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A facile access to natural and unnatural dialkylsubstituted maleic anhydrides☆

Anirban Kar and Narshinha P. Argade*

Division of Organic Chemistry (Synthesis), National Chemical Laboratory, Pune 411 008, India

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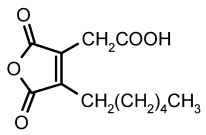
Dedicated to Dr B. G. Hazra, OCS, NCL, Pune

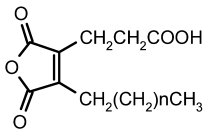
Abstract—A facile new route to the potential building blocks 2-bromomethyl-3-alkylmaleic anhydrides **15a/b** for the synthesis of natural and unnatural dialkylsubstituted maleic anhydrides has been demonstrated, starting from dimethyl citraconate (**9**) via NBS-bromination, S_N2' Grignard coupling reactions, hydrolysis, molecular bromine addition and dehydrative ring closure reactions pathway with 49–51% overall yield in 5-steps. Chemoselective allylic substitution of bromoatom in **15a/b** with Grignard reagents has been described to obtain the unsymmetrical maleic anhydride **16** and symmetrically dialkylsubstituted maleic anhydrides **25a/b** in 55% yield. The naturally occurring 2-carboxymethyl-3-hexylmaleic anhydride (**1**) has been synthesized from **16** via esterification, ozonolysis and an oxidation route. The synthesis of two naturally occurring 2-(β-carboxyethyl)-3-alkylmaleic anhydrides **2a/b** have been completed via a chemoselective diethylmalonate coupling reaction followed by acid induced hydrolysis. In our hands the S_N2 or S_N2' coupling of Grignard reagent with **21** to obtain **1** and Reformatsky reaction with **15a/b** to obtain **2c/d** met with failure.

1. Introduction

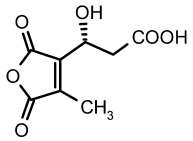
During the past decade several structurally interesting compounds with dialkylsubstituted maleic anhydride moieties have been isolated as bioactive natural products and synthesized in view of their promising bioactivities.[1–3]



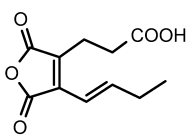
2-Carboxymethyl-3-hexyl-maleic anhydride (1)[4]



2-(ß-Carboxyethyl)-3-alkylmaleic anhydrides (2a/b, n = 4/6)[5]

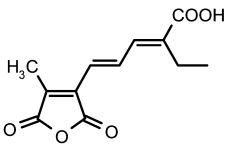


Maleic anhydride segment of Tautomycin (3)[6]

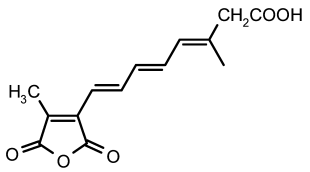


2-(*E*)-But-1-enyl-3-(ß-Carboxyethyl) -maleic anhydride (4)[7]

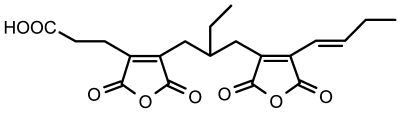
In Figure 1 we have listed the recently isolated bioactive naturally occurring dialkylsubstituted maleic anhydrides with free carboxylic group,[4–9] viz 2-carboxymethyl-3-hexylmaleic anhydride (**1**),[4] 2-(β-carboxyethyl)-3-hexylmaleic anhydride (**2a**),[5] 2-(β-carboxyethyl)-3-octylmaleic anhydride (**2b**),[5] tautomycin part structure (**3**),[6] (*E*)-2-but-1-enyl-3-(β-carboxyethyl)maleic anhydride (**4**),[7] telfairic



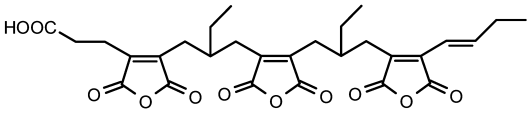
Telfairic Anhydride (5)[8]



Itaconitin (6)[9]



Cordyanhydride A (7)[7]



Cordyanhydride B (8)[7]

Figure 1.

☆ NCL Communication No. 6639. For preliminary communication see Ref. 11.

Keywords: Grignard reagent; maleic anhydrides; NBS-bromination.

* Corresponding author. Tel./fax: +91-20-5893153;
e-mail: argade@dalton.ncl.res.in

