Regioselective Monoalkylation of Dimethyl Alkylidenesuccinates: Simple Approach to Dialkyl-Substituted Maleic Anhydrides Including Chaetomellic Acid A

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Abstract: Natural and nonnatural dialkylmaleic anhydrides were readily prepared from dimethyl alkylidenesuccinates by sodium hexamethyldisilazide-induced selective monoalkylation followed by base-catalyzed hydrolysis.

Key words: esters, alkylations, furans, heterocycles, maleic anhydrides

Maleic anhydrides and their derivatives are potentially useful as building blocks for the synthesis of a diverse range of structurally interesting, complex, bioactive, natural and nonnatural products or polymers with the tailored material characteristics.[1] Recently, large number of alkylated methyl-substituted maleic anhydrides has been isolated as bioactive natural products, and we surmise that these might be produced naturally by condensation of suitable long-chain acids with pyruvic acid (Figure 1).[2–12] Many well-designed product-specific syntheses of these natural products have been reported in recent times, including several from our research group.[13,14] In continuation of our studies on cyclic anhydride chemistry,[14,15] we felt that the selective alkylation of readily available dimethyl alkylidenesuccinates would provide a robust and general approach to the target compounds. With this perspective, we report our results on simple and efficient syntheses of natural and nonnatural dialkylmaleic anhydrides.

Dimethyl alkylidenesuccinates can be readily obtained by treatment of dimethyl maleate with trialkylphosphine and aldehydes[16] or with 1,8-diazabicyclo[5.4.0]undec-7-ene and nitroalkanes.[17] As shown in Table 1, the reactions of an in situ generated Wittig adduct from dimethyl maleate and tributylphosphine with variety of aldehydes at room temperature provided the desired (*E*)-dimethyl alkylidenesuccinates (**2a**–**g**) in 68–78% yields within 24–30 hours.

