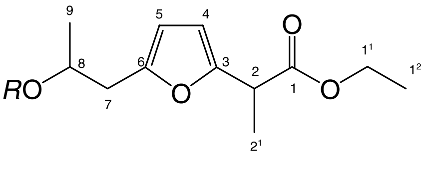


Fig. 1. Labeling used for NMR assignment

Dimethyl 2-(5-(2-hydroxyethyl)furan-2-yl)malonate (**2**, $C_{11}H_{14}O_6$)

A stirred solution of 2-(furan-2-yl)ethanol (**1a**) (1.60 g, 14 mmol) and dimethyl malonate (9.25 g, 7 mmol) in *Me*OH/$H_2O = 9/1$ was reacted at rt with $CeSO_4$ (5.66 g, 14 mmol) added slowly in a minimum of H_2O. After 1 h, 5 g celite were added, after 11 h, 23 h, and 28 h 1.42 g, 2.84 g, and 1.42 g $CeSO_4$ were added. After 2 h, the solution was filtered, washed with NaOH (0.1 M) and *Me*OH was removed by evaporation *in vacuo*. The product was extracted 6 times with *Ac*O*Et*, and the combined organic layers were washed with brine. The organic layer was dried (Na_2SO_4), and the *Ac*O*Et* removed by evaporation *in vacuo*. Purification by chromatography on a silica gel column using CH_2Cl_2/Et_2O increasing the diethyl ether ratio afforded **2** (1.03 g, 4.25 mmol, 31%). Oil; $R_f = 0.20$ ($CH_2Cl_2/Et_2O = 4/1$); IR (film): $\bar{\nu} = 3133$, 3008, 2957, 2890, 2849, 1742, 1611, 1559, 1437, 1317, 1283, 1239, 1202, 1152, 1028 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.34$ (d, $J = 3.2$ Hz, H-4), 6.10 (dt, $J = 3.2$, 0.4 Hz, H-5), 4.76 (s, H-2), 3.85 (t, $J = 6.2$ Hz, H-8), 3.79 (s, H-1^1), 2.88 (t, $J = 6.2$ Hz, H-7), 1.87 (br, OH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 166.7$ (C=O), 153.4 (C-3), 144.3 (C-6), 110.2 (C-4), 107.7 (C-5), 60.9 (C-8), 53.1 (C-1^1), 51.7 (C-2), 31.6 (C-7) ppm; EI-MS: $m/z = 242$ (8, $[M]^+$), 212 (61, $[(M+H)-CH_3O]^+$), 183 (23, $[M-CO_2CH_3]^+$), 153 (52), 152 (89), 121 (100), 111 (31), 65 (30).

Dimethyl 2-(5-(2-hydroxyethyl)-5-methoxyfuran-2(5H)-ylidene)malonate (**4**, $C_{12}H_{16}O_7$)

A stirred solution of **1a** (200 mg, 1.8 mmol) and dimethyl malonate (236 mg, 1.8 mmol) in 50 cm^3 *Me*OH was reacted at rt with *CAN* (1.96 g, 3.6 mmol) added over a 0.5 h period. *Me*OH was removed by evaporation *in vacuo*, 50 cm^3 brine were added, and the product was extracted 10 times with diethyl ether. The combined organic layers were dried (Na_2SO_4), and the diethyl ether was removed by evaporation *in vacuo*. Purification by chromatography on a silica gel column using $CH_2Cl_2/Et_2O = 4/1$ afforded **4** (155 mg, 0.57 mmol, 32%). Oil; $R_f = 0.10$ ($CH_2Cl_2/Et_2O = 4/1$); IR (film): $\bar{\nu} = 3129$, 3091, 3000, 2954, 2894, 2842, 1713, 1636, 1583, 1437, 1337, 1275, 1217, 1193, 1167, 1129, 1079, 1035, 995, 947, 929, 818 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.36$ (d, $J = 6.0$ Hz, H-4), 6.63 (d, $J = 6.0$ Hz, H-5), 3.79 (s, H-1^1), 3.81–3.69 (m, H-8), 3.15 (s, H-6^1), 2.15–2.05 (m, H-7) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 168.9$ (C-6), 165.2, 165.1 (C=O), 142.8 (C-5), 127.5 (C-4), 117.8 (C-2), 99.9 (C-3), 57.7 (C-8), 52.4, 52.0 (OCH_3), 51.3 (OCH_3), 40.2 (C-7) ppm; DCI-MS: $m/z = 273$ (100, $[M+H]^+$), 258 (18, $[M-CH_3]^+$), 241 (20), 227 (8).