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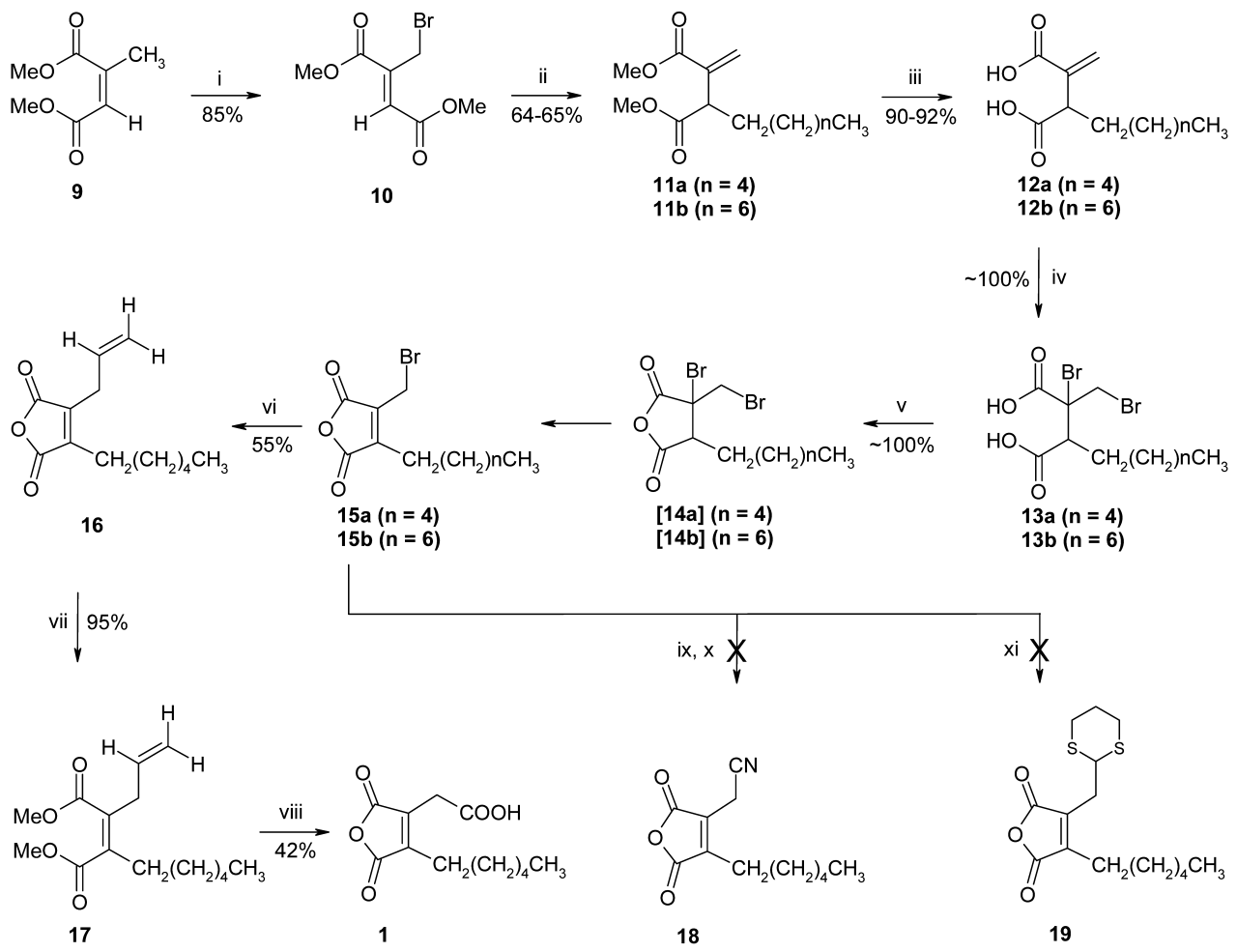
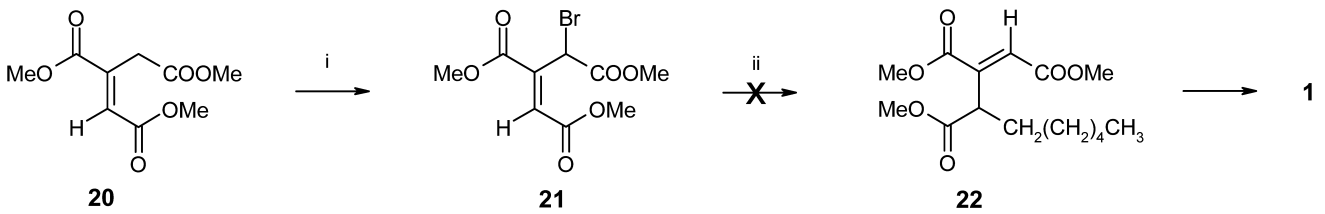
anhydride (**5**),[8] itaconitin (**6**),[9] cordyanhydride A (**7**)[7] and cordyanhydride B (**8**).[7] The anhydride **1** has been isolated[4] as a novel metabolite of the *Aspergillus* FH-X-213 from an apple. In 1994, Soda et al. reported the biotransformation of stearic acid with a microbial strain isolated from soil, *Pseudomonas cepacica* A-1419, to produce two new maleic anhydride derivatives **2a** and **2b**.[5] Very recently, the first general synthetic route to these diverse dialkylsubstituted maleic anhydride analogs was demonstrated[1] by Baldwin et al. using a versatile copper mediated tandem vicinal difunctionalization of dimethyl acetylenedicarboxylate. In our continuing interest[10] to provide facile synthetic routes to natural and unnatural alkylsubstituted maleic anhydrides, we herein report[11] another general approach to this type of compounds via the chemoselective S_N2/S_N2' coupling of Grignard reagents/diethylmalonate with dimethyl bromomethylfumarate (**10**)/2-bromomethyl-3-alkylmaleic anhydrides **15a/b** (Schemes 1, 3 and 4).

2. Results and discussion

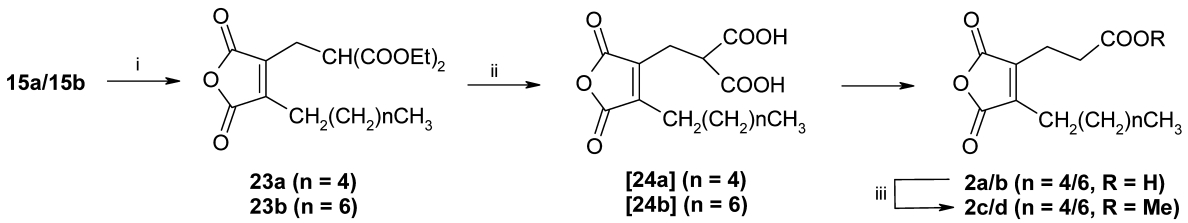
We planned the preparation of 2-(bromomethyl)-3-hexylmaleic anhydride (**15a**) as a suitable starting material for the synthesis of the natural products 2-carboxymethyl-3-hexylmaleic anhydride (**1**) and 2-carboxyethyl-3-hexylmaleic anhydride (**2a**). Several methods for the synthesis of alkylmethylmaleic anhydrides have been reported,[10] but the NBS-bromination of these anhydrides is known to take place at the allylic methylene carbon[12] and hence we thought of preparing **15a** via a chemoselective S_N2' coupling reaction of a Grignard reagent with **10**.[13] The dimethyl methylmaleate (**9**) on NBS-bromination gave dimethyl bromomethylfumarate (**10**) in 85% yield and both allylic bromination and isomerization of the carbon–carbon double bond from maleate to fumarate took place in one pot (Scheme 1). The freshly prepared hexylmagnesium bromide was chemoselectively coupled with **10** in an S_N2' fashion to yield the diester **11a** in 64% yield. The LiOH induced hydrolysis of **11a** followed by bromination of the diacid **12a** with molecular bromine gave a mixture of all four possible stereoisomers of **13a** in nearly equal proportions with ~100% yield. The diacid **13a** in refluxing acetic anhydride yielded the desired (bromomethyl)-hexylmaleic anhydride (**15a**) in quantitative yield and both the dehydrative ring closure of diacid **13a** to succinic



Scheme 1. *Reagents, conditions and yields*: (i) NBS (1.5 equiv.), AIBN, CCl_4, reflux, 12 h (85%); (ii) $CH_3(CH_2)_nCH_2MgBr$ (1.5 equiv., n=4/6), Et_2O, HMPA, −20°C, 0.5 h (64–65%); (iii)) LiOH (10 equiv.), THF+H_2O (3:1), room temperature, 18 h (90–92%); (iv) Br_2 (1.5 equiv.), CCl_4, room temperature, 6 h (~100%); (v) Ac_2O, reflux, 1.5 h (~100%); (vi) C_2H_3MgBr (5 equiv.), CuI (0.1 equiv.), Et_2O, HMPA, −5 to 0°C (55%); (vii) CH_2N_2, Et_2O, MeOH, 0°C, 3 h (95%); (viii) O_3, $(CH_3)_2CO$, −78°C, 3 min then $Na_2Cr_2O_7{\cdot}H_2O$, H_2SO_4, H_2O, Et_2O, 0°C, 3 h then 1 M aq. NaOH then 1 M aq. HCl, (42%); (ix) NaCN (1.1 equiv.), MeOH, room temperature, 2 h (0%); (x) CuCN (5 equiv.), MeOH, reflux, 8 h (0%); (xi) 1,3-dithiane (1.1 equiv.), n-BuLi (1.2 equiv.), THF, HMPA, 6 h (0%).



