Succinylation of Tertiary Alcohols under High Pressure

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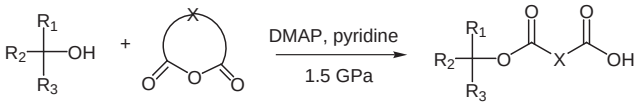
Abstract: The efficient succinylation of the sterically hindered tertiary alcohols **1** was performed by reaction with succinic acid monomethyl and monoallyl ester (**4a** and **4b)**, respectively, in CH_2Cl_2 in the presence of dicyclohexylcarbodiimide and 4-(dimethylamino)pyridine under high pressure to give the methyl and allyl succinates **5a** and **5b**, respectively, in high yields. The succinates **5a**,**b** were efficiently converted into the hemisuccinate **3a** by treatment with lithium propyl mercaptide or by palladium(0)-catalyzed deallylation.

Key words: succinates, hemisuccinates, acylation, tertiary alcohols, high pressure

Introduction and Background

Dicarboxylic acid monoester groups are unique substituents found in several biologically active natural products such as reveromycins,[1] (–)-A26771B,[2] malolactomycin A and B,[3] etc. In addition, the dicarboxylic acid monoesters attract much attention as the prodrugs of steroids,[4] anthracyclins,[5,6] and taxol[7–9] because of their water-soluble property. Several methods for preparation of dicarboxylic acid monoesters with cyclic anhydrides, acid chlorides and carboxylate anions have been reported.[4–9] However, few methods are known for the acylation of sterically hindered alcohols.[10,11] We have already reported the one-step and efficient synthesis of dicarboxylic acid monoesters **3a**–**c** of sterically hindered alcohols **1** including tertiary alcohols with cyclic anhydrides **2a**–**c** in pyridine in the presence of DMAP under high pressure (Scheme 1).[12]



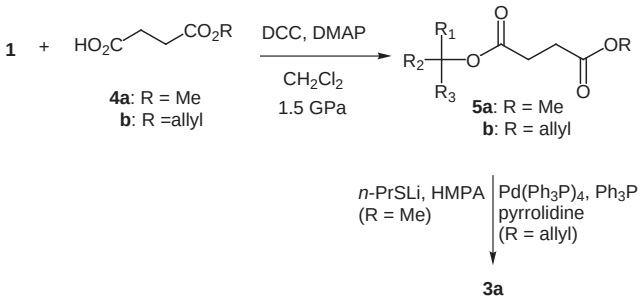
1

2a: X = -CH_2CH_2-
b: X = -$CH_2CH_2CH_2$-
c: X = -CH_2OCH_2-

3a: X = -CH_2CH_2-
b: X = -$CH_2CH_2CH_2$-
c: X = -CH_2OCH_2-

Scheme 1

However, in the synthetic studies of reveromycin A having a tertiary alcohol hemisuccinate, we have encountered difficulty in the acylation of the tertiary alcohol even using our developed method with cyclic anhydride under high pressure. Thus, more efficient methods for the synthesis of the hemisuccinates **3a** of the sterically hindered tertiary alcohols **1** were further investigated. We now report an efficient synthesis of the methyl and allyl succinates **5a**,**b** of the hindered tertiary alcohols **1** with succinic acid monomethyl and monoallyl esters **4a**,**b** in CH_2Cl_2 in the presence of dicyclohexylcarbodiimide (DCC) or 1,3-diisopropylcarbodiimide (DIC) and 4-(dimethylamino)pyridine (DMAP) under high pressure (1.5 GPa) and the conversion of the succinates **5a**,**b** into the hemisuccinates **3a** (X = CH_2CH_2) (Scheme 2).



Scheme 2

Succinylation of Tertiary Alcohol

To develop more efficient methods for the succinylation, several intermediates in the synthetic studies of reveromycin A[13,14] were chosen as the substrates having a sterically hindered tertiary hydroxyl group. We first examined the introduction of the hemisuccinate or succinate to the alcohol **7**[15] derived from the known lactone **6**[13] (Scheme 3). These results are shown in Table 1 (entries 1–4). The initial attempt using our reported procedure under high pressure (succinic anhydride **2a** in pyridine in the presence of DMAP at 1.5 GPa)[12] resulted in the recovery of **7** (entry 1). 3-Methoxycarbonylpropionyl chloride (**14**) and the mixed anhydride **15** (Figure 1) also did not give the desired succinate **8** even under high pressure (entries 2 and 3). After several attempts, we found that the succinylation of **7** with succinic acid monomethyl ester (**4a**) in the presence of DCC and DMAP in CH_2Cl_2 at 1.5 GPa proceeded to give the methyl succinate **8** in 19% yield, with a 70% recovery of **7** (entry 4). This result means that the method using the succinic acid monomethyl ester (**4a**) and DCC under high pressure is more efficient than our previous procedure[12] for the succinylation of hindered alcohols. This new method was then applied to the alcohol **10**[16] having an alkyne group in place of the CH_2OBOM group. The

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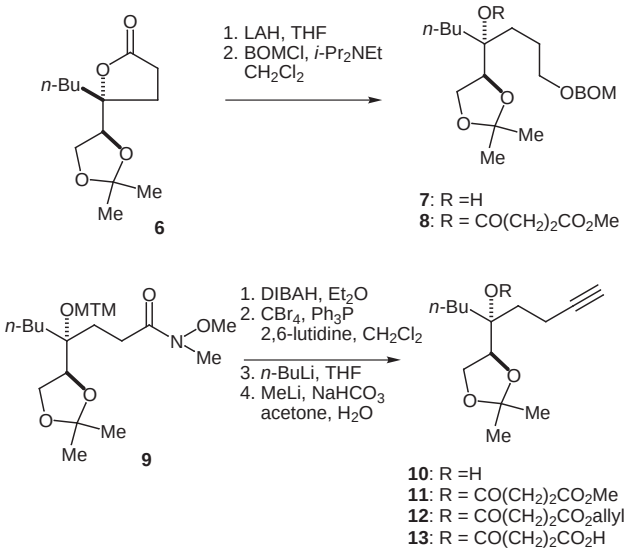