General Procedure for the Synthesis of Di- and Triethyl Furylmethanedi- and -tricarboxylates with Mn(III)

$KMnO_4$ (0.57 eq) was added to a 100°C and stirred solution of $Mn(OAc)_2 \cdot 4H_2O$ (2.27 eq) in *Ac*OH ($2\,cm^3 \cdot mmol^{-1}$ $Mn(OAc)_2 \cdot 4H_2O$). After 0.5 h, Ac_2O (6.8 eq) was added cautiously and then the mixture was cooled to rt. Di- or triethyl methanedi- or -tricarboxylate (0.5–2 eq), the appropriate furan derivative (0.5–2 eq), and Na*OAc* (1.82 eq) were added and the resulting mixture was stirred at 65°C in an Ar atmosphere for 24 h. After cooling at rt, H_2O (1 $cm^3 \cdot mmol^{-1}$ Na*OAc*) was added and the product was extracted with toluene ($4 \times 5\,cm^3/cm^3$ H_2O). The extract was washed with H_2O and brine, dried ($MgSO_4$), and evaporated *in vacuo*. Purification by chromatography on a silica gel column using *n*-hexane/*Ac*O*Et* increasing the *Ac*O*Et* ratio afforded the product.

Diethyl 2-(furan-2-yl)-2-methylmalonate (**6**, $C_{12}H_{16}O_5$) and *Diethyl 2-(5-(1,1-bis(ethoxycarbonyl)ethyl)furan-2-yl)-2-methylmalonate* (**7**, $C_{20}H_{28}O_9$)

General procedure with furan (0.53 cm^3, 7.3 mmol) and diethyl methylmalonate (1.89 cm^3, 11.1 mmol). Compounds **6** (484 mg, 2.0 mmol, 28%) and **7** (1.352 g, 3.3 mmol, 45%) were obtained.

6: Oil; $R_f = 0.36$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu}$ = 2985, 2942, 2907, 2877, 1737, 1664, 1585, 1501, 1453, 1378, 1272, 1246, 1228, 1159, 1109, 1082, 1019 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (dd, *J* = 1.7, 1.0 Hz, H-6), 6.36 (dd, *J* = 3.3, 1.0 Hz, H-4), 6.35 (dd, *J* = 3.3, 1.7 Hz, H-5), 4.26–4.16 (m, *J* = 7.1 Hz, H-1^1), 1.82 (s, H-2^1), 1.26 (t, *J* = 7.1 Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.5 (C=O), 150.7 (C-3), 142.2 (C-6), 110.2 (C-5), 107.7 (C-4), 61.8 (C-1^1), 55.1 (C-2), 20.3 (C-2^1), 13.8 (C-1^2) ppm; EI-MS: m/z = 241 (10, $[M+H]^+$), 240 (20, $[M]^+$), 221 (16), 211 (9, $[M-C_2H_5]^+$), 183 (11), 182 (12), 174 (19), 168 (29), 167 (84, $[M-COOC_2H_5]^+$),147 (24), 140 (12), 139 (30), 137 (15), 129 (77), 128 (21), 127 (12), 123 (13), 122 (18), 121 (50), 119 (11), 117 (13), 111 (35), 110 (11), 109 (13), 108 (24), 107 (25), 106 (27), 105 (53), 104 (11), 1 (23), 101 (44), 100 (34), 99 (25), 98 (18), 97 (19), 96 (12), 95 (30), 94 (30), 93 (100), 92 (21), 91 (52), 90 (12), 89 (15), 88 (53), 87 (24).

7: Oil; $R_f = 0.20$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu}$ = 2985, 2942, 2909, 2876, 1737, 1601, 1455, 1378, 1245, 1174, 1110, 1023 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.32 (s, CH), 4.21 (q, *J* = 7.1 Hz, H-1^1), 1.78 (s, H-2^1), 1.24 (t, *J* = 7.1 Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.3 (C=O), 150.4 (C-3), 108.5 (C-4), 61.8 (C-1^1), 55.1 (C-2), 20.2 (C-2^1), 13.8 (C-1^2) ppm; EI-MS: m/z = 413 (5, $[M+H]^+$), 412 (11, $[M]^+$), 340 (18, $[M+H-CO_2C_2H_5]^+$), 339 (85, $[M-CO_2C_2H_5]^+$), 294 (14), 267 (47, $[M+H-2xCO_2C_2H_5]^+$), 266 (17, $[M-2xCO_2C_2H_5]^+$), 239 (26, $[M-CH_3C(CO_2C_2H_5)_2]^+$), 222 (16), 221 (100), 220 (25), 211 (12), 194 (14), 193 (38), 192 (15), 183 (11), 165 (21), 163 (15), 155 (12), 149 (11), 147 (22), 137 (13), 127 (12), 121 (10), 119 (20), 117 (11), 99 (17), 98 (14), 93 (61), 92 (14), 91 (24), 90 (10), 89 (11), 86 (22), 84 (39), 83 (21), 77 (19), 65 (28), 44 (71).

Diethyl 2-(furan-2-yl)-2-octylmalonate (**8**, $C_{19}H_{30}O_5$) and *Diethyl 2-(5-(1,1-bis(ethoxycarbonyl)ethyl)furan-2-yl)-2-octylmalonate* (**9**, $C_{34}H_{56}O_9$)

General procedure with furan (0.8 cm^3, 11.0 mmol) and diethyl octylmalonate (2.37 g, 8.5 mmol). Compounds **8** (1.10 g, 3.2 mmol, 38%) and **9** (970 mg, 1.6 mmol, 19%) were obtained.