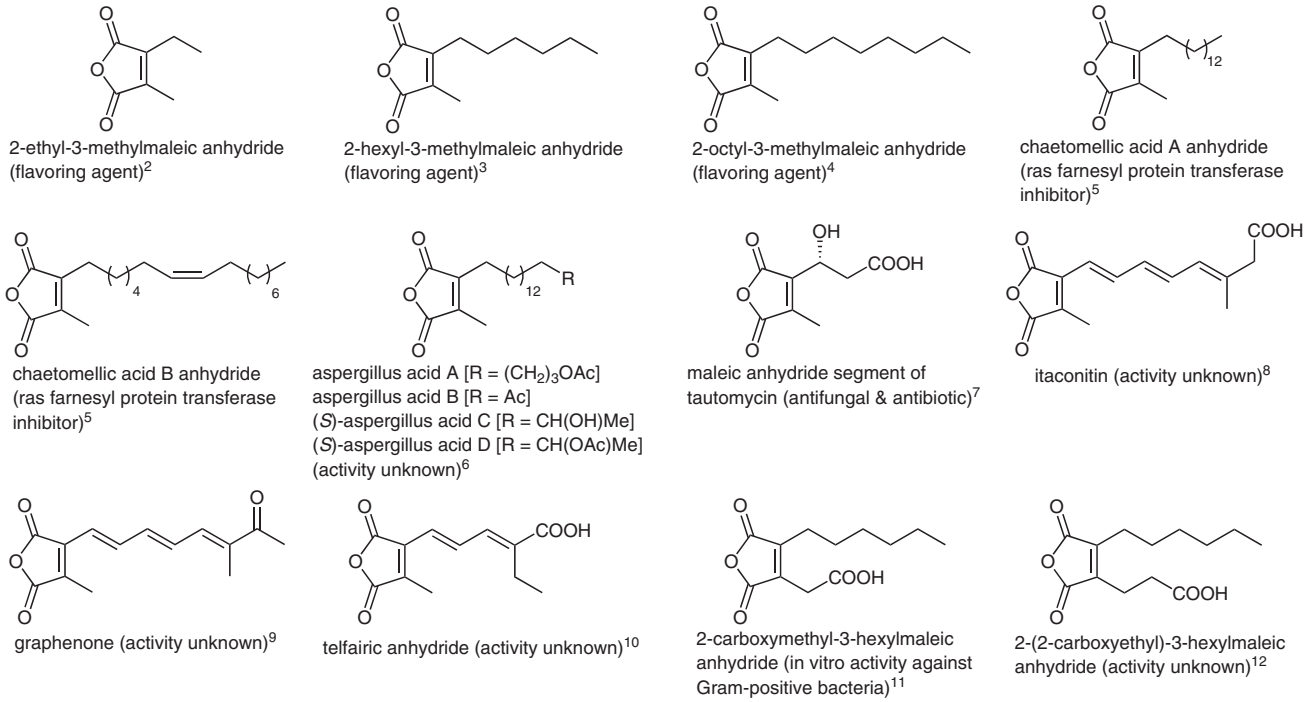

Figure 1 Naturally occurring dialkyl-substituted maleic anhydrides

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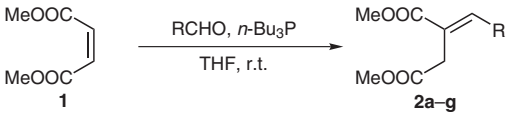
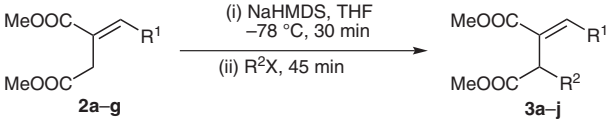
Table 1 Synthesis of Dimethyl (2*E*)-2-Alkylidenesuccinates



Entry	RCHO	Time (h)	Product	Yield (%)
1	$MeCH_2CHO$	24	**2a**	72
2	$Me(CH_2)_4CHO$	24	**2b**	78
3	$Me(CH_2)_8CHO$	24	**2c**	71
4	$Me(CH_2)_{12}CHO$	24	**2d**	68
5	$PMBO(CH_2)_2CHO$	30	**2e**	74
6	$PMBO(CH_2)_3CHO$	30	**2f**	72
7	PhCHO	24	**2g**	76

We devised a systematic plan for studying the base-catalyzed alkylation of our prospective precursors **2a**–**g**, with the aim of developing a new and simple approach to a diverse range of dialkylmaleic anhydrides. In principle, the action of a base on substrates **2a**–**f** should form reactive allylic carbanions at either the α-position of the ester unit or the γ-position of α,β-unsaturated systems with effective extended delocalization of the π-cloud. In our hands, the use of sodium hydride as the base for generating carbanions from substrates **2a** and **2d** resulted in excessive decomposition of the starting materials. The best results were obtained by using sodium hexamethyldisilazide (1.20 equiv) as the base in tetrahydrofuran as solvent at –78 °C; this produced the allylic carbanion regioselectively at the α-position of the ester unit of the substrates **2a**–**f**. As expected, substrate **2g** also formed the corresponding allylic carbanion on treatment with sodium hexamethyldisilazide. As summarized in Table 2, the carbanionic species generated from compounds **2a**–**g** reacted smoothly with methyl iodide, allyl bromide, benzyl bromide, or methyl bromoacetate to give the required monoalkylated products **3a**–**j** in 79–93% yields. Unfortunately, however, the allylic carbanionic species generated from substrates **3b** and **3h** failed to react with a secondary halide (2-bromopropane) under similar conditions.

Table 2 Regioselective Monoalkylation of Dimethyl (2*E*)-2-Alkylidenesuccinates

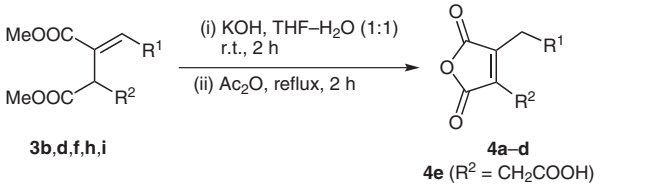


Entry	R^1	R^2X	Product	Yield (%)
1	Et	MeI	**3a**	93
2	$(CH_2)_4Me$	MeI	**3b**	91
3	$(CH_2)_8Me$	MeI	**3c**	85
4	$(CH_2)_{12}Me$	MeI	**3d**	88
5	$(CH_2)_2OPMB$	MeI	**3e**	85
6	$(CH_2)_3OPMB$	MeI	**3f**	81
7	$(CH_2)_4Me$	$CH_2=CHCH_2Br$	**3g**	82
8	Ph	BnBr	**3h**	92
9	$(CH_2)_4Me$	MeO_2CCH_2Br	**3i**	86
10	$(CH_2)_8Me$	MeO_2CCH_2Br	**3j**	79