Scheme 3

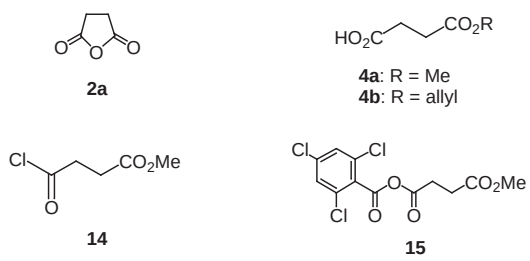

Figure 1 Acylating reagents

yield of the methyl succinate **11** increased to 77% yield, which should be due to the reduced steric hindrance of the alkyne group (entry 10). The succinic acid monoallyl ester (**4b**) also afforded the allyl succinate **12** under the same conditions in 75% yield (entry 11). The use of DIC in place of DCC under high pressure was also effective for producing **11** in a similar yield (entry 12), while the same reaction did not proceed at atmospheric pressure (entry 6). Succinic anhydride (**2a**), 3-methoxycarbonylpropionyl chloride (**14**) and the mixed anhydride **15** did not react at all with the tertiary hydroxyl group of **10** even under high pressure and **10** was quantitatively recovered in every case (entries 7, 8 and 9).

We next extended the acylation method using the succinic acid monoester under high pressure to a variety of tertiary alcohols such as linalool (**16**), α-terpineol (**20**) and the 6,6-spiroacetal derivatives, **24**,[13] **26**[13] and **28**[17] (Figure 2, Table 2). The reactions of the acyclic alcohols **16** and **20** with succinic acid monomethyl ester (**4a**) smoothly proceeded to afford the methyl succinates **17** and **21** in 92% and 92% yields, respectively (entries 1 and 3). The succinic acid monoallyl ester (**4b**) also reacted with **16** and **20** to give the corresponding allyl succinates **18** and **22** in 97% and 95% yields, respectively (entries 2 and 4). In comparison with the new method, **16** and **20** were converted into the hemisuccinates in 66% and 79% yields along with the recovered **16** and **20** by our previous procedure with succinic anhydride (**2a)** under high pressure.[12] The reaction

Table 1 Succinylation of Tertiary Alcohols **7** and **10**

Entry	Alcohol	Reagent (equiv)	Additive (equiv)	Solvent	Conditions	Succinate[a]	Yield (%)
1	**7**	**2a** (5)	DMAP (0.1)	pyridine	1.5 GPa, r.t., 1 d	**8***	0[b]
2	**7**	**14** (2)	DMAP (0.1)	pyridine	1.5 GPa, r.t., 1 d	**8**	0[b]
3	**7**	**15** (5)	DMAP (0.1)	pyridine	1.5 GPa, r.t., 1 d	**8**	0[b]
4	**7**	**4a** (5)	DCC (5), DMAP (0.1)	CH_2Cl_2	1.5 GPa, r.t., 3 d	**8**	19[c]
5	**10**	**14** (2)	DMAP (0.1)	pyridine	r.t., 1 d[d]	**11**	0[b]
6	**10**	**4a** (2)	DIC (2), DMAP (0.1)	CH_2Cl_2	r.t., 1 d[d]	**11**	0[b]
7	**10**	**2a** (5)	DMAP (0.1)	pyridine	1.5 GPa, r.t., 1 d	**11***	0[b]
8	**10**	**14** (2)	DMAP (0.1)	pyridine	1.5 GPa, r.t., 1 d	**11**	0[b]
9	**10**	**15** (2)	DMAP (0.1)	pyridine	1.5 GPa, r.t., 1 d	**11**	0[b]
10	**10**	**4a** (3)	DCC (3), DMAP (0.1)	CH_2Cl_2	1.5 GPa, r.t., 2 d	**11**	77[e]
11	**10**	**4b** (3)	DCC (3), DMAP (0.1)	CH_2Cl_2	1.5 GPa, r.t., 2 d	**12**	75
12	**10**	**4a** (3)	DIC (3), DMAP (0.1)	CH_2Cl_2	1.5 GPa, r.t., 2 d	**11**	71[f]

[a] **8*** and **11*** denote the corresponding hemisuccinates, respectively.
[b] The alcohol **7** was recovered in >90%.
[c] The alcohol **7** was recovered in 70%.
[d] The reaction was carried out at atmospheric pressure.
[e] The alcohol **10** was recovered in 10%.
[f] The alcohol **10** was recovered in 18%.

Table 2 Succinylation of Tertiary Alcohols **16**, **20**, **24**, **26** and **28** under High Pressure and Deprotection of the Succinates **17**, **18**, **21** and **22**

Entry	Alcohol	Reagent (equiv)	Additive (equiv)	Solvent	Succinate[a]	Yield (%)	Deprotection[b]	Hemisuccinate	Yield (%)
1	**16**	**4a** (3)	DCC (3), DMAP (0.1)	CH_2Cl_2	**17**	92	A	**19**	(98)
2	**16**	**4b** (3)	DCC (3), DMAP (0.1)	CH_2Cl_2	**18**	97	B	**19**	(96)
3	**20**	**4a** (3)	DCC (3), DMAP (0.1)	CH_2Cl_2	**21**	92	A	**23**	(96)
4	**20**	**4b** (3)	DCC (3), DMAP (0.1)	CH_2Cl_2	**22**	95	B	**23**	(96)
5	**24**	**2a** (5)	DMAP (0.1)	pyridine	**25***	0			
6	**24**	**4b** (3)	DCC (3), DMAP (0.1)	CH_2Cl_2	**25**	85			
7	**26**	**4b** (3)	DCC (3), DMAP (0.1)	CH_2Cl_2	**27**	76			
8	**28**	**4b** (3)	DCC (3), DMAP (0.1)	CH_2Cl_2	**29**	74			

[a] The reaction was carried out at 1.5 GPa at r.t. for 1 d. **25*** denotes the corresponding hemisuccinate.
[b] A: PrSLi, HMPA, B: $Pd(Ph_3P)_4$, Ph_3P, pyrrolidine.