8: Oil; $R_f = 0.56$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu}$ = 2958, 2927, 2857, 1741, 1586, 1501, 1466, 1447, 1390, 1368, 1299, 1239, 1223, 1189, 1154, 1118, 1097, 1031, 1017, 1023 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (dd, *J* = 1.9, 0.8 Hz, H-6), 6.59 (dd, *J* = 3.3, 0.8 Hz, H-4), 6.34 (dd, *J* = 3.3, 1.9 Hz, H-5), 4.28–4.15 (m, H-1^1), 2.27–2.23 (m, H-2^1), 1.30–1.12 (m, H-2^2 to H-2^7), 1.24 (t, *J* = 7.1 Hz, H-1^2), 0.85 (t, *J* = 6.8 Hz, H-2^8) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7 (C=O), 149.7 (C-3), 141.8 (C-6), 110.2 (C-5), 109.2 (C-4), 61.6 (C-1^1), 59.4 (C-2), 34.3 (C-2^1), 31.7, 29.5, 29.1, 24.5, 22.6, 14.0 (C-2^8), 13.9 (C-1^2) ppm; DCI-MS: m/z = 340 (11, $[M+2H]^+$), 339 (67, $[M+H]^+$), 290 (11), 273 (30), 265 (24, $[M-CO_2C_2H_5]^+$), 192 (11), 191 (29), 160 (12), 107 (15), 95 (21), 94 (23), 93 (30), 92 (20), 91 (23), 82 (12), 81 (28), 59 (11), 58 (30), 57 (14), 56 (24), 55 (46), 54 (18), 53 (17), 52 (16), 51 (10), 46 (100).

9: Oil; $R_f = 0.47$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu}$ = 2959, 2927, 2856, 1741, 1601, 1544, 1466, 1447, 1390, 1368, 1299, 1237, 1189, 1128, 1097, 1069, 1027 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.57 (s, CH), 4.28–4.13 (m, *J* = 7.1, H-1^1), 2.23–2.18 (m, H-2^1), 1.30–1.09 (m, H-2^2 to H-2^7, H-1^2), 0.86 (t, *J* = 6.9 Hz, H-2^8) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5 (C=O), 148.9 (C-3), 110.1 (C-4), 61.5 (C-1^1), 59.3 (C-2), 34.4 (C-2^1), 31.8, 29.7, 29.3, 29.2, 24.6, 22.6 (C-2^2 to C-2^7), 14.0 (C-2^8), 13.9 (C-1^2) ppm; EI-MS: m/z = 609 (6, $[M+H]^+$), 608 (5, $[M]^+$), 536 (27, $[M+H-CO_2C_2H_5]^+$), 535 (30, $[M-CO_2C_2H_5]^+$), 205 (10), 193 (12), 191 (17), 189 (20), 179 (17), 175 (10), 173 (16), 161 (11), 147 (20), 141 (25), 135 (20), 133 (17), 131 (12), 127 (12), 123 (22), 122 (10), 121 (20), 120 (12), 119 (15), 118 (10), 117 (11), 110 (11), 109 (11), 108 (20), 107 (16), 106 (16), 105 (14), 100 (12), 99 (15), 98 (10), 97 (16), 96 (17), 95 (19), 94 (20), 93 (23), 92 (27), 91 (19), 89 (15), 88 (16), 87 (52), 86 (50), 85 (84), 84 (74), 83 (20), 82 (48), 81 (30), 80 (28), 79 (24), 78 (15), 77 (10),73 (14), 72 (30), 71 (37), 70 (42), 69 (40), 68 (40), 67 (17), 66 (12), 59 (44), 58 (75), 57 (89), 56 (100), 55 (12), 54 (12), 52 (21), 51 (24); ESI-HR-MS: m/z $[M+H]^+$ = calcd 609.3997, found 609.4003.

Diethyl 2-ethoxycarbonyl-2-(5-(tris(ethoxycarbonyl)methyl)furan-2-yl)malonate (**10**, $C_{24}H_{32}O_{13}$)

General procedure with furan (0.8 cm^3, 11 mmol) and triethyl methanetricarboxylate (4.6 cm^3, 22 mmol). Compound **10** (4.27 g, 8.08 mmol, 73%) was obtained. Oil; $R_f = 0.16$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.70 (s, H-4), 4.30 (q, *J* = 7.1 Hz, H-1^1), 1.30 (t, *J* = 7.1 Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.8 (C=O), 146.3 (C-3), 111.5 (C-4), 67.7 (C-2), 63.2 (C-1^1), 14.2 (C-1^2) ppm; ESI-MS: m/z = 311 (11), 285 (21), 270.3 (15), 270 (100, $[M-C(CO_2C_2H_5)_3–C_2H_5]^+$).

Diethyl 2-(5-(2-acetoxyethyl)furan-2-yl)-2-methylmalonate (**12**, $C_{16}H_{22}O_7$) and *Diethyl 2-(5-(2-hydroxyethyl)furan-2-yl)-2-methylmalonate* (**11**, $C_{14}H_{20}O_6$)

General procedure with **1a** (1.26 g, 11.2 mmol) and diethyl methylmalonate (1.88 cm^3, 11.0 mmol). Compounds **12** (978 mg, 3.0 mmol, 27%) and **11** (886 mg, 3.1 mmol, 28%) were obtained.