The base-catalyzed hydrolysis of two different ester units in compounds **3b**, **3d**, **3f**, and **3h** to give the corresponding dicarboxylic acids, followed by acetic anhydride-induced ring closure and concomitant exocyclic to endocyclic carbon–carbon double-bond isomerization gave the corresponding dialkylated maleic anhydrides **4a**–**d** in 73–91% yields (Table 3); product **4d** is a precursor of maculalactones A–C.[18] Base-catalyzed hydrolysis of triester **3i** followed by acidification with hydrochloric acid gave the natural product **4e** in 65% yield through isomerization of the carbon–carbon double bond followed by instantaneous dehydrative ring closure. The analytical and spectral data obtained for all the above-mentioned natural products were in complete agreement with the reported data.[3,5,11,14a,18d] More distinctively, starting from dimethyl maleate (**1**), the naturally occurring ras FPTase inhibitor chaetomellic acid A anhydride (**4b**) was obtained in three straightforward steps with 53% overall yield.

In summary, we have demonstrated a new general protocol for the synthesis of natural and unnatural symmetrical/unsymmetrical dialkyl-substituted maleic anhydrides through regioselective generation of carbanions from dimethyl alkylidenesuccinates, followed by selective monocondensation with primary alkyl halides, allyl halides, benzyl halides, or activated alkyl halides, and subsequent base-catalyzed hydrolysis and ring closure with the exocyclic to endocyclic carbon–carbon double-bond rearrangement. We feel that the present approach to dialkylmaleic anhydrides is noteworthy and will be useful for producing a focused library of derivatives and congeners for studies of structure–activity relationships.

Table 3 Synthesis of Natural and Nonnatural Dialkylmaleic Anhydrides



Entry	R^1	R^2	Product	Yield (%)
1	$(CH_2)_4Me$	Me	**4a**	83
2	$(CH_2)_{12}Me$	Me	**4b**	89
3	$(CH_2)_3OPMB$	Me	**4c**	73
4	Ph	Bn	**4d**	91
5[a]	$(CH_2)_4Me$	CH_2CO_2Me	**4e**	65

[a] Reaction conditions: (i) aq KOH, THF–MeOH (1:2), reflux, 2 h; (ii) H^+/HCl.

The ^{1}H NMR spectra were recorded on Bruker NMR spectrometers operating at 200, 400 and 500 MHz, respectively, with TMS as an internal standard. The ^{13}C NMR spectra were recorded on the same instruments operating at 50, 100 and 125 MHz. The IR spectra were recorded on a Shimadzu FT-IR spectrometer. Column chromatographic separations were carried out on silica gel (60–120 mesh). Commercially available dimethyl maleate, NaHMDS, and *n*-Bu_3P were used.

Dimethyl (2*E*)-2-Propylidenesuccinate (2a)[17d]; Typical Procedure

n-Bu_3P (1.30 mL, 5.21 mmol) was slowly added by syringe to a stirred soln of dimethyl maleate (**1**, 0.50 g, 3.47 mmol) and EtCHO (0.20 g, 3.47 mmol) in THF (1 mL) at r.t. under N_2. The mixture was stirred for 24 h and then diluted with CH_2Cl_2 (15 mL). 35% aq H_2O_2 (5 mL) was added to oxidize unreacted *n*-Bu_3P, and the mixture was stirred for additional 30 min. The organic layer was washed with H_2O (10 mL), sat. aq $NaHCO_3$ (10 mL), and brine (10 mL) then dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography [silica gel, PE–EtOAc (85:15)] to give a thick oil; yield: 0.47 g (72%).

IR (neat): 1742, 1723, 1653 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.03 (t, *J* = 8 Hz, 3 H), 2.17 (quint, *J* = 8 Hz, 2 H), 3.32 (s, 2 H), 3.65 (s, 3 H), 3.71 (s, 3 H), 6.93 (t, *J* = 4 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 12.8, 22.2, 31.8, 51.8, 51.9, 124.6, 147.4, 167.3, 171.2.

Dimethyl (2*E*)-2-Hexylidenesuccinate (2b)[17b]

IR (neat): 1733, 1715, 1657 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.89 (t, *J* = 8 Hz, 3 H), 1.25–1.37 (m, 4 H), 1.46 (quint, *J* = 8 Hz, 2 H), 2.19 (q, *J* = 8 Hz, 2 H), 3.36 (s, 2 H), 3.68 (s, 3 H), 3.75 (s, 3 H), 6.98 (t, *J* = 8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.8, 22.3, 28.0, 28.8, 31.3, 32.0, 51.8, 51.9, 125.1, 146.1, 167.3, 171.2.