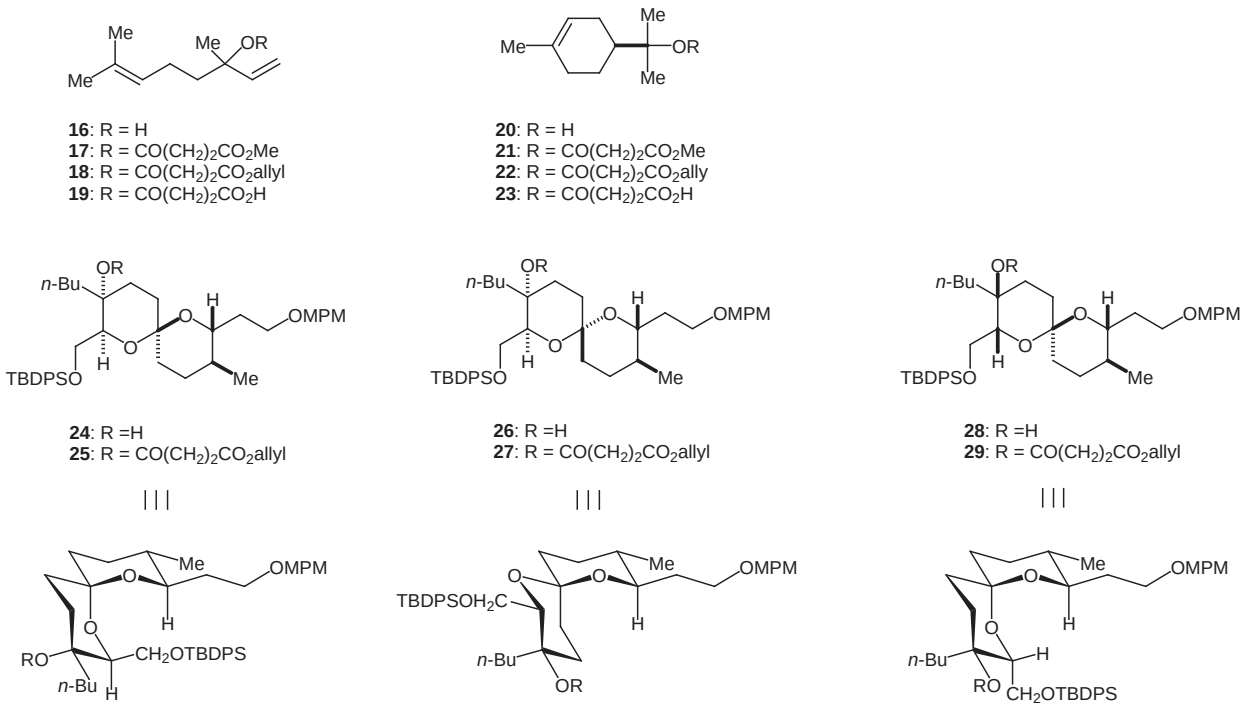

Figure 2 Structures of compounds **16–29**

of **24**, having an axial hydroxyl group, with **2a** resulted in the recovery of **24** (entry 5). As expected, however, the new method with succinic acid monoallyl ester (**4b**), DCC and DMAP under high pressure efficiently produced the desired succinate **25** in 85% yield (entry 6). The diastereomers **26** and **28**, having an equatorial hydroxyl group, also reacted with **4b**, DCC and DMAP under high pressure to give the corresponding succinates **27** and **29** in 76% and 74% yields, respectively, together with unidentified polar compounds (entries 7 and 8).

Conversion of Succinates into the Hemisuccinates

The hemisuccinates are essential groups for the biological activity and solubility of reveromycins and other prodrugs. The conversions of the tertiary alcohol succinates into the hemisuccinates were then examined using the methyl succinate **30**[18] and allyl succinate **31**[18] as the model compounds (Figure 3). Treatment of the methyl succinate **30** with potassium trimethylsilanolate[19] gave a mixture of the acid **32** and 2-methly-1-phenylpropan-2-ol formed by the non-selective hydrolysis. Lithium propyl mercaptide[20] smoothly reacted with **30** to give the acid **32** by the selec-

tive *O*-alkyl cleavage of the methyl ester in 95% yield (Method A). The method using lithium propyl mercaptide could not be applied to the methyl sorbate (**33**), which corresponds to the side chain of reveromycin A, because the competitive Michael addition reactions occurred. On the other hand, the allyl ester **31** was efficiently converted into the acid **32** by the palladium(0)-catalyzed hydrogenolysis of the allyl ester using $Pd(Ph_3P)_4$[21] or $Pd_2(dba)_3CHCl_3$[22] (Method B). The present methods using lithium propyl mercaptide for the methyl succinates and $Pd(Ph_3P)_4$ for the allyl succinates were applied to a variety of succinates, **11**, **12**, **17**, **18**, **21** and **22** (Table 2, entries 1–4) to afford the corresponding hemisuccinates in almost quantitative yields. The allyl succinates, **34**[14] and **36**[14], having an unsaturated allyl ester were also effectively converted into the hemisuccinates, **35** and **37**, by the palladium(0)-catalyzed deallylation, respectively (Figure 3).