Scheme 2. *Reagents, conditions and yields*: (i) NBS (10 equiv.), AIBN, CCl_4, reflux, 32 h (85%); (ii) $C_6H_{13}MgBr$ (1.5 equiv.), Et_2O, HMPA, −20°C, 0.5 h (0%).



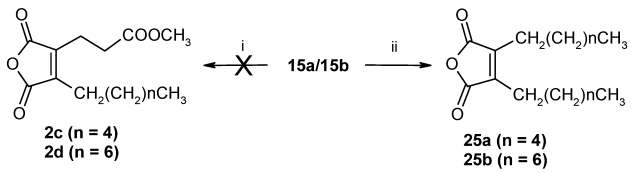
Scheme 3. *Reagents, conditions and yields*: (i) (a) diethyl malonate (1.1 equiv.), NaH (1.1 equiv.), C_6H_6, room temperature, 8 h; (b) H^+/HCl (72–74%) (ii) AcOH+HCl (1:1), reflux, 12 h (95–96%); (iii) CH_2N_2, Et_2O, 0°C, 3 h (95%).

anhydride derivative **14a** and the dehydrobromination took place in one pot. Similarly, the coupling reaction of **10** with octylmagnesium bromide followed by repetition of above sequence of reactions furnished **15b**. Highly chemoselective S_N2 displacement of allylic bromoatom in **15a** with vinylmagnesium bromide in the presence of HMPA and a copper catalyst gave the desired anhydride **16** in 55% yield.[10b] The anhydride **16** on treatment with diazomethane gave the diester **17** in 95% yield. The diester **17** on ozonolysis followed by an in situ oxidation and hydrolysis gave[1] the natural product carboxymethylhexylmaleic anhydride (**1**) in 42% yield.

Starting from diester **9**, the final product **1** was obtained in 8-steps with 11% overall yield. The analytical and spectroscopic data obtained for **1** were in complete agreement with reported data.[4] We investigated the displacement of allylic bromide **15a** with sodium cyanide, copper cyanide[14] and 2-lithio-1,3-dithiane[15] to obtain **18** and **19**, but all our attempts met with failure and always ended with the formation of complex reaction mixtures and/or polymeric gums. We felt that the S_N2 or S_N2' coupling of a hexylmagnesium bromide with bromotriester **21** will provide an easy access to **1** via **22** (Scheme 2). The triester **20**[16] on NBS-bromination gave **21** with 85% yield. In our hands, all our attempts to chemoselectively couple Grignard reagents with **21** met with failure and complex reaction mixtures were formed. We feel that **21** is prone to polymerization reactions and hence we were unable to complete the short synthesis of **1**.

Starting from **15a/b**, we planned for the synthesis of natural products **2a/b**. The highly chemoselective diethyl malonate coupling with **15a/b** in benzene using sodium hydride as base furnished the anhydride derivatives **23a/b** in 72–74% yield (Scheme 3). Acid catalysed hydrolysis of these diesters **23a/b** and an in situ decarboxylation of the intermediate *gem*-dicarboxylic acids gave the natural products **2a/b** in 95–96% yield. The overall yield of **2a/b** in 7-steps was 34–36%. The analytical and spectroscopic data obtained for **2a/b** were in complete agreement with reported data. The anhydrides **2a/b** were also characterized further as the methyl esters **2c/d**.

The chemoselective coupling of freshly prepared pentylmagnesium bromide with **15a** and heptylmagnesium bromide with **15b** in the presence of HMPA and a copper catalyst gave the desired dihexylmaleic anhydride (**25a**) and dioctylmaleic anhydride (**25b**) in 55% yield, thus providing a new simple route to symmetrical and unsymmetrical dialkylsubstituted maleic anhydrides (Scheme 4). In our hands, all attempts to obtain **2c/d** via a chemoselective Reformatsky reaction with **15a/b** in the presence/absence of HMPA met with failure and we recovered starting material only.



Scheme 4. *Reagents, conditions and yields*: (i) $BrCH_2COOMe$ (1.5 equiv.), Zn (2 equiv.), THF, room temperature/reflux, 12 h (0%); (ii) $CH_3(CH_2)_n$-CH_2MgBr (5 equiv, n=3/5), CuI (0.1 equiv.), Et_2O, HMPA, −5 to 0°C (55–56%).

3. Conclusion

In summary, we have demonstrated a facile route to natural products 2-carboxymethyl-3-hexylmaleic anhydride (**1**) [8-steps (11%)], 2-(β-carboxyethyl)-3-alkylmaleic anhydrides **2a/b** [7-steps (34–36%)], and symmetrical/unsymmetrical dialkylsubstituted maleic anhydrides **16**, **25a/b** [6-steps (27–28%)] via a highly chemoselective S_N2' reaction with dimethyl bromomethylfumarate (**10**) and S_N2 reaction with 2-bromomethyl-3-alkylmaleic anhydrides **15a/b** as key steps. We feel that the bromoanhydrides **15a/b** and their analogs will be a potential building blocks for synthesis of several important natural/synthetic products bearing maleic anhydride moieties.

4. Experimental

4.1. General

Melting points are uncorrected. Column chromatographic separations were carried out on silica gel (60–120 mesh). Commercially available citraconic anhydride, alkyl bromides, magnesium turnings, HMPA, CuI, lithium hydroxide, diethyl malonate, NaH and acetic anhydride were used.