Dimethyl (2*E*)-2-Decylidenesuccinate (2c)

IR ($CHCl_3$): 1736, 1718, 1655 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (t, *J* = 8 Hz, 3 H), 1.26 (br s, 12 H), 1.45 (quint, *J* = 8 Hz, 2 H), 2.18 (q, *J* = 8 Hz, 2 H), 3.36 (s, 2 H), 3.68 (s, 3 H), 3.75 (s, 3 H), 6.98 (t, *J* = 8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.0, 22.6, 28.4, 28.9, 29.2, 29.25, 29.34, 29.4, 31.8, 32.0, 51.87, 51.91, 125.2, 146.2, 167.4, 171.3.

Anal. Calcd for $C_{16}H_{28}O_4$: C, 67.57; H, 9.92. Found: C, 67.19; H, 9.65.

Dimethyl (2*E*)-2-Tetradecylidenesuccinate (2d)

IR ($CHCl_3$): 1735, 1718, 1654 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (t, *J* = 6 Hz, 3 H), 1.26 (br s, 20 H), 1.45 (quint, *J* = 8 Hz, 2 H), 2.18 (q, *J* = 8 Hz, 2 H), 3.36 (s, 2 H), 3.69 (s, 3 H), 3.75 (s, 3 H), 6.98 (t, *J* = 8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.0, 22.6, 28.4, 28.9, 29.26, 29.29, 29.34, 29.5, 29.6 (4 C), 31.9, 32.0, 51.87, 51.91, 125.1, 146.2, 167.4, 171.3.

Anal. Calcd for $C_{20}H_{36}O_4$: C, 70.55; H, 10.66. Found: C, 70.27; H, 10.46.

Dimethyl (2*E*)-2-{3-[(4-Methoxybenzyl)oxy]propylidene}succinate (2e)

IR ($CHCl_3$): 1740, 1714, 1657 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.48 (q, *J* = 8 Hz, 2 H), 3.37 (s, 2 H), 3.54 (t, *J* = 6 Hz, 2 H), 3.66 (s, 3 H), 3.74 (s, 3 H), 3.80 (s, 3 H), 4.44 (s, 2 H), 6.80–6.95 (m, 2 H), 6.97 (t, *J* = 8 Hz, 1 H), 7.20–7.30 (m, 2 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 29.6, 32.2, 52.0 (2 C), 55.2, 67.9, 72.7, 113.7, 126.8, 129.2, 130.1, 142.3, 159.2, 167.1, 171.1.

Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.46; H, 7.16.

Dimethyl (2*E*)-2-{4-[(4-Methoxybenzyl)oxy]butylidene}succinate (2f)

IR ($CHCl_3$): 1740, 1712, 1653 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.76 (quint, *J* = 8 Hz, 2 H), 2.30 (q, *J* = 8 Hz, 2 H), 3.37 (s, 2 H), 3.46 (t, *J* = 8 Hz, 2 H), 3.68 (s, 3 H), 3.75 (s, 3 H), 3.81 (s, 3 H), 4.42 (s, 2 H), 6.80–6.95 (m, 2 H), 6.97 (t, *J* = 8 Hz, 1 H), 7.20–7.32 (m, 2 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.5, 28.3, 31.9, 51.83, 51.85, 55.1, 68.7, 72.5, 113.6, 125.7, 129.1, 130.3, 145.2, 159.0, 167.2, 171.2.

Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 63.92; H, 7.27.

Dimethyl (2*E*)-2-Benzylidenesuccinate (2g)[16b]

IR ($CHCl_3$): 1733, 1715, 1641 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.55 (s, 2 H), 3.74 (s, 3 H), 3.84 (s, 3 H), 7.30–7.50 (m, 5 H), 7.92 (s, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 33.3, 52.0, 52.1, 125.7, 128.5, 128.8, 128.9, 134.8, 142.0, 167.6, 171.5.