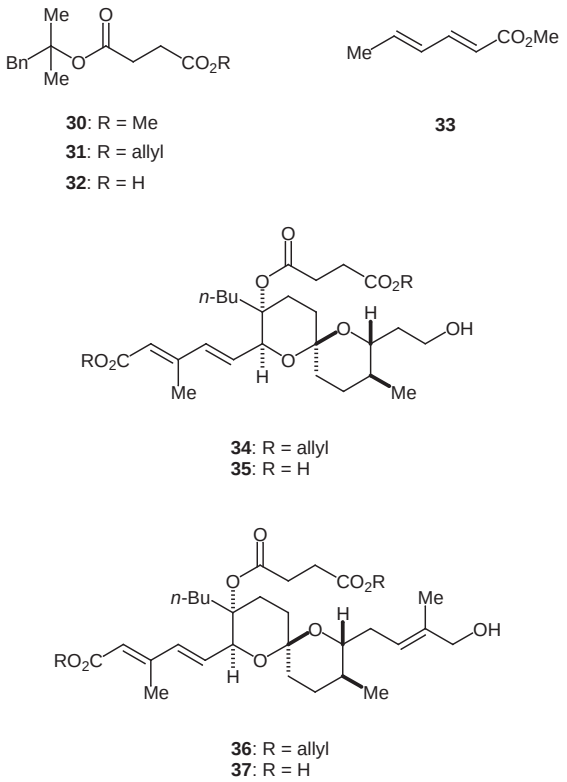

Figure 3 Structures of compounds **30–37**

Conclusion

In conclusion, we have found an efficient method for the preparation of the methyl and allyl succinates of a variety of sterically hindered tertiary alcohols by reaction with succinic acid monoester in CH_2Cl_2 in the presence of DCC and DMAP under high pressure. The methyl and allyl succinates were quantitatively converted into the hemisuccinates by treatment with lithium propyl mercaptide and by palladium(0)-catalyzed deallylation, respectively.

The apparatus for chemical reaction under high pressure has been developed at RIKEN instrumentation center. The RIKEN high-pressure apparatus using a direct piston-cylinder equipment is capable of holding a 150 mL reaction volume at 1.5 GPa. The optical rotations were measured using a Jasco DIP-370 digital polarimeter. IR spectra were measured with a JASCO VALOR-III FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-EX270 (270 MHz and 67.5 MHz), JNM-GSX (500 MHz and 125 MHz), and JNM-ECP (500 MHz and 125 MHz). Chemical shifts are reported in ppm relative to TMS (0 ppm) for the ^{1}H NMR and to the center of $CDCl_3$ (77.0 ppm) for the ^{13}C NMR as internal standards. Mass specta were recorded on Jeol JMA-HX110 and Shimadzu Kratos Maldi III mass spectrometers. Flash column chromatography was performed using silica gel 60N (spherical, neutral, 40–100 μm) (Kanto Chemical Co. Inc.). HPLC was performed using Sensyu Pak PEGASIL Silica 120–5 (300 × 250 mm) (Sensyu Scientific Co., Ltd.).

Succinylation of Tertiary Alcohols; Succinic Acid (1*R*)-1-Butyl-1-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]pent-4-ynyl Ester Methyl Ester (11); Typical Procedure

In a 1 mL teflon vessel were placed **10**[16] (84.1 mg, 0.35 mmol), succinic acid monomethyl ester (**4a**; 138.7 mg, 1.05 mmol), DCC (216.6 mg, 1.05 mmol) and DMAP (4 mg, 0.04 mmol). The vessel was filled with CH_2Cl_2 and compressed to 1.5 GPa at r.t. for 2 d in a high pressure instrument. The resulting mixture was diluted with EtOAc (50 mL) and washed with 1 N HCl (1 mL), 2 N aq Na_2CO_3 (2 × 1 mL) and brine (2 × 5 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by column chromatography with hexane–EtOAc (2:1) to give **11** (91.7 mg, 77%) as a colorless oil and **10** (8.4 mg, 10%) (Table 1, entry 10).

11

R_f 0.35 (hexane–EtOAc, 5:1); $[\alpha]_D$ –3.0 (*c* = 1.5, $CHCl_3$).

^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 6.9 Hz, 3 H), 1.23–1.40 (m, 4 H), 1.32 (s, 3 H), 1.42 (s, 3 H), 1.84 (m, 2 H), 1.94 (dd, *J* = 2.6, 2.6 Hz, 1 H), 2.11 (m, 1 H), 2.22–2.40 (m, 3 H), 2.59 (m, 4 H), 3.69 (s, 3 H), 3.88 (dd, *J* = 8.7, 6.9 Hz, 1 H), 3.96 (dd, *J* = 8.7, 7.1 Hz, 1 H), 4.57 (dd, *J* = 7.1, 6.9 Hz, 1 H).

^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 13.4, 14.0, 23.1, 24.6, 25.4, 26.1, 28.9, 29.9, 32.6, 33.9, 51.8, 65.2, 68.1, 78.2, 84.1, 85.4, 109.0, 170.9, 172.3.

IR (neat): ν = 3289, 2958, 2936, 1736 cm^{-1}.

HRMS (FAB, M + Na$^+$): *m*/*z* calcd for $C_{19}H_{30}O_6Na$ 377.1940, found 377.1940.

Succinylation of 10 with DIC

Following the typical procedure for the succinylation of **10**, the alcohol **10** (48.0 mg, 0.2 mmol) was succinylated with DIC in place of DCC to give **11** (48.3 mg, 71%) as a colorless oil and **10** (8.6 mg, 18%) (Table 1, entry 12).