4.1.1. Dimethyl bromomethylfumarate (10). A mixture of **9** (9.48 g, 60 mmol), *N*-bromosuccinimide (16.02 g, 90 mmol) and catalytic amount of AIBN (200 mg, 1.22 mmol) in carbon tetrachloride (300 mL) was gently refluxed for 12 h in a 500 mL round bottom flask. The mixture was left overnight at room temperature and then filtered. The residue was washed with CCl_4 (25 mL×2); the combined organic layer was washed with water (100 mL), brine (50 mL) and then dried over Na_2SO_4. The organic layer was concentrated in vacuo to furnish thick yellow oil, which was purified by chromatography on silica gel column using petroleum ether/ethyl acetate (9:1) to give the desired bromo diester **10**: 12.10 g (85% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.83 (s, 3H), 3.88 (s, 3H), 4.72 (s, 2H), 6.83 (s, 1H); ^{1}H NMR (CCl_4, 200 MHz) δ 3.87 (s, 3H), 3.93 (s, 3H), 4.70 (s, 2H), 6.79 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.1, 51.7, 52.5, 127.9, 142.4, 164.5, 164.7; MS (*m/e*) 238 (2%), 236 (2%), 206 (78%), 204 (79%), 179 (9%), 177 (9%), 125 (78%), 98 (18%), 68 (20%), 59 (49%); IR (Neat) ν_{max} 1730, 1726, 1643 cm^{-1}. Anal. calcd for $C_7H_9BrO_4$: C, 35.47; H, 3.83. Found: C, 35.59; H, 3.72.

4.1.2. Dimethyl 1-nonen-2,3-dicarboxylate (11a). A fresh solution of *n*-hexylmagnesium bromide in ether was prepared as follows. A solution of *n*-hexyl bromide (1.98 g, 12 mmol) in LAH–dried ether (10 mL) was added at room temperature to magnesium turnings (864 mg, 36 mmol) in ether (10 mL) under argon with constant stirring in three equal portions at an interval of 10 min. The reaction mixture was further stirred at room temperature for 4 h. TLC of the reaction mixture in *n*-pentane showed quantitative conversion of the halide to the Grignard reagent. This freshly generated Grignard reagent was added drop wise to a solution of HMPA (7.17 g, 40 mmol) and **10** (1.90 g, 8 mmol) in anhydrous ether (20 mL) under argon at −20°C and the reaction mixture was further stirred at the same temperature for 0.5 h. The reaction was quenched by the addition of a saturated ammonium chloride solution (30 mL). An additional ether (30 mL) was added to the reaction mixture and the organic layer was separated. The aqueous layer was extracted with ether (20 mL×3), the combined ethereal extracts were washed with water (30 mL), brine (20 mL) and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was chromatographed over silica gel using petroleum ether/ethyl acetate (9.5:0.5) to give **11a**: 1.23 g (64% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.85 (t, J=8 Hz, 3H), 1.26 (bs, 8H), 1.50–1.75 (m, 1H), 1.75–2.00 (m, 1H), 3.48 (t, J=8 Hz, 1H), 3.66 (s, 3H), 3.74 (s, 3H), 5.74 (s, 1H), 6.34 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.5, 22.1, 27.0, 28.6, 30.9, 31.2, 46.1, 51.2, 51.4, 125.9, 138.2, 166.0, 173.1; IR (Neat) ν_{max} 1738, 1726, 1632, 1439 cm^{-1}. Anal. calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.52; H, 9.06.

4.1.3. Dimethyl 1-undecen-2,3-dicarboxylate (11b). Repetition of above procedure using *n*-octylmagnesium bromide [prepared from *n*-octyl bromide (2.32 g, 12 mmol) and magnesium (864 mg, 36 mmol)] and **10** (1.90 g, 8 mmol) gave the corresponding diester **11b**: 1.40 g (65% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J=6 Hz, 3H), 1.26 (bs, 12H), 1.55–1.78 (m, 1H), 1.78–2.00 (m, 1H), 3.51 (t, J=8 Hz, 1H), 3.69 (s, 3H), 3.77 (s, 3H), 5.76 (s, 1H), 6.36 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.8, 22.5, 27.3, 29.1 (4-carbons), 31.2, 31.6, 46.4, 51.8, 126.3, 138.5, 166.5, 173.5; MS (*m/e*) 270 (3%), 239 (6%), 211 (50%), 171 (11%), 157 (68%), 139 (16%), 126 (67%), 109 (13%), 95 (28%), 81 (43%), 67 (42%), 55 (60%); IR (Neat) ν_{max} 1738, 1728, 1630, 1458, 1437 cm^{-1}. Anal. calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.56; H, 9.73.

4.1.4. 1-Nonen-2,3-dicarboxylic acid (12a). A aqueous solution of lithium hydroxide (600 mg in 6 mL water) was added to a solution of **11a** (960 mg, 4 mmol) in tetrahydrofuran (18 mL) at room temperature and the reaction mixture was stirred for 18 h. The reaction mixture was then concentrated in vacuo, and the residue was dissolved in ethyl acetate (50 mL) and acidified to pH 2 with 2N hydrochloric acid (10 mL). The organic layer was separated and the aqueous layer was further extracted with ethyl acetate (20 mL×3). The combined organic layer was washed with water (20 mL), brine (20 mL) and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was chromatographed over silica gel using petroleum ether/ethyl acetate (6:4) to give **12a**: 767 mg (90% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, J=6 Hz, 3H), 1.29 (bs, 8H), 1.60–1.85 (m, 1H), 1.85–2.10 (m, 1H), 3.44 (t, J=8 Hz, 1H), 5.87 (s, 1H), 6.55 (s, 1H), 10.24 (bs, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.9, 22.5, 27.2, 28.9, 30.7, 31.5, 46.2, 129.5, 137.4, 171.8, 179.9; IR ($CHCl_3$) ν_{max} 2700–2500, 1708, 1705, 1628, 1217 cm^{-1}. Anal. calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.75. H, 8.41.

4.1.5. 1-Undecen-2,3-dicarboxylic acid (12b). It was prepared similarly from **11b** (1.08 g, 4 mmol) and aqueous lithium hydroxide solution (613 mg in 6 mL water) as described above to obtain the corresponding dicarboxylic acid **12b**: 891 mg (92% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J=6 Hz, 3H), 1.27 (bs, 12H), 1.60–1.85 (m, 1H), 1.85–2.10 (m, 1H), 3.39 (t, J=8 Hz, 1H), 5.84 (s, 1H), 6.55 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0, 22.6, 27.3, 29.6 (3-carbons), 30.8, 31.8, 46.4, 129.5, 137.5, 171.8, 179.7; MS (*m/e*) 242 (1%), 224 (1%), 206 (1%), 197 (6%), 143 (3%), 129 (12%), 112 (22%), 95 (5%), 81 (8%), 67 (9%), 55 (21%); IR ($CHCl_3$) ν_{max} 2700–2500, 1708, 1705, 1628, 1215 cm^{-1}. Anal. calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.37; H, 9.23.