Dimethyl (3*E*)-2-Methyl-3-propylidenesuccinate (3a); Typical Procedure

A 1 M soln of NaHMDS in THF (1.30 mL, 1.30 mmol) was added to a stirred soln of alkylidenesuccinate **2a** (0.20 g, 1.08 mmol) in THF (5 mL) at –78 °C, and reaction mixture was stirred at –78 °C for 30 min. MeI (0.07 mL, 1.08 mmol) was then added dropwise at –78 °C, and the mixture was stirred at –78 °C for 45 min. The reaction was quenched with sat. aq NH_4Cl (2 mL), and the mixture was concentrated in vacuo. The residue was dissolved in EtOAc (20 mL), and the organic layer was washed with H_2O (10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography [silica gel, PE–EtOAc (85:15)] to give a thick oil; yield: 0.20 g (93%).

IR ($CHCl_3$): 1746, 1715, 1643 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.07 (t, *J* = 8 Hz, 3 H), 1.32 (d, *J* = 8 Hz, 3 H), 2.20 (d quint, *J* = 8, 4 Hz, 2 H), 3.59 (q, *J* = 8 Hz, 1 H), 3.65 (s, 3 H), 3.71 (s, 3 H), 6.83 (t, *J* = 8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 13.0, 15.8, 21.8, 37.5, 51.7, 51.9, 131.5, 145.5, 166.9, 174.1.

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.37; H, 7.69.

Dimethyl (2*E*)-2-Hexylidene-3-methylsuccinate (3b)[15b]

IR (neat): 1742, 1730 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.85 (t, *J* = 8 Hz, 3 H), 1.20–1.35 (m, 4 H), 1.29 (d, *J* = 6 Hz, 3 H), 1.43 (quint, *J* = 6 Hz, 2 H), 2.14 (dq, *J* = 8, 4 Hz, 2 H), 3.56 (q, *J* = 6 Hz, 1 H), 3.61 (s, 3 H), 3.67 (s, 3 H), 6.80 (t, *J* = 8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 13.8, 15.7, 22.3, 28.1, 28.4, 31.4, 37.5, 51.5, 51.7, 131.9, 144.1, 166.8, 174.0.

Dimethyl (2*E*)-2-Decylidene-3-methylsuccinate (3c)

IR ($CHCl_3$): 1734, 1726, 1647 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (t, *J* = 6 Hz, 3 H), 1.26 (br s, 12 H), 1.34 (d, *J* = 6 Hz, 3 H), 1.46 (quint, *J* = 6 Hz, 2 H), 2.19 (dq,

J = 7, 4 Hz, 2 H), 3.60 (q, *J* = 8 Hz, 1 H), 3.66 (s, 3 H), 3.72 (s, 3 H), 6.85 (t, *J* = 8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.0, 15.8, 22.6, 28.51, 28.53, 29.2, 29.3, 29.36, 29.43, 31.8, 37.6, 51.7, 51.9, 131.9, 144.3, 166.9, 174.2.

Anal. Calcd for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13. Found: C, 68.13; H, 9.81.

Dimethyl (3*E*)-2-Methyl-3-tetradecylidenesuccinate (3d)[15b]
IR ($CHCl_3$): 1739, 1712, 1646 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (t, *J* = 6 Hz, 3 H), 1.26 (br s, 20 H), 1.34 (d, *J* = 8 Hz, 3 H), 1.47 (quint, *J* = 6 Hz, 2 H), 2.19 (dq, *J* = 7, 4 Hz, 2 H), 3.61 (q, *J* = 8 Hz, 1 H), 3.66 (s, 3 H), 3.73 (s, 3 H), 6.86 (t, *J* = 8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.1, 15.9, 22.7, 28.6, 29.3, 29.36, 29.40, 29.5, 29.6 (5 C), 31.9, 37.6, 51.8, 52.0, 131.9, 144.4, 166.9, 174.2.

Dimethyl (2*E*)-2-{3-[(4-Methoxybenzyl)oxy]propylidene}-3-methylsuccinate (3e)
IR (neat): 1740, 1716, 1648 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.34 (d, *J* = 6 Hz, 3 H), 2.50 (dq, *J* = 8, 2 Hz, 2 H), 3.55 (t, *J* = 6 Hz, 2 H), 3.60 (q, *J* = 6 Hz, 1 H), 3.64 (s, 3 H), 3.73 (s, 3 H), 3.81 (s, 3 H), 4.46 (s, 2 H), 6.86–6.93 (m, 3 H), 7.21–7.30 (m, 2 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 15.7, 29.2, 37.8, 51.7, 51.9, 55.2, 68.0, 72.7, 113.7, 129.2, 130.1, 133.5, 140.3, 159.2, 166.6, 173.9.

Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 63.87; H, 6.94.

Dimethyl (2*E*)-2-{4-[(4-Methoxybenzyl)oxy]butylidene}-3-methylsuccinate (3f)
IR ($CHCl_3$): 1735, 1715, 1647 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.34 (d, *J* = 6 Hz, 3 H), 1.77 (quint, *J* = 8 Hz, 2 H), 2.18–2.42 (m, 2 H), 3.48 (t, *J* = 6 Hz, 2 H), 3.62 (q, *J* = 6 Hz, 1 H), 3.66 (s, 3 H), 3.73 (s, 3 H), 3.81 (s, 3 H), 4.42 (s, 2 H), 6.80–6.93 (m, 3 H), 7.21–7.30 (m, 2 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 15.8, 25.3, 28.6, 37.6, 51.7, 51.9, 55.2, 68.9, 72.6, 113.8, 129.2, 130.4, 132.5, 143.4, 159.2, 166.8, 174.1.

Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 65.43; H, 7.90.

Dimethyl (3*E*)-2-Allyl-3-hexylidenesuccinate (3g)
IR ($CHCl_3$): 1743, 1716, 1644 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.90 (t, *J* = 10 Hz, 3 H), 1.26–1.36 (m, 4 H), 1.77 (quint, *J* = 10 Hz, 2 H), 2.10–2.25 (m, 2 H), 2.36–2.45 (m, 1 H), 2.81–2.88 (m, 1 H), 3.57 (dd, *J* = 10, 5 Hz, 1 H), 3.66 (s, 3 H), 3.72 (s, 3 H), 4.98 (dd, *J* = 10, 2 Hz, 1 H), 5.03 (dd, *J* = 15, 5 Hz, 1 H), 5.66–5.76 (m, 1 H), 6.94 (t, *J* = 10 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 13.9, 22.4, 28.2, 28.8, 31.5, 34.4, 43.1, 51.8, 52.0, 116.8, 129.5, 135.8, 145.8, 166.9, 173.2.

Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 66.83; H, 9.40.

Dimethyl (3*E*)-2-Benzyl-3-benzylidenesuccinate (3h)[15g]
IR ($CHCl_3$): 1735, 1715, 1637 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.98 (dd, *J* = 14, 10 Hz, 1 H), 3.41 (dd, *J* = 14, 6 Hz, 1 H), 3.73 (s, 3 H), 3.84 (s, 3 H), 4.00 (dd, *J* = 10, 6 Hz, 1 H), 6.80–6.92 (m, 4 H), 7.05–7.17 (m, 2 H), 7.18–7.31 (m, 4 H), 7.75 (s, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 35.9, 45.2, 52.0, 52.2, 126.1, 128.06, 128.11, 128.15, 128.19, 129.1, 130.4, 135.0, 138.9, 142.9, 167.0, 173.1.

Trimethyl (3*E*)-Non-3-ene-1,2,3-tricarboxylate (3i)[17a]
IR ($CHCl_3$): 1735, 1650 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.89 (t, *J* = 6 Hz, 3 H), 1.20–1.40 (m, 4 H), 1.47 (quint, *J* = 6 Hz, 2 H), 2.14–2.40 (m, 2 H), 2.44 (dd, *J* = 12, 6 Hz, 1 H), 3.21 (dd, *J* = 16, 8 Hz, 1 H), 3.66 (s, 3 H), 3.69 (s, 3 H), 3.73 (s, 3 H), 4.13 (dd, *J* = 8, 6 Hz, 1 H), 6.95 (t, *J* = 8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 13.9, 22.4, 28.2, 28.7, 31.5, 35.2, 39.4, 51.8, 51.9, 52.3, 129.2, 146.8, 166.6, 172.4, 172.6.

Trimethyl (3*E*)-Tridec-3-ene-1,2,3-tricarboxylate (3j)
IR ($CHCl_3$): 1735, 1646 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (t, *J* = 8 Hz, 3 H), 1.26 (br s, 12 H), 1.46 (quint, *J* = 8 Hz, 2 H), 2.13–2.40 (m, 2 H), 2.44 (dd, *J* = 12, 6 Hz, 1 H), 3.21 (dd, *J* = 18, 8 Hz, 1 H), 3.66 (s, 3 H), 3.69 (s, 3 H), 3.72 (s, 3 H), 4.12 (dd, *J* = 8, 8 Hz, 1 H), 6.95 (t, *J* = 8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.0, 22.6, 28.5, 28.7, 29.2, 29.3, 29.35, 29.43, 31.8, 35.2, 39.4, 51.75, 51.78, 52.2, 129.2, 146.7, 166.5, 172.4, 172.5.