Succinic Acid (1*R*)-5-Benzyloxy-1-butyl-1-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]pentyl Ester Methyl Ester (8)

Following the typical procedure for the succinylation of **10**, the alcohol **7**[15] (36.7 mg, 0.1 mmol) was succinylated to give **8** (8.9 mg, 19%) as a colorless oil and **7** (25.7 mg, 70%) (Table 1, entry 4).

8

R_f 0.60 (hexane–EtOAc, 1:1); $[\alpha]_D$ –1.5 (*c* = 1.0, $CHCl_3$).

^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.9 Hz, 3 H), 1.21–1.40 (m, 6 H), 1.32 (s, 3 H), 1.42 (s, 3 H), 1.68 (m, 2 H), 1.88 (m, 2 H), 2.58 (s, 4 H), 3.56 (t, *J* = 6.5 Hz, 2 H), 3.68 (s, 3 H), 3.90 (dd, *J* = 8.5, 6.9 Hz, 1 H), 3.95 (dd, *J* = 8.5, 6.9 Hz, 1 H), 4.55 (dd, *J* = 6.9, 6.9 Hz, 1 H), 4.60 (s, 2 H), 4.75 (s, 2 H), 7.25–7.40 (m, 5 H).

^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 14.0, 23.3, 24.0, 24.8, 25.6, 26.1, 29.0, 30.0, 31.6, 33.1, 51.8, 65.3, 68.2, 69.3, 78.7, 86.4, 94.6, 109.1, 127.7, 127.8, 128.4, 137.9, 171.2, 172.7.

IR (neat): ν = 2955, 2935, 2874, 1736, 1456, 1380, 1370 cm^{-1}.

HRMS (FAB, M + Na^+): *m/z* calcd for $C_{26}H_{40}O_7Na$ 487.2672, found 487.2674.

Succinic Acid Allyl Ester (1*R*)-1-Butyl-1-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl] Ester (12)

Following the typical procedure for the succinylation of **10**, the alcohol **10**[16] (48.0 mg, 0.2 mmol) was succinylated with the succinic acid monomallyl ester (**4b**) in place of **4a** to give **12** (57.1 mg, 75%) as a colorless oil (Table 1, entry 11); R_f 0.40 (hexane–/EtOAc, 5:1); $[\alpha]_D$ –1.3 (*c* = 1.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 6.9 Hz, 3 H), 1.25–1.40 (m, 4 H), 1.32 (s, 3 H), 1.43 (s, 3 H), 1.84 (m, 2 H), 1.94 (dd, *J* = 2.8, 2.8 Hz, 1 H), 2.10 (ddd, *J* = 13.8, 10.5, 5.5 Hz, 1 H), 2.27 (ddd, *J* = 13.8, 10.5, 5.5 Hz, 1 H), 2.27–2.40 (m, 2 H), 2.61 (m, 4 H), 3.89 (dd, *J* = 8.3, 6.9 Hz, 1 H), 3.97 (dd, *J* = 8.3, 6.9 Hz, 1 H), 4.57 (dd, *J* = 6.9, 6.9 Hz, 1 H), 4.60 (ddd, *J* = 5.3, 1.4, 1.4 Hz, 1 H), 5.24 (ddt, *J* = 10.6, 1.4, 1.4 Hz, 1 H), 5.32 (ddt, *J* = 17.0, 1.4, 1.4 Hz, 1 H), 5.92 (ddt, *J* = 17.2, 10.6, 5.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.4, 13.9, 23.2, 24.7, 25.4, 26.1, 29.1, 29.1, 29.9, 34.0, 65.3, 65.4, 68.2, 78.3, 84.2, 85.6, 109.2, 118.3, 132.0, 171.2, 171.8.

IR (neat): ν = 3292, 2934, 1736, 1648 cm^{-1}.

HRMS (FAB, M + Na^+): *m/z* calcd for $C_{21}H_{32}O_6Na$ 403.2097, found 403.2098.

Succinic Acid 1,5-Dimethyl-1-vinylhex-4-enyl Ester Methyl Ester (17)

Following the typical procedure for the succinylation of **10**, the alcohol **16** (46.3 mg, 0.3 mmol) was succinylated to give **17** (73.8 mg, 92%) as a colorless oil (Table 2, entry 1); R_f 0.70 (hexane–EtOAc, 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.54 (s, 3 H), 1.59 (br s, 3 H), 1.67 (br s, 3 H), 1.75 (ddd, *J* = 13.7, 10.1, 6.9 Hz, 1 H), 1.84 (ddd, *J* = 13.7, 9.2, 7.3 Hz, 1 H), 1.97 (m, 2 H), 2.60 (br s, 4 H), 3.69 (s, 3 H), 5.08 (tq, *J* = 7.4, 0.9 Hz, 1 H), 5.12 (dd, *J* = 11.0, 0.9 Hz, 1 H), 5.15 (dd, *J* = 17.4, 0.9 Hz, 1 H), 5.96 (dd, *J* = 17.4, 11.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.5, 22.3, 23.5, 25.6, 29.0, 30.1, 39.8, 51.7, 83.4, 113.2, 123.7, 131.8, 141.6, 170.9, 172.8.

IR (neat): ν = 2975, 2929, 1739, 1646 cm^{-1}.

HRMS (FAB, M + Na^+): *m/z* calcd for $C_{15}H_{24}O_4Na$ 291.1572, found 291.1572.