4.1.6. 1,2-Dibromononan-2,3-dicarboxylic acid (13a). A solution of bromine (720 mg, 4.50 mmol) in CCl_4 (5 mL) was added drop wise to a solution of **12a** (639 mg, 3 mmol) in carbon tetrachloride (15 mL) at room temperature and the reaction mixture was stirred for 6 h. The reaction mixture

was then concentrated in vacuo, and the residue was diluted with ethyl acetate (20 mL). The organic layer was washed with saturated sodium metabisulphite (10 mL), water (10 mL), brine (10 mL) and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was chromatographed over silica gel using petroleum ether/ethyl acetate (6:4) to give **13a**: 1.11 g (~100% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (t, J=6 Hz, 3H), 1.30 (bs, 8H), 1.80–2.05 (m, 2H), 3.15–3.40 (m, 1H), 3.98 (t, J=10 Hz, 1H), 4.15 (t, J=10 Hz, 1H), 8.73 (bs, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0 (2-carbons), 22.4 (2-carbons), 27.5, 27.7, 28.8–29.6 (4-carbons), 31.4 (2-carbons), 34.7, 36.2, 49.3, 51.3, 60.8, 63.4, 173.1, 173.4, 177.6, 178.5; IR (Neat) ν_{max} 2700–2500, 1720, 1715, 1215 cm^{-1}. Anal. calcd for $C_{11}H_{18}Br_2O_4$: C, 35.32; H, 4.85. Found: C, 35.40; H, 4.78.

4.1.7. 1,2-Dibromoundecan-2,3-dicarboxylic acid (13b). It was prepared similarly from **12b** (726 mg, 3 mmol) and bromine (720 mg, 4.50 mmol) as described above to obtain the corresponding diacid **13b**: 1.20 g (~100% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89 (t, J=6 Hz, 3H), 1.29 (bs, 12H), 1.80–2.05 (m, 2H), 3.20–3.50 (m, 1H), 3.90–4.30 (m, 2H), 8.90–9.50 (bs, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0 (2-carbons), 22.6 (2-carbons), 27.6, 27.9, 29.2–29.6 (8-carbons), 31.6 (2-carbons), 34.9, 36.3, 49.5, 51.6, 61.1, 63.4, 172.9, 173.3, 177.5, 178.4; MS (*m/e*) 403 (1%), 402 (2%), 401 (1%), 305 (5%), 303 (5%), 223 (10%), 177 (11%), 149 (15%), 125 (42%), 109 (12%), 95 (20%), 81 (41%), 69 (35%), 55 (50%); IR (Neat) ν_{max} 2700–2500, 1726, 1713, 1460 cm^{-1}. Anal. calcd for $C_{13}H_{22}Br_2O_4$: C, 38.83; H, 5.51. Found: C, 38.75; H, 5.47.

4.1.8. 2-Bromomethyl-3-hexylmaleic anhydride (15a). A solution of **13a** (1.11 g, 3 mmol) in acetic anhydride (7 mL) was refluxed for 1.5 h and the reaction mixture was concentrated under vacuo at 50°C. The residue was diluted with ethyl acetate (20 mL) and the organic layer was washed with water (15 mL), brine (15 mL) and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was chromatographed over silica gel using petroleum ether/ethyl acetate (9.5:0.5) to give **15a**: 820 mg (~100% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89 (t, J=6 Hz, 3H), 1.33 (bs, 6H), 1.65 (quintet, J=8 Hz, 2H), 2.56 (t, J=8 Hz, 2H), 4.18 (s, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.7, 16.0, 22.2, 24.7, 27.0, 29.0, 31.1, 138.7, 147.3, 163.7, 164.6; IR (Neat) ν_{max} 1852, 1827, 1774, 1769, 1666, 1462 cm^{-1}. Anal. calcd for $C_{11}H_{15}BrO_3$: C, 48.02; H, 5.50. Found: C, 48.11; H, 5.45.

4.1.9. 2-Bromomethyl-3-octylmaleic anhydride (15b). It was prepared similarly from **13b** (1.20 g, 3 mmol) and acetic anhydride (7 mL) as described above to obtain the corresponding anhydride **15b**: 909 mg (~100% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89 (t, J=6 Hz, 3H), 1.28 (bs, 10H), 1.67 (quintet, J=8 Hz, 2H), 2.56 (t, J=8 Hz, 2H), 4.18 (s, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.9, 15.8, 22.5, 24.9, 27.1, 29.0–29.4 (3-carbons), 31.6, 138.8, 147.4, 163.7, 164.7; MS (*m/e*) 304 (1%), 302 (1%), 223 (5%), 195 (3%), 177 (6%), 149 (6%), 125 (25%), 97 (6%), 79 (10%), 69 (11%), 55 (22%); IR (Neat) ν_{max} 1848, 1828, 1771, 1769, 1666, 1462 cm^{-1}. Anal. calcd for $C_{13}H_{19}BrO_3$: C, 51.50; H, 6.32. Found: C, 51.61; H, 6.45.

4.1.10. 2-(Prop-2-enyl)-3-hexylmaleic anhydride (16). A fresh solution of vinylmagnesium bromide in ether was prepared as follows. A solution of vinyl bromide (535 mg, 5 mmol) in LAH-dried ether (10 mL) was added at room temperature to magnesium turnings (360 mg, 15 mmol) in ether (10 mL) under argon with constant stirring in three equal portions at an interval of 10 min. The reaction mixture was further stirred at room temperature for 4 h. TLC of the reaction mixture in *n*-pentane showed quantitative conversion of the halide to the Grignard reagent. This freshly generated Grignard reagent was added drop wise to the solution of **15a** (275 mg, 1 mmol) and copper(I) iodide (19 mg, 0.01 mmol) in ether (10 mL) and HMPA (2 mL) under argon at −5 to 0°C over 15–20 min under stirring. The reaction mixture was allowed to reach room temperature and further stirred for 8 h. It was diluted with ether (15 mL) and acidified with 4N H_2SO_4 (10 mL). The organic layer was separated and the aqueous layer was further extracted with ether (15 mL×3). The combined organic layer was washed with water (20 mL), brine (20 mL) and dried over Na_2SO_4 and concentrated in vacuo. The residue was chromatographed over silica gel using petroleum ether/ethyl acetate (9.5:0.5) to give **16**: 122 mg (55% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89 (t, J=6 Hz, 3H), 1.30 (bs, 6H), 1.58 (m, 2H), 2.48 (t, J=8 Hz, 2H), 3.23 (d, J=6 Hz, 2H), 5.05–5.30 (m, 2H), 5.70–6.00 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0, 22.4, 24.4, 27.8, 28.4, 29.2, 31.3, 118.7, 131.1, 141.5, 145.4, 165.6, 165.8; IR (Neat) ν_{max} 1848, 1767, 1665, 1639, 1215, 924, 669 cm^{-1}. Anal. calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.31; H, 8.09.