Anal. Calcd for $C_{19}H_{32}O_6$: C, 64.02; H, 9.05. Found: C, 63.64; H, 8.94.

3-Hexyl-4-methylfuran-2,5-dione (4a);[14i] Typical Procedure
20% aq KOH (5 mL) was added to a stirred soln of diester **3b** (100 mg, 0.42 mmol) in THF (5 mL), and the mixture was stirred at r.t. for 2 h. The solvent was removed in vacuo and the residue was acidified to pH 2 with 2 M HCl. The mixture was extracted with Et_2O (3 × 10 mL) and the organic layer was washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. Ac_2O (5 mL) was added to the residue and the mixture was refluxed for 2 h. The mixture was then concentrated in vacuum and the residue was purified by column chromatography [silica gel, PE–EtOAc (8:2)] to give a thick oil; yield: 68 mg (83%).

IR (neat): 1765, 1655 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.90 (m, 3 H), 1.15–1.45 (m, 6 H), 1.45–1.70 (m, 2 H), 2.08 (s, 3 H), 2.46 (t, *J* = 7 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 9.4, 12.0, 22.4, 24.4, 27.6, 29.0, 31.3, 140.5, 144.7, 165.8, 166.4.

3-Methyl-4-tetradecylfuran-2,5-dione (4b; Chaetomellic Acid A Anhydride)[14i]
IR (neat): 1770, 1680 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.15–1.45 (br s, 22 H), 1.46–1.69 (m, 2 H), 2.07 (s, 3 H), 2.45 (t, *J* = 7 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 9.6, 14.3, 22.9, 24.6, 27.7, 29.0–31.0 (9 C), 32.1, 140.6, 144.9, 166.0, 166.4.

3-{4-[(4-Methoxybenzyl)oxy]butyl}-4-methylfuran-2,5-dione (4c)
IR ($CHCl_3$): 1822, 1764, 1613 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.55–1.80 (m, 4 H), 2.05 (s, 3 H), 2.48 (t, *J* = 8 Hz, 2 H), 3.46 (t, *J* = 6 Hz, 2 H), 3.81 (s, 3 H), 4.43 (s, 2 H), 6.89 (d, *J* = 10 Hz, 2 H), 7.26 (d, *J* = 12 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 9.5, 24.1, 24.4, 29.4, 55.2, 69.1, 72.6, 113.7, 129.3, 130.3, 140.7, 144.3, 159.1, 165.8, 166.2.

Anal. Calcd for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 67.37; H, 6.96.

3,4-Dibenzylfuran-2,5-dione (4d)[18d]
IR ($CHCl_3$): 1769 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 3.78 (s, 4 H), 7.05–7.20 (m, 4 H), 7.20–7.35 (m, 6 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 29.9, 127.1, 128.6, 128.8, 134.9, 142.7, 165.6.

2-(4-Hexyl-2,5-dioxo-2,5-dihydrofuran-3-yl)acetic Acid (4e)[14c]
20% aq KOH (5 mL) was added to a stirred soln of triester **3i** (100 mg, 0.34 mmol) in 1:2 THF–MeOH (5 mL) and the mixture was stirred and refluxed for 2 h. The mixture was then concentrated in vacuo and the residue was acidified to pH 2 with 2 M HCl. The mixture was extracted with Et_2O (3 × 10 mL) and the organic layer was washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography [silica gel, PE–EtOAc (7:3)] to give a thick oil; yield: 52 mg (65%).

IR (neat): 1820, 1771, 1718, 1216, 925, 670 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 0.89 (t, *J* = 8 Hz, 3 H), 1.15–1.45 (m, 6 H), 1.60 (quint, *J* = 8 Hz, 2 H), 2.50 (t, *J* = 8 Hz, 2 H), 3.57 (s, 2 H), 8.60 (br s, 1 H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 13.9, 22.4, 24.9, 27.5, 29.1 (2 C), 31.3, 135.5, 148.1, 165.1 (2 C), 173.0.

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