Succinic Acid 1,5-Dimethyl-1-vinylhex-4-enyl Ester Prop-1-ynyl Ester (18)

Following the typical procedure for the succinylation of **10**, the alcohol **16** (46.3 mg, 0.3 mmol) was succinylated with the succinic acid monoallyl ester (**4b**) in place of **4a** to give **18** (85.7 mg, 97%) as a colorless oil (Table 2, entry 2); R_f 0.75 (hexane–EtOAc, 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.54 (s, 3 H), 1.59 (br s, 3 H), 1.67 (br s, 3 H), 1.75 (ddd, *J* = 13.7, 10.1, 6.9 Hz, 1 H), 1.84 (ddd, *J* = 13.7, 9.2, 7.3 Hz, 1 H), 1.97 (m, 2 H), 2.61 (m, 4 H), 4.59 (br d, *J* = 5.5 Hz, 2 H), 5.08 (br t, *J* = 7.0 Hz, 1 H), 5.12 (d, *J* = 11.0 Hz, 1 H), 5.15 (d, *J* = 17.4 Hz, 1 H), 5.23 (br d, *J* = 10.5 Hz, 1 H), 5.31 (br dd, *J* = 17.4, 1.4 Hz, 1 H), 5.90 (ddt, *J* = 17.4, 10.5, 5.5 Hz, 1 H), 5.96 (dd, *J* = 17.4, 11.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.5, 22.3, 23.5, 25.6, 29.1, 30.0, 39.8, 65.3, 83.4, 113.2, 118.3, 123.7, 131.8, 132.0, 141.6, 170.9, 172.0.

IR (neat): ν = 2973, 2931, 1737, 1648 cm^{-1}.

HRMS (FAB, M + Na^+): *m/z* calcd for $C_{17}H_{26}O_4Na$ 317.1729, found 317.1727.

Succinic Acid Methyl Ester 1-Methyl-1-(4-methylcyclohex-3-enyl)ethyl Ester (21)

Following the typical procedure for the succinylation of **10**, the alcohol **20** (46.3 mg, 0.3 mmol) was succinylated to give **21** (74.0 mg, 92%) as a colorless oil (Table 2, entry 3); R_f 0.75 (hexane–EtOAc, 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.42 (s, 3 H), 1.44 (s, 3 H), 1.64 (br s, 3 H), 1.75–1.87 (m, 2H), 1.90–2.18 (m, 5 H), 2.52–2.60 (m, 4 H), 3.69 (s, 3 H), 5.36 (br s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.1, 23.3, 23.3, 23.8, 26.3, 29.1, 30.3, 37.3, 42.7, 51.7, 85.4, 120.2, 133.9, 171.3, 172.9.

IR (neat): ν = 2931, 1732, 1438 cm^{-1}.

HRMS (FAB, M + Na^+): *m/z* calcd for $C_{15}H_{24}O_4Na$ 291.1572, found 291.1573.

Succinic Acid Allyl Ester 1-Methyl-1-(4-methylcyclohex-3-enyl)ethyl Ester (22)

Following the typical procedure for the succinylation of **10**, the alcohol **20** (46.3 mg, 0.3 mmol) was succinylated with the succinic acid monoallyl ester (**4b**) in place of **4a** to give **22** (83.9 mg, 95%) as a colorless oil (Table 2, entry 4); R_f 0.80 (hexane–EtOAc, 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (s, 3 H), 1.44 (s, 3 H), 1.64 (br s, 3 H), 1.75–1.87 (m, 2 H), 1.90–2.07 (m, 5 H), 2.54–2.64 (m, 4 H), 4.59 (d, *J* = 5.5 Hz, 1 H), 5.23 (ddt, *J* = 10.5, 1.4, 1.4 Hz, 1 H), 5.32 (ddt, *J* = 17.4, 1.4, 1.4 Hz, 1 H), 5.36 (br s, 1 H), 5.91 (ddt, *J* = 17.4, 10.5, 5.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.1, 23.3, 23.3, 23.8, 25.1, 29.3, 30.3, 37.3, 42.7, 65.3, 85.4, 118.3, 120.3, 132.1, 133.9, 171.3, 172.1.

IR (neat): ν = 2975, 2930, 1732, 1680, 1650 cm^{-1}.

HRMS (FAB, M + Na^+): *m/z* calcd for $C_{17}H_{26}O_4Na$ 317.1729, found 317.1726.

Succinic Acid Allyl Ester (2*S*,3*R*,6*S*,8*R*,9*S*)-3-Butyl-2-(*tert*-butyldiphenylsilanyloxymethyl)-8-[2-(4-methoxybenzyloxy)-ethyl]-9-methyl-1,7-dioxaspiro[5.5]undec-3-yl ester (25)

Following the typical procedure for the succinylation of **10**, the alcohol **24**[13] (243.2 mg, 0.36 mmol) was succinylated with the succinic acid monoallyl ester (**4b**) in place of **4a** to give **25** (249.6 mg, 85%) as a colorless oil (Table 2, entry 6); R_f 0.50 (hexane–EtOAc, 3:1); $[\alpha]_D$ –6.3 (*c* = 1.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.77 (t, *J* = 6.9 Hz, 3 H), 0.79 (d, *J* = 6.4 Hz, 3 H), 1.05 (s, 9 H), 1.05–2.00 (m, 16 H), 2.27 (m, 1 H), 2.57 (m, 4 H), 3.37 (ddd, *J* = 9.2, 9.2, 5.5 Hz, 1 H), 3.56 (ddd, *J* = 9.2, 9.2, 5.5 Hz, 1 H), 3.67 (ddd, *J* = 7.8, 7.3, 2.7 Hz, 1 H), 3.73 (dd, *J* = 11.0, 4.6 Hz, 1 H), 3.79 (s, 3 H), 3.81 (dd, *J* = 11.0, 6.9 Hz, 1 H), 4.22 (dd, *J* = 6.9, 4.6 Hz, 1 H), 4.28 (d, *J* = 11.5 Hz, 1 H), 4.30 (d, *J* = 11.5 Hz, 1 H), 4.58 (ddd, *J* = 6.0, 1.4, 1.4 Hz, 2 H), 5.23 ((ddt, *J* = 10.5, 1.4, 1.4 Hz, 1 H), 5.31 (ddt, *J* = 17.0, 1.4, 1.4 Hz, 1 H), 5.90 (ddt, *J* = 17.0, 10.5, 6.0 Hz, 1 H), 6.85 (d, *J* = 8.7 Hz, 2 H), 7.21 (d, *J* = 8.7 Hz, 2 H), 7.3–7.8 (m, 10 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.8, 17.8, 19.1, 22.9, 24.5, 25.2, 26.8, 27.5, 29.2, 30.1, 32.8, 32.8, 33.2, 34.2, 34.6, 55.2, 63.7, 65.3, 67.1, 72.5, 73.6, 77.6, 83.5, 95.9, 113.7, 118.3, 127.7, 129.1, 129.7, 130.9, 132.1, 133.3, 133.6, 135.6, 135.7, 159.0, 171.1, 171.9.