4.1.11. 2,3-Dihexylmaleic anhydride (25a). Repetition of above procedure using pentylmagnesium bromide [prepared from *n*-pentyl bromide (378 mg, 2.50 mmol) and magnesium (180 mg, 7.50 mmol)], **15a** (138 mg, 0.50 mmol), copper(I) iodide (9.50 mg, 0.05 mmol) and HMPA (1 mL) gave the corresponding **25a**: 74 mg (56% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (t, J=6 Hz, 6H), 1.31 (bs, 12H), 1.58 (quintet, J=6 Hz, 4H), 2.45 (t, J=8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 22.6, 24.5, 28.0, 29.1, 31.8, 144.5, 166.0; IR ($CHCl_3$) ν_{max} 1846, 1767, 1705, 1663, 1466, 1215, 758 cm^{-1}. Anal. calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.21; H, 9.79.

4.1.12. 2,3-Dioctylmaleic anhydride (25b). Repetition of above procedure using heptylmagnesium bromide [prepared from *n*-heptyl bromide (448 mg, 2.50 mmol) and magnesium (180 mg, 7.50 mmol)], **15b** (152 mg, 0.50 mmol), copper(I) iodide (9.50 mg, 0.05 mmol) and HMPA (1 mL) gave **25b**: 89 mg (55% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89 (t, J=6 Hz, 6H), 1.27 (bs, 20H), 1.57 (quintet, J=6 Hz, 4H), 2.44 (t, J=8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.9, 22.6, 24.5, 27.9, 29.1–29.6 (3-carbons), 31.8, 144.5, 165.9; MS (*m/e*) 322 (3%), 277 (4%), 250 (3%), 224 (7%), 205 (5%), 126 (9%), 95 (11%), 79 (15%), 67 (20%), 55 (36%); IR ($CHCl_3$) ν_{max} 1836, 1767, 1466, 1215 cm^{-1}. Anal. calcd for $C_{20}H_{34}O_3$: C, 74.49; H, 10.63. Found: C, 74.56; H, 10.71.

4.1.13. Dimethyl 2-(prop-2-enyl)-3-hexylmaleate (17).[1] A solution of **16** (111 mg, 0.50 mmol) in methanol (10 mL) was treated with a solution of diazomethane in ether at 0°C

until the starting material was completely consumed (3 h). The excess diazomethane was quenched with acetic acid (0.5 mL) and the reaction mixture was concentrated in vacuo. The residue was chromatographed over silica gel using petroleum ether/ethyl acetate (9.5:0.5) to give **17**: 127 mg (95% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J=6 Hz, 3H), 1.27 (bs, 6H), 1.50–1.80 (m, 2H), 2.35 (t, J=8 Hz, 2H), 3.12 (d, J=6 Hz, 2H), 3.74 (s, 3H), 3.78 (s, 3H), 5.00–5.20 (m, 2H), 5.65–5.90 (m, 1H); IR (Neat) ν_{max} 1713, 1638, 1217, 758 cm^{-1}. Anal. calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 67.25; H, 9.07.

4.1.14. 2-Carboxymethyl-3-hexylmaleic anhydride (1).[4] A solution of **17** (100 mg, 0.37 mmol) was dissolved in acetone and the system was flushed with argon gas. The reaction mixture was cooled to −78°C using acetone-dry ice bath and ozone was slowly bubbled in reaction mixture for 3 min at the same temperature. The reaction mixture was flushed with argon and concentrated under vacuum. The residue was dissolved in diethyl ether and cooled to 0°C. A solution of 5% $Na_2Cr_2O_7$ in 4N sulfuric acid (2 mL) was added in a drop wise fashion for 10 min. The reaction mixture was further stirred for 3 h and neutralized with 2N sodium hydroxide (5 mL) solution till alkaline. The aqueous layer was washed with ether (10 mL×3) and then acidified with 2N hydrochloric acid (10 mL). Acidified aqueous layer was extracted with ethyl acetate (10 mL×3). The combined organic layer was washed with water (20 mL), brine (20 mL) and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was chromatographed over silica gel using petroleum ether/ethyl acetate (7.5:2.5) to give **1**: 37 mg (42% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (t, J=6 Hz, 3H), 1.30 (bs, 6H), 1.50–1.80 (m, 2H), 2.49 (t, J=8 Hz, 2H), 3.61 (s, 2H); IR (Neat) ν_{max} 1820, 1771, 1718, 1216, 925, 670 cm^{-1}. Anal. calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 60.20; H, 6.83.

4.1.15. Trimethyl 1-propene-1,2,3-tricarboxylate (20). A solution of 1-propene-1,2,3-tricarboxylic acid (6.96 g, 40 mmol) in methanol (50 mL) and H_2SO_4 (0.5 mL) mixture was refluxed for 12 h under nitrogen. The reaction mixture was concentrated in vacuo. The residue was diluted with water (20 mL) and extracted with ethyl acetate (20 mL×3). The combined organic layer was washed with water (20 mL), brine (20 mL) and dried over Na_2SO_4. Concentration of organic layer in vacuo followed by silica gel column chromatographic purification of the crude product using petroleum ether/ethyl acetate (7:3) as eluent furnished pure triester **20**: 6.48 g (75% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.68 (s, 3H), 3.76 (s, 3H), 3.81 (s, 3H), 3.95 (s, 2H), 6.95 (s, 1H); IR ($CHCl_3$) ν_{max} 1738, 1728, 1655, 1437, 1283, 1200, 1173, 758 cm^{-1}. Anal. calcd for $C_9H_{12}O_6$: C, 50.00; H, 5.59. Found: C, 50.09; H, 5.48.

4.1.16. Trimethyl 3-bromo-1-propene-1,2,3-tricarboxylate (21). A mixture of **20** (2.16 g, 10 mmol), *N*-bromosuccinimide (17.80 g, 100 mmol) and catalytic amount of AIBN (200 mg, 1.22 mmol) in carbon tetrachloride (300 mL) was gently refluxed for 32 h in a 500 mL round bottom flask. The reaction mixture was left overnight at room temperature and then filtered. The residue was washed with CCl_4 (50 mL×2); the combined organic layer was washed with water (100 mL), brine (50 mL) and then dried over Na_2SO_4. The organic layer was concentrated in vacuo to a furnish thick yellow oil, which was purified by chromatography on silica gel column using petroleum ether/ethyl acetate (7:3) to give the desired bromo triester **21**: 2.50 g (85% yield, 90% purity by ^{1}H NMR); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.76 (s, 3H), 3.81 (s, 3H), 3.83 (s, 3H), 6.78 (s, 1H), 6.85 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 37.7, 52.1, 52.7, 53.3, 127.6, 141.4, 163.7, 164.5, 166.4; IR (Neat) ν_{max} 1736, 1726, 1655, 1437, 1329, 1283, 1200, 1173, 1022, 789 cm^{-1}.