12: Oil; $R_f = 0.21$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu}$ = 2984, 2908, 1741, 1608, 1555, 1452, 1378, 1240, 1110, 1023 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 6.25$ (d, $J = 3.2$ Hz, H-4), 6.04 (d, $J = 3.2$ Hz, H-5), 4.27 (t, $J = 7.0$ Hz, H-8), 4.22 (q, $J = 7.2$ Hz, H-1^1), 2.94 (t, $J = 7.0$ Hz, H-7), 2.03 (s, C*H*$_3$–C=O), 1.79 (*s*, H-2^1), 1.25 (t, $J = 7.2$ Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.9$ (C=O), 169.6 (2C, C=O), 151.7 (C-3), 149.6 (C-6), 108.5 (C-4), 107.1 (C-5), 62.2 (C-8), 61.8 (C-1^1), 55.1 (C-2), 27.7 (C-7), 20.8 (*C*H$_3$–C=O), 20.3 (C-2^1), 13.9 (C-1^2) ppm; EI-MS: $m/z = 266$ (19, [M − CH$_3$CO$_2$H]$^+$), 194 (16), 193 (100), 165 (13), 120 (13), 119 (48), 107 (14); DCI-MS: $m/z = 345$ (29), 344 (100, [M + H + H$_2$O]$^+$), 328 (16), 327 (62, [M + H]$^+$), 268 (14), 267 (59), 266 (37, [M − CH$_3$CO$_2$H]$^+$), 194 (14), 193 (57), 166 (13), 165 (15), 135 (12), 119 (14), 92 (13); ESI-HR-MS: m/z [M + H]$^+$ = calcd 327.1437, found 327.1438.

11: Oil; $R_f = 0.06$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu} = 3462$, 3131, 2983, 2942, 2907, 1736, 1607, 1554, 1451, 1378, 1245, 1173, 1108, 1051, 1021 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 6.25$ (d, $J = 3.2$ Hz, H-4), 6.07 (dt, $J = 3.2$, 0.6 Hz, H-5), 4.23 (q, $J = 7.1$ Hz, H-1^1), 3.83 (t, $J = 6.2$ Hz, H-8), 2.87 (td, $J = 6.2$, 0.6 Hz, H-7), 2.02 (br, OH), 1.80 (s, H-2^1), 1.26 (t, $J = 7.1$ Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 169.6$ (C=O), 152.9 (C-3), 149.6 (C-6), 108.5 (C-4), 107.2 (C-5), 61.9 (C-1^1), 61.0 (C-8), 55.1 (C-2), 31.5 (C-7), 20.2 (C-2^1), 13.9 (C-1^2) ppm; EI-MS: $m/z = 284$ (2, [M]$^+$), 254 (6), 211 (7, [M − CO$_2$C$_2$H$_5$]$^+$), 93 (11), 92 (11), 88 (28), 87 (22), 77 (10), 73 (16), 70 (34), 46 (12), 44 (100); ESI-HR-MS: m/z [M + H]$^+$ = calcd 285.1332, found 285.1333.

Diethyl 2-(5-(2-acetoxyethyl)furan-2-yl)-2-octylmalonate (**14**, C$_{23}$H$_{36}$O$_7$) and *Diethyl 2-(5-(2-hydroxyethyl)furan-2-yl)-2-octylmalonate* (**13**, C$_{21}$H$_{34}$O$_6$)

General procedure with **1a** (1.24 g, 11.1 mmol) and diethyl octylmalonate (3.12 g, 11.2 mmol). Compounds **14** (938 mg, 2.2 mmol, 20%) and **13** (735 mg, 1.9 mmol, 17%) were obtained.

14: Oil; $R_f = 0.24$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu} = 2958$, 2928, 2857, 1741, 1609, 1466, 1387, 1368, 1298, 1235, 1186, 1125, 1096, 1038 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 6.48$ (d, $J = 3.2$ Hz, H-4), 6.04 (dt, $J = 3.2$, 0.6 Hz, H-5), 4.25 (t, $J = 6.9$ Hz, H-8), 4.22 (dq, $J = 12.3$, 7.1 Hz, H-1^{1a}, H-1$^{1a'}$), 4.21 (dq, $J = 12.3$, 7.1 Hz, H-1^{1b}, H-1$^{1b'}$), 2.92 (td, $J = 6.4$, 0.4 Hz, H-7), 2.24–2.20 (m, H-2^1), 2.03 (s, C*H*$_3$–C=O), 1.30–1.14 (m, H-2^2 to H-2^7), 1.23 (t, $J = 7.1$ Hz, H-1^2), 0.85 (t, $J = 6.9$ Hz, H-2^8) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.8$ (C=O), 168.7 (2C, C=O), 151.2 (C-3), 148.6 (C-6), 109.9 (C-4), 107.1 (C-5), 62.2 (C-8), 61.5 (C-1^1), 59.3 (C-2), 34.2 (C-2^1), 31.5 (C-7), 31.7, 29.6, 29.1, 29.1, 24.5, 22.6 (C-2^2 to C-2^7), 20.8 (*C*H$_3$–C=O), 14.0 (C-2^8), 13.9 (C-1^2) ppm; ESI-MS: $m/z = 443$ (18, [M + H + H$_2$O]$^+$), 442 (100, [M + H$_2$O]$^+$), 425 (28, [M + H]$^+$), 365 (12); ESI-HR-MS: m/z [M + H]$^+$ = calcd 425.2534, found 425.2532.