IR (neat): ν = 2956, 2860, 1736, 1650, 1614, 1589, 1514 cm^{-1}.

HRMS (FAB, M + Na^+) *m/z* calcd for $C_{48}H_{66}O_9Na$ 837.4374, found 837.4378.

Succinic Acid Allyl Ester (2*S*,3*R*,6*R*,8*R*,9*S*)-3-Butyl-2-(*tert*-butyldiphenylsilanyloxymethyl)-8-[2-(4-methoxybenzyloxy)-ethyl]-9-methyl-1,7-dioxaspiro[5.5]undec-3-yl Ester (27)

Following the typical procedure for the succinylation of **10**, the alcohol **26**[13] (182.8 mg, 0.27 mmol) was succinylated with the succinic acid monoallyl ester (**4b**) in place of **4a** to give **27** (167.8 mg, 76%) as a colorless oil (Table 2, entry 7); R_f 0.53 (hexane–EtOAc, 3:1); $[\alpha]_D$ +0.4 (*c* = 1.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 6.9 Hz, 3 H), 0.84 (d, *J* = 6.4 Hz, 3 H), 1.06 (s, 9 H), 1.10–2.08 (m, 16 H), 2.20 (m, 1 H), 2.27–2.54 (m, 4 H), 3.27 (ddd, *J* = 9.6, 9.6, 1.8 Hz, 1 H), 3.69 (m, 1 H), 3.73 (dd, *J* = 11.0, 7.3 Hz, 1 H), 3.79 (m, 1 H), 3.79 (s, 3 H), 3.87 (dd, *J* = 11.0, 3.2 Hz, 1 H), 4.43 (d, *J* = 11.5 Hz, 1 H), 4.48 (d, *J* = 11.5 Hz, 1 H), 4.50 (ddd, *J* = 5.0, 1.4, 1.4 Hz, 2 H), 4.79 (dd, *J* = 7.3, 3.2 Hz, 1 H), 5.19 (ddt, *J* = 10.5, 1.4, 1.4 Hz, 1 H), 5.26 (ddt, *J* = 17.0, 1.4, 1.4 Hz, 1 H), 5.85 (ddt, *J* = 17.0, 10.5, 5.0 Hz, 1 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 7.27 (d, *J* = 8.7 Hz, 2 H), 7.3–7.8 (m, 10 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 17.4, 19.4, 23.1, 25.6, 26.8, 26.9, 27.3, 29.1, 29.4, 30.1, 30.4, 34.0, 34.9, 35.3, 55.2, 62.9, 65.2, 66.8, 72.6, 73.6, 75.2, 83.1, 96.7, 113.7, 118.3, 127.4, 127.5, 129.4, 129.4, 131.1, 132.1, 134.1, 135.8, 160.0, 170.7, 171.9.

IR (neat): ν = 2955, 2859, 1737, 1650, 1614, 1514 cm^{-1}.

HRMS (FAB, M + Na^+): *m*/*z* calcd for $C_{48}H_{66}O_9Na$ 837.4374, found 837.4388.

Succinic Acid Allyl Ester (2*R*,3*S*,6*S*,8*R*,9*S*)-3-Butyl-2-(*tert*-butyldiphenyl-silanyloxymethyl)-8-[2-(4-methoxybenzyloxy)-ethyl]-9-methyl-1,7-dioxaspiro[5.5]undec-3-yl Ester (29)

Following the typical procedure for the succinylation of **10**, the alcohol **28**[17] (28.4 mg, 0.04 mmol) was succinylated with the succinic acid monoallyl ester (**4b**) in place of **4a** to give **29** (25.4 mg, 74%) as a colorless oil (Table 2, entry 8); R_f 0.50 (hexane–EtOAc, 3:1); $[\alpha]_D$ +14.2 (*c* = 1.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.80 (d, *J* = 6.4 Hz, 3 H), 0.81 (t, *J* = 6.9 Hz, 3 H), 1.03 (s, 9 H), 1.05–2.15 (m, 17 H), 2.41–2.60 (m, 4 H), 3.65 (dd, *J* = 10.5, 8.7 Hz, 1 H), 3.69 (ddd, *J* = 9.6, 9.6, 6.0 Hz, 1 H), 3.73 (ddd, *J* = 10.1, 10.1, 2.3 Hz, 1 H), 3.77 (s, 3 H), 3.79 (dd, *J* = 10.5, 0.5 Hz, 1 H), 3.92 (ddd, *J* = 9.6, 9.6, 5.0 Hz, 1 H), 4.49 (s, 2 H), 4.50 (dd, *J* = 8.7, 0.5 Hz, 1 H), 4.54 (ddd, *J* = 6.0, 1.4, 1.4 Hz, 2 H), 5.20 (ddt, *J* = 10.5, 1.4, 1.4 Hz, 1 H), 5.27 (ddt, *J* = 17.0, 1.4, 1.4 Hz, 1 H), 5.85 (ddt, *J* = 17.0, 10.5, 6.0 Hz, 1 H), 6.84 (d, *J* = 8.7 Hz, 2 H), 7.29 (d, *J* = 8.7 Hz, 2 H), 7.30–7.80 (m, 10 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 17.5, 19.1, 23.1, 25.5, 26.7, 26.9, 28.1, 29.2, 30.1, 30.2, 33.3, 34.1, 35.0, 35.1, 55.2, 62.5, 65.3, 68.0, 72.2, 72.7, 73.6, 83.0, 95.1, 113.6, 118.3, 127.6, 127.6, 129.4, 129.4, 129.5, 129.6, 131.1, 132.0, 133.6, 135.6, 135.7, 159.0, 170.6, 171.8.