4.1.17. 2-(β-*gem*-Dicarbethoxy)ethyl-3-hexylmaleic anhydride (23a). To a slurry of sodium hydride (26 mg, 1.10 mmol) in benzene (5 mL), a solution of diethyl malonate (176 mg, 1.10 mmol) in benzene (5 mL) was added drop wise at room temperature and the reaction mixture was stirred for 5 min. A solution of **15a** (275 mg, 1 mmol) in benzene (10 mL) was added to the reaction mixture at room temperature and it was stirred for another 8 h. The mixture was acidified with dil. HCl (10 mL, 4%) and extracted with ethyl acetate (30 mL×3). The combined organic layers were washed with water (20 mL), brine (20 mL) and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was chromatographed over silica gel using petroleum ether/ethyl acetate (9.5:0.5) to give **23a**: 255 mg (72% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J=6 Hz, 3H), 1.26 (bs, 6H), 1.26 (t, J=8 Hz, 6H), 1.55 (quintet, J=6 Hz, 2H), 2.49 (t, J=8 Hz, 2H), 3.02 (d, J=8 Hz, 2H), 3.90 (t, J=8 Hz, 1H), 4.20 (q, J=8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.9, 22.4, 23.6, 24.6, 27.7, 29.2, 29.6, 31.3, 49.0, 62.0, 139.7, 147.2, 165.2, 165.4, 167.9; IR ($CHCl_3$) ν_{max} 1827, 1767, 1753, 1732, 1464 cm^{-1}. Anal. calcd for $C_{18}H_{26}O_7$: C, 61.00; H, 7.40. Found: C, 61.03; H, 7.49.

4.1.18. 2-(β-*gem*-Dicarbethoxy)ethyl-3-octylmaleic anhydride (23b). Repetition of above procedure using sodium hydride (26 mg, 1.10 mmol), diethyl malonate (176 mg, 1.10 mmol) and **15b** (304 mg, 1 mmol) gave the corresponding diester **23b**: 283 mg (74% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J=6 Hz, 3H), 1.27 (bs, 10H), 1.27 (t, J=8 Hz, 6H), 1.50–1.70 (m, 2H), 2.50 (t, J=8 Hz, 2H), 3.03 (d, J=8 Hz, 2H), 3.91 (t, J=8 Hz, 1H), 4.21 (q, J=8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.9 (2-carbons), 22.5, 23.7, 24.6, 27.7, 29.1–29.6 (3-carbons), 31.7, 49.1, 61.9, 139.8, 147.1, 165.2, 165.4, 167.8; MS (*m*/*e*) 382 (3%), 337 (28%), 308 (3%), 290 (30%), 252 (11%), 238 (35%), 222 (7%), 206 (12%), 192 (46%), 160 (37%), 133 (15%), 93 (16%), 79 (24%), 69 (26%), 55 (38%); IR ($CHCl_3$) ν_{max} 1769, 1746, 1732, 1215 cm^{-1}. Anal. calcd for $C_{20}H_{30}O_7$: C, 62.81; H, 7.90. Found: C, 62.73; H, 7.79.

4.1.19. 2-(β-Carboxyethyl)-3-hexylmaleic anhydride (2a). A solution of diester **23a** (177 mg, 0.50 mmol) in concentrated HCl (5 mL) and acetic acid (5 mL) was refluxed with stirring for 12 h. The reaction mixture was then allowed to reach room temperature and then saturated by adding solid sodium chloride. The filtered aqueous layer was extracted with ethyl acetate (10 mL×3) and the organic layer was washed with brine (10 mL) and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was chromatographed over silica gel using petroleum ether/ethyl acetate (7:3) to give **2a**: 122 mg (96%

yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J=6 Hz, 3H), 1.28 (bm, 6H), 1.57 (quintet, J=6 Hz, 2H), 2.49 (t, J=8 Hz, 2H), 2.76 (s, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.9, 19.6, 22.4, 24.6, 27.8, 29.2, 31.0, 31.3, 141.5, 146.3, 165.4, 165.6, 177.4; MS (*m/e*) 254 (28%), 236 (62%), 208 (15%), 162 (5%), 148 (34%), 91 (10%), 60 (70%); IR (Neat) ν_{max} 2700–2500, 1840, 1765, 1713, 1437, 1273 cm^{-1}. Anal. calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.13. Found: C, 61.33; H, 7.05.

4.1.20. 2-(β-Carboxyethyl)-3-octylmaleic anhydride (2b). Repetition of above procedure using **23b** (191 mg, 0.50 mmol) gave the corresponding **2b**: 134 mg (95% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J=6 Hz, 3H), 1.29 (bs, 10H), 1.57 (quintet, J=6 Hz, 2H), 2.50 (t, J=8 Hz, 2H), 2.77 (s, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.9, 19.6, 22.5, 24.5, 27.8, 29.0–29.5 (3-carbons), 31.0, 31.7, 141.4, 146.2, 165.3, 165.5, 177.2; MS (*m/e*) 282 (2%), 265 (4%), 252 (2%), 236 (9%), 219 (7%), 208 (9%), 180 (3%), 166 (7%), 138 (6%), 105 (4%), 91 (8%), 79 (11%), 69 (16%), 55 (42%); IR (Neat) ν_{max} 2700–2500, 1840, 1767, 1713, 1668, 1447, 1267 cm^{-1}. Anal. calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.92; H, 7.73.

4.1.21. 2-(β-Carbmethoxy)ethyl-3-hexylmaleic anhydride (2c). A solution of **2a** (64 mg, 0.25 mmol) in diethyl ether (5 mL) was treated with a solution of diazomethane in ether at 0°C until the starting material was completely consumed (3 h). The excess diazomethane was quenched with acetic acid (0.5 mL) and the reaction mixture was concentrated in vacuo. The residue was chromatographed over silica gel using petroleum ether/ethyl acetate (9.5:0.5) to give **2c**: 63 mg (95% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89 (t, J=6 Hz, 3H), 1.28 (bm, 6H), 1.57 (quintet, J=8 Hz, 2H), 2.51 (t, J=8 Hz, 2H), 2.60–2.90 (m, 4H), 3.69 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.9, 19.9, 22.4, 24.5, 27.8, 29.2, 31.2, 31.3, 51.9, 141.9, 146.1, 165.5, 165.6, 172.0; IR ($CHCl_3$) ν_{max} 1844, 1767, 1740, 1670, 1439, 1269 cm^{-1}. Anal. calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.56; H, 7.39.