13: Oil; $R_f = 0.10$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu} = 3475$, 2957, 2928, 2857, 2086, 1737, 1608, 1553, 1466, 1447, 1390, 1369, 1298, 1239, 1191, 1126, 1097, 1047, 1031 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 6.44$ (d, $J = 3.2$ Hz, H-4), 6.06 (dt, $J = 3.2$, 0.7 Hz, H-5), 4.21 (q, $J = 7.1$ Hz, H-1^1), 3.81 (t, $J = 6.2$ Hz, H-8), 2.85 (t, $J = 6.2$ Hz, H-7), 2.24 – 2.20 (m, H-2^1), 1.90 (br, OH), 1.29 – 1.15 (m, H-2^2 to H-2^7), 1.24 (t, $J = 7.1$ Hz, H-1^2), 0.85 (t, $J = 6.9$ Hz, H-2^8) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 168.8$ (C=O), 152.3 (C-3), 148.6 (C-6), 109.8 (C-4), 107.2 (C-5), 61.6 (C-1^1), 61.0 (C-8), 59.3 (C-2), 34.2 (C-2^1), 31.5 (C-7), 31.7, 29.6, 29.1, 29.1, 24.5, 22.6 (C-2^2 to C-2^7), 14.0 (C-2^8), 13.9 (C-1^2) ppm; ESI-MS: $m/z = 401$ (11), 401 (13), 400 (100, [M + H + H$_2$O]$^+$), 399 (12, [M + H$_2$O]$^+$), 384 (11), 383 (47, [M + H]$^+$), 309 (15); ESI-HR-MS: m/z [M + H]$^+$ = calcd 383.2428, found 383.2427.

Triethyl 1-(5-(2-acetoxyethyl)furan-2-yl)ethane-1,1,2-tricarboxylate (**16**, C$_{18}$H$_{24}$O$_9$) and *Triethyl 1-(5-(2-hydroxyethyl)furan-2-yl)ethane-1,1,2-tricarboxylate* (**15**, C$_{16}$H$_{22}$O$_8$)

General procedure with **1a** (2.35 g, 21 mmol) and triethyl methanetricarboxylate (4.6 cm^3, 21 mmol). Compounds **16** (2.89 g, 7.5 mmol, 36%) and **15** (1.47 g, 4.3 mmol, 20%) were obtained.

16: Oil; $R_f = 0.14$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu} = 2985$, 2941, 2907, 2875, 1755, 1607, 1549, 1467, 1446, 1389, 1368, 1249, 1096, 1057 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 6.60$ (d, $J = 3.2$ Hz, H-4), 6.10 (dt, $J = 3.2$, 0.7 Hz, H-5), 4.32 (q, $J = 7.1$ Hz, H-1^1), 4.28 (t, $J = 6.8$ Hz, H-8), 2.97 (t, $J = 6.8$ Hz, H-7), 2.05 (s, C*H*$_3$–C=O) 1.31 (t, $J = 7.1$ Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 171.3$ (C=O), 165.1 (3C, C=O), 153.2 (C-3), 144.4 (C-6), 111.5 (C-4), 107.7 (C-5), 67.7 (C-2), 63.2 (C-1^1), 62.5 (C-8), 28.5 (C-7), 21.3 (*C*H$_3$–C=O), 14.3 (C-1^2) ppm; ESI-MS: $m/z = 408.1$ (17), 407.1 (100, [M + Na]$^+$).

15: Oil; $R_f = 0.04$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu} = 3463$, 2984, 1742, 1467, 1446, 1390, 1369, 1231, 1096, 1057 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 6.62$ (d, $J = 3.2$ Hz, H-4), 6.13 (dt, $J = 3.2$, 0.7 Hz, H-5), 4.34 (q, $J = 7.1$ Hz, H-1^1), 3.87 (t, $J = 6.0$ Hz, H-8), 2.91 (t, $J = 6.0$ Hz, H-7), 1.32 (t, $J = 7.1$ Hz, H-1^2), 1.90 (br, OH) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 165.1$ (C=O), 154.4 (C-3), 144.5 (C-6), 111.6 (C-4), 107.8 (C-5), 63.3 (C-1^1), 61.6 (C-8), 53.8 (C-2), 32.0 (C-7), 14.3 (C-1^2) ppm; ESI-MS: $m/z = 397$ (14), 381 (23), 366 (28), 366 (100, [M + Na]$^+$).

Triethyl 1-(5-(2-acetoxyethyl)furan-2-yl)ethane-1,1,2-tricarboxylate (**16**, C$_{18}$H$_{24}$O$_9$)

General procedure with 2-(furan-2-yl)ethyl acetate (**1d**) (1.63 g, 10.6 mmol) and triethyl methanetricarboxylate (2.3 cm^3, 10.9 mmol). Compound **16** (3.06 g, 8.0 mmol, 75%) was obtained as the lone product. Data are the same as above.

Diethyl 2-(5-(2-(benzyloxy)ethyl)furan-2-yl)-2-octylmalonate (**17**, C$_{28}$H$_{40}$O$_6$)

General procedure with 2-(2-(benzyloxy)ethyl)furan (**1b**) (3.44 g, 17.0 mmol) and diethyl octylmalonate (4.79 g, 17.2 mmol). Compound **17** (4.93 g, 10.4 mmol, 61%) was obtained. Oil; $R_f = 0.42$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu} = 3030$, 2957, 2927, 2857, 1741, 1607, 1466, 1455, 1389, 1367, 1299, 1235, 1185, 1100, 1029 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.36 - 7.28$ (m, *Ph*), 6.48 (d, $J = 3.2$ Hz, H-4), 6.04 (d, $J = 3.2$ Hz, H-5), 4.51 (s, C*H*$_2$-*Ph*), 4.21 (dq, $J = 14.2$, 7.1 Hz, H-1^{1a}), 4.20 (dq, $J = 14.2$, 7.1 Hz, H-1^{1b}), 3.70 (t, $J = 6.9$ Hz, H-8), 2.92 (t, $J = 6.9$ Hz, H-7), 2.25 – 2.21 (m, H-2^1), 1.29 – 1.16 (m, H-2^2 to H-2^7), 1.23 (t, $J = 7.1$ Hz, H-1^2), 0.87 (t, $J = 6.9$ Hz, H-2^8) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 168.8$ (C=O), 152.3 (C-3), 148.1 (C-6), 138.1 (1C, *Ph*), 128.3, 127.6, 127.6 (5C, *Ph*), 109.9 (C-4), 106.8 (C-5), 73.0 (*C*H$_2$-*Ph*), 68.3 (C-8), 61.5 (C-1^1), 59.3 (C-2), 34.3 (C-2^1), 31.8, 29.6, 29.2, 29.1, 24.5, 22.6 (C-2^2 to C-2^7), 28.8 (C-7), 14.1 (C-2^8), 14.0 (C-1^2) ppm; ESI-MS: $m/z = 541$ (16), 527 (32), 511 (11), 496 (100, [M + Na]$^+$); ESI-HR-MS: m/z [M + H]$^+$ = calcd 473.2898, found 473.2890.

Diethyl 2-benzyl-2-(5-(2-(benzyloxy)ethyl)furan-2-yl)malonate (**18**, $C_{27}H_{30}O_6$)

General procedure with **1b** (2.19 g, 10.8 mmol) and diethyl benzylmalonate (2.57 cm^3, 11.0 mmol). Compound **18** (3.77 g, 8.4 mmol, 77%) was obtained. Oil; $R_f = 0.34$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu} =$ 3031, 2981, 2938, 2905, 2863, 1881, 1741, 1606, 1555, 1497, 1455, 1390, 1367, 1298, 1279, 1230, 1182, 1098, 1083, 1039, 739, 701 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.41 - 7.23$ (m, *Ph*), 7.18 – 7.11 (m, *Ph*), 6.86 – 6.83 (m, *Ph*), 6.45 (d, $J = 3.2$ Hz, H-4), 6.04 (d, $J = 3.2$ Hz, H-5), 4.55 (s, C*H*$_2$-*Ph*), 4.215 (dq, $J = 10.8$, 7.1 Hz, H-1^{1a}), 4.185 (dq, $J = 10.8$, 7.1 Hz, H-1^{1b}), 4.20 (q, $J = 7.1$ Hz, H-1$^{1'}$), 3.74 (t, $J = 6.9$ Hz, H-8), 3.63 (s, H-2^1), 2.97 (t, $J = 6.9$ Hz, H-7), 1.22 (t, $J = 7.1$ Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 168.0$ (C=O), 152.2 (C-3), 147.0 (C-6), 138.1, 135.7, 129.8, 128.3, 127.8, 127.6, 126.8 (12C, *Ph*), 111.3 (C-4), 107.1 (C-5), 73.0 (*C*H$_2$-*Ph*), 68.3 (C-8), 61.7 (C-1^1), 40.7 (C-2^1), 28.8 (C-7), 13.6 (C-1^2) ppm; ESI-MS: $m/z = 489$ (11), 474 (25, [M + H + Na]$^+$), 473 (100, [M + Na]$^+$); ESI-HR-MS: m/z [M + H]$^+$ = calcd 451.2115, found 451.2119.

Diethyl 2-(5-(2-(benzyloxy)ethyl)furan-2-yl)-2-methylmalonate (**19**, $C_{21}H_{26}O_6$)