4.1.22. 2-(β-Carbmethoxy)ethyl-3-octylmaleic anhydride (2d). Repetition of the above procedure with **2b** (71 mg, 0.25 mmol) gave the corresponding **2d**: 70 mg (95% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89 (t, J=6 Hz, 3H), 1.27 (bs, 10H), 1.57 (quintet, J=6 Hz, 2H), 2.51 (t, J=8 Hz, 2H), 2.60–2.90 (m, 4H), 3.70 (s, 3H); MS (*m/e*) 296 (3%), 277 (6%), 265 (37%), 250 (11%), 218 (10%), 207 (13%), 198 (18%), 180 (22%), 166 (67%), 151 (15%), 138 (21%), 91 (13%), 79 (26%), 67 (31%), 55 (67%); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 21.2, 22.6, 24.3, 28.0, 29.1, 29.2, 29.4, 30.0, 31.7, 51.6, 142.0, 146.1, 165.4, 165.5, 172.7; IR ($CHCl_3$) ν_{max} 1836, 1767, 1738, 1450, 1215 cm^{-1}. Anal. calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.76; H, 8.25.

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References

1. Adlington, R. M.; Baldwin, J. E.; Cox, R. J.; Pritchard, G. J. *Synlett* **2002**, 820 and references cited therein.
2. (a) Baldwin, J. E.; Adlington, R. M.; Roussi, F.; Bulger, P. G.; Marqwez, A. V. W. *Tetrahedron* **2001**, *57*, 7409. (b) Nicolaou, K. C.; Baran, P. S.; Zong, Y.-L.; Fong, K. C.; He, Y.; Yoon, W. H.; Choi, H.-S. *Angew. Chem., Int. Ed.* **1999**, *38*, 1676 and references cited therein.
3. (a) Singh, S. B.; Jayasuriya, H.; Silverman, K. C.; Bonfiglio, C. A.; Williamsons, J. M.; Lingham, R. B. *Bioorg. Med. Chem.* **2000**, *8*, 571. (b) Singh, S. B.; Zink, D. L.; Liesch, J. M.; Goetz, M. A.; Jenkins, R. G.; Nalin-Omstead, M.; Silverman, K. C.; Bills, G. F.; Mosley, R. T.; Gibbs, J. B.; Albers-Schonberg, G.; Lingham, R. B. *Tetrahedron* **1993**, *49*, 5917. (c) Weber, W.; Semar, M.; Anke, T.; Bross, M.; Steglich, W. *Planta Med.* **1992**, *58*, 56. (d) Raistrick, H.; Smith, G. *Biochem. J.* **1933**, *27*, 1814.
4. Weidenmuller, H.-L.; Cavagna, F.; Fehlhaber, H.-W.; Prave, P. *Tetrahedron Lett.* **1972**, *13*, 3519.
5. (a) Itoh, S.; Esaki, N.; Masaki, K.; Blank, W.; Soda, K. *J. Ferment. Bioeng* **1994**, *77*, 513. (b) Gama, Y.; Yasumoto, M.; Suzuki, H.; Ishigami, Y. *Yukagaku* **1989**, *38*, 292.
6. (a) Cheng, X. C.; Kihara, T.; Kusakabe, H.; Magae, J.; Kobayashi, Y.; Fang, R. P.; Ni, Z. F.; Shen, Y. C.; Ko, K.; Yamaguchi, I.; Isono, K. *J. Antibiot.* **1987**, *40*, 907. (b) Naganawa, A.; Ichikawa, Y.; Isobe, M. *Tetrahedron* **1994**, *50*, 8969.
7. (a) Isaka, M.; Tanticharoen, M.; Thebtaranonth, Y. *Tetrahedron Lett.* **2000**, *41*, 1657. (b) Yamanishi, R.; Okada, K.; Tamugi, N.; Iwashima, M.; Iguchi, K. *Bull. Chem. Soc. Jpn* **2000**, *73*, 2087 and refs. cited therein. (c) Aldridge, D. C.; Carman, R. M.; Moore, R. B. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2134.
8. Adeboya, M. O.; Edwards, R. L.; Laessoe, T.; Maitland, D. J.; Whalley, A. J. S. *Liebigs Ann. Chem.* **1996**, 1437.
9. (a) Kinoshita, K.; Nakajima, S. *Chem. Pharm. Bull.* **1958**, *6*, 31. (b) Nakajima, S. *Chem. Pharm. Bull.* **1965**, *13*, 73. (c) Sankawa, U.; Shibata, S. *Chem. Pharm. Bull.* **1969**, *17*, 2025.
10. (a) Desai, S. B.; Argade, N. P. *J. Org. Chem.* **1997**, *62*, 4862. (b) Deshpande, A. M.; Natu, A. A.; Argade, N. P. *J. Org. Chem.* **1998**, *63*, 9557. (c) Deshpande, S. G.; Argade, N. P. *Synthesis* **1999**, 1306. (d) Deshpande, A. M.; Natu, A. A.; Argade, N. P. *Synthesis* **2001**, 702. (e) Mangaleswaran, S.; Argade, N. P. *J. Org. Chem.* **2001**, *66*, 5259. (f) Mangaleswaran, S.; Argade, N. P. *Synthesis* **2002**, 865. (g) Kar, A.; Argade, N. P. *J. Org. Chem.* **2002**, *67*, 7131. (h) Sahoo, M. K.; Mhaske, S. B.; Argade, N. P. *Synthesis* **2003**, 346.
11. Kar, A.; Argade, N. P. *Tetrahedron Lett.* **2002**, *43*, 6563.
12. Desai S. B.; Argade N. P. Unpublished results.
13. (a) Beltaief, I.; Besbes, R.; Amor, F. B.; Amri, H.; Villieras, M.; Villieras, J. *Tetrahedron* **1999**, *55*, 3949. (b) Amri, H.; Villieras, J. *Tetrahedron Lett.* **1987**, *28*, 5521. (c) Loh, T.-P.; Lye, P.-L. *Tetrahedron Lett.* **2001**, *42*, 3511. (d) Calo, V.; Lopez, L.; Pesce, G. *J. Organomet. Chem.* **1988**, *353*, 405.
14. Vogel, A. I. *Vogel's Textbook of Practical Organic Chemistry*,

5th ed.; Furniss, B. S., Stanley, B., Eds.: Longman: Harlow, 1989; Chapter 5, p 714.
15. Bulman Page, P. C.; van Neil, M. B.; Prodger, J. C. *Tetrahedron* **1989**, *45*, 7643.
16. Bruce, W. F. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. 2, p 12.