General procedure with **1b** (9.65 g, 47.7 mmol) and diethyl methylmalonate (7.91 cm^3, 47.6 mmol). Compound **19** (14.34 g, 38.35 mmol, 81%) was obtained. Oil; $R_f = 0.40$ (*n*-hexane/*Ac*O*Et* = 80/20); IR (film): $\bar{\nu} = 2979$, 1734, 1553, 1454, 1376, 1243, 1108, 1020, 737, 698 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.37 - 7.31$ (m, *Ph*), 6.29 (d, $J = 3.2$ Hz, H-4), 6.06 (d, $J = 3.2$ Hz, H-5), 4.54 (s, C*H*$_2$-*Ph*), 4.24 (q, $J = 7.1$ Hz, H-1^1), 3.73 (t, $J = 6.9$ Hz, H-8), 2.96 (t, $J = 6.9$ Hz, H-7), 1.82 (*s*, H-2^1), 1.27 (t, $J = 7.1$ Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.2$ (C=O), 149.7 (C-3), 144.0 (C-6), 138.7, 128.8, 128.1 (6C, *Ph*), 109.0 (C-4), 107.4 (C-5), 73.4 (*C*H$_2$-*Ph*), 68.7 (C-8), 67.2 (C-2), 62.2 (C-1^1), 29.4 (C-7), 20.8 (C-2^1), 14.4 (C-1^2) ppm; ESI-MS: $m/z = 398$ (22, [M + H + Na]$^+$, 397 (100, [M + Na]$^+$); APCI-MS: m/z = 398 (100, [M + H + Na]$^+$), 397 (100, [M + Na]$^+$), 392 (3.5, [M + 18]$^+$, 375 (3.5, [M + H]$^+$), 301 (5, [M-CO$_2$C$_2$H$_5$]$^+$).

Triethyl 1-(5-(2-(benzyloxy)ethyl)furan-2-yl)ethane-1,1,2-tricarboxylate (**20**, $C_{23}H_{28}O_8$)

General procedure with **1b** (9.98 g, 49.4 mmol) and triethyl methanetricarboxylate (10.41 cm^3, 49.5 mmol). Compound **20** (18.73 g, 43.3 mmol, 89%) was obtained. Oil; $R_f = 0.26$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu} = 3089$, 3064, 3030, 2984, 2939, 2906, 2868, 1746, 1606, 1549, 1497, 1466, 1455, 1391, 1368, 1213, 1098, 1060, 862, 739, 700 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.39 - 7.27$ (m, *Ph*), 6.61 (d, $J = 3.3$ Hz, H-4), 6.11 (d, $J = 3.3$ Hz, H-5), 4.54 (s, C*H*$_2$-*Ph*), 4.32 (q, $J = 7.1$ Hz, H-1^1), 3.73 (t, $J = 7.0$ Hz, H-8), 2.98 (t, $J = 7.0$ Hz, H-7), 1.30 (t, $J = 7.1$ Hz, H-1^2) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 165.2$ (C=O), 154.4 (C-3), 144.0 (C-6), 138.7, 128.8, 128.1 (6C, *Ph*), 111.5 (C-4), 107.4 (C-5), 73.4 (*C*H$_2$-*Ph*), 68.7 (C-8), 67.7 (C-2), 63.1 (C-1^1), 29.4 (C-7), 14.3 (C-1^2) ppm; ESI-MS: $m/z = 456$ (23), 455 (100, [M + Na]$^+$), 451 (26, [M + H$_2$O]$^+$), 434 (19, [M + H]$^+$).

Triethyl 1-(5-(2-(benzyloxy)propyl)furan-2-yl)ethane-1,1,2-tricarboxylate (**21**, $C_{24}H_{30}O_8$)

General procedure with 2-(2-(benzyloxy)propyl)furan (**1c**) (2.22 g, 10.3 mmol) and triethyl methanetricarboxylate (2.16 cm^3, 10.3 mmol). Compound **21** (2.52 g, 5.64 mmol, 55%) was obtained. Oil; $R_f = 0.23$ (*n*-hexane/*Ac*O*Et* = 75/25 + 1% *Me*OH); IR (film): $\bar{\nu} = 3064$, 2982, 2938, 2906, 2872, 1747, 1605, 1547, 1496, 1466, 1454, 1369, 1342, 1212, 1131, 1096, 1057, 1019 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.37 - 7.26$ (m, *Ph*), 6.62 (d, $J = 3.2$ Hz, H-4), 6.10 (d, $J = 3.2$ Hz, H-5), 4.55 (d, $J = 11.7$ Hz, CH*H*-*Ph*), 4.50 (d, $J = 11.7$ Hz, C*H*H-*Ph*), 4.32 (q, $J = 7.1$ Hz, H-1^1), 3.86 – 3.80 (m, H-8), 3.00 (dd, $J = 14.8$, 5.9 Hz, H-7a), 2.76 (dd, $J = 14.8$, 6.9 Hz, H-7b), 1.30 (t, $J = 7.1$ Hz, H-1^2), 1.23 (d, $J = 6.3$ Hz, H-9) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 165.2$ (C=O), 154.4 (C-3), 144.0 (C-6), 139.1, 128.7, 128.0, 127.9 (6C, *Ph*), 111.5 (C-4), 108.1 (C-5), 74.4 (C-8), 71.2 (*C*H$_2$-*Ph*), 67.8 (C-2), 63.2 (C-1^1), 37.7 (C-7), 20.1 (C-9), 14.3 (C-1^2) ppm; ESI-MS: $m/z = 495$ (19), 487 (33), 486 (89, [M + K]$^+$), 472 (12), 471 (16), 470 (45), 469 (100, [M + Na]$^+$), 389 (10).

Dimethyl 2-(5-(2-hydroxyethyl)furan-2-yl)-2-methylmalonate (**3a**, $C_{12}H_{16}O_6$)

A stirred solution of malonate **2** (0.4 g, 1.65 mmol) and *DBU* (0.75 g, 4.95 mmol) in 10 cm^3 CH$_2$Cl$_2$ was reacted under a N$_2$ atmosphere with *Me*I (0.21 cm^3, 3.30 mmol). The solution was stirred at rt for 3 h and the solvent was evaporated *in vacuo*. Purification by chromatography on a silica gel column using CH$_2$Cl$_2$/*Et*$_2$O = 8.5/1 afforded **3a** (418 mg, 1.62 mmol, 97%). Oil; $R_f = 0.17$ (*Et*$_2$O/*n*-hexane = 75/25); IR (film): $\bar{\nu} = 3441$, 3133, 3003, 2955, 2887, 2848, 1741, 1608, 1456, 1436, 1378, 1255, 1163, 1118, 1051, 1034 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 6.25$ (d, $J = 3.2$ Hz, H-4), 6.08 (d, $J = 3.2$ Hz, H-5), 3.84 (t, $J = 6.2$ Hz, H-8), 3.77 (s, H-1^1), 2.87 (t, $J = 6.2$ Hz, H-7), 1.87 (br, OH), 1.81 (s, 3H, H-2^1) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 170.1$ (C=O), 153.1 (C-3), 149.4 (C-6), 108.7 (C-4), 107.3 (C-5), 61.0 (C-8), 55.0 (C-2), 53.0 (C-1^1), 31.6 (C-7), 20.3 (C-2^1) ppm; EI-MS: $m/z = 257$ (16, [M + H]$^+$), 256 (18, [M]$^+$), 239 (12, [M + H + H$_2$O]$^+$), 226 (32); 198 (12), 197 (100, [M – CO$_2$CH$_3$]$^+$), 179 (22), 167

(52), 166 (48), 137 (18), 135 (66), 111(23), 107 (27), 106 (11), 77 (10), 44 (10), 40 (14); ESI-HR-MS: m/z $[M+H]^+$ = calcd 257.1020, found 257.1019.

Dimethyl 2-(5-(2-hydroxyethyl)furan-2-yl)-2-octylmalonate (**3b**, $C_{19}H_{30}O_6$)

A stirred solution of malonate **2** (1.93 g, 7.96 mmol) and *DBU* (3.64 g, 23.90 mmol) in 30 cm^3 CH_2Cl_2 was reacted under a N_2 atmosphere with octyl iodide (5.74 g, 23.90 mmol). The solution was stirred at reflux for 6.5 h and the solvent was evaporated *in vacuo*. Purification by chromatography on a silica gel column using $CH_2Cl_2/Et_2O = 8.5/1$ increasing the diethyl ether ratio afforded **3b** (1.92 g, 5.42 mmol, 68%). Oil; $R_f = 0.36$ (Et_2O/n-hexane = 75/25); IR (film): $\bar{\nu} = 3475$, 2955, 2927, 2856, 1742, 1649, 1457, 1436, 1378, 1241, 1128, 1050 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.42$ (d, $J = 3.1$ Hz, H-4), 6.05 (dd, $J = 3.2$, 0.8 Hz, H-5), 3.80 (t, $J = 6.3$ Hz, H-8), 3.73 (*s*, H-1^1), 2.84 (t, $J = 6.3$ Hz, H-7), 2.22 – 2.18 (m, H-2^1), 2.02 (br, OH), 1.29 – 1.15 (m, H-2^2 to H-2^7), 0.84 (t, $J = 6.9$ Hz, H-2^8) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 169.3$ (C=O), 156.2 (C-3), 148.3 (C-6), 109.9 (C-4), 107.2 (C-5), 61.0 (C-8), 52.8 (C-1^1), 59.3 (C-2), 34.3 (C(2^1), 31.5 (C-7), 31.7, 29.6, 29.2, 29.1, 24.6, 22.6 (C-2^2 to C-2^7), 14.0 (C-2^8), ppm; EI-MS: $m/z = 355$ (9, $[M+H]^+$), 354 (14, M^+), 324 (33, $[(M+H)\text{–}CH_3O]^+$), 296 (19), 295 (85, $[M-CH_3OCO]^+$), 277 (11), 266 (21), 265 (100), 264 (52), 263 (13), 236 (16), 235 (86), 233 (24), 217 (16), 211 (14), 210 (27), 205 (37), 183 (11), 180 (20), 179 (68), 166 (27), 165 (41), 163 (15), 161(12), 153 (22), 151 (13), 147 (15), 145 (10), 135 (15), 125 (15), 121 (19), 111 (64), 107 (22), 105 (16), 97 (11), 95 (18), 93 (14), 91 (19), 86 (11), 85 (14), 84 (16), 83 (26), 82 (10), 81 (43), 80 (37), 79 (42), 78 (15), 77 (26), 73 (38), 71 (15), 69 (23), 67 (21), 65 (15), 59 (28), 57 (12), 55 (24), 44 (30), 42 (32); ESI-HR-MS: m/z $[M+Na]^+$ = calcd 377.1935, found 377.1935, $[M+H]^+$ = calcd 355.2115, found 355.2115.

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