IR (neat): ν = 2931, 2859, 1737, 1650, 1615, 1588, 1513 cm^{-1}.

HRMS (FAB, M + Na^+): *m*/*z* calcd for $C_{48}H_{66}O_9Na$ 837.4374, found 837.4374.

Conversion of Succinates into the Hemisuccinates; Succinic Acid Mono-(1,1-dimethyl-2-phenylethyl) Ester (32); Typical Procedure

Method A: A 0.55 M solution of PrSLi in HMPA[20] (273 μL, 0.15 mmol) was added to **30** (26.4 mg, 0.1 mmol) at r.t. under N_2. After stirring for 1 h, ice and Et_2O (15 mL) were added to the mixture. The aqueous layer was acidified with 1 N HCl and extracted with EtOAc (4 × 10 mL). The combined extracts were washed with brine and dried ($MgSO_4$). After removal of the solvent, the residue was purified by column chromatography with hexane–EtOAc, (2:1) to give **32** (23.8 mg, 95%) as a colorless solid.

Method B: Pyrrolidine (50 μL, 0.6 mmol) was added to a stirred mixture of **31** (29.0 mg, 0.1 mmol), $Pd(Ph_3P)_4$ (2.9 mg, 2.5 μmol) and Ph_3P (1.3 mg, 5.0 μmol) in CH_2Cl_2 (10 mL) at 0 °C under N_2. After stirring for 1 h, the resulting mixture was diluted with EtOAc (50 mL) and extracted with 2 N aq Na_2CO_3 (6 × 1 mL). The combined extracts were acidified with 1 N HCl (pH 1–3) and extracted with EtOAc (6 × 10 mL). The combined extracts were washed with brine and dried ($MgSO_4$). After removal of the solvent, the residue was purified by column chromatography with hexane–EtOAc, (2:1) to give **32** (23.8 mg, 95%) as a colorless solid; R_f 0.65 (hexane–EtOAc–AcOH, 50:50:1); mp 77–79 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.46 (s, 6 H), 2.56 (m, 4 H), 3.11 (s, 2 H), 7.20–7.40 (m, 5 H).

^{13}C NMR (125 MHz, CD_3OD): δ = 26.0, 29.0, 30.1, 46.2, 82.9, 126.5, 128.0, 130.5, 137.1, 171.5, 178.4.

IR (ATR): ν = 1708, 1230, 1168, 1111 cm^{-1}.

HRMS (FAB, M + Na^+): *m*/*z* calcd for $C_{14}H_{18}O_4Na$ 273.1103, found 273.1109.

Succinic Acid (1*R*)-Mono-{1-butyl-1-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]pent-4-ynyl} Ester (13)

Following the typical procedure for the preparation of **32**, the hemisuccinate **13** was formed from **11** (17.7 mg, 0.05 mmol) and **12** (15.2 mg, 0.04 mmol) as a colorless oil in 94% and 97% yields, respectively; R_f 0.50 (hexane–EtOAc–AcOH, 50:50:1); $[\alpha]_D$ +4.7 (*c* = 0.2, $CHCl_3$).

^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 6.9 Hz, 3 H), 1.25–1.38 (m, 4 H), 1.33 (s, 3 H), 1.43 (s, 3 H), 1.82–1.88 (m, 2 H), 1.95 (dd, *J* = 2.8, 2.8 Hz, 1 H), 2.10 (ddd, *J* = 13.7, 10.1, 6.0 Hz, 1 H), 2.27 (ddd, *J* = 13.7, 10.5, 5.5 Hz, 1 H), 2.30–2.42 (m, 2 H), 2.59 (m, 4 H), 3.89 (dd, *J* = 8.7, 6.9 Hz, 1 H), 3.97 (dd, *J* = 8.7, 7.3 Hz, 1 H), 4.57 (dd, *J* = 7.3, 6.9 Hz, 1 H).

^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 13.4, 13.9, 23.2, 24.6, 25.4, 26.1, 29.0, 30.0, 32.6, 34.0, 65.3, 68.2, 78.3, 84.3, 85.4, 109.2, 171.4, 175.2.

IR (neat): ν = 3309, 2958, 2929, 2857, 1733, 1717, 1457, 1371 cm^{-1}.

HRMS (FAB, M + Na^+): *m*/*z* calcd for $C_{18}H_{28}O_6Na$ 363.1784, found 363.1783.

Succinic Acid Mono-(1,5-dimethyl-1-vinylhex-4-enyl) Ester (19)

Following the typical procedure for the preparation of **32**, the hemisuccinate **19** was formed from **16** (26.8 mg, 0.1 mmol) and **17** (29.4 mg, 0.1 mmol) as a colorless oil in 98% and 96% yields, respectively (Table 2, entries 1, 2); R_f 0.30 (hexane–EtOAc–AcOH, 50:25:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.54 (s, 3 H), 1.59 (br s, 3 H), 1.67 (br s, 3 H), 1.76 (ddd, *J* = 13.7, 10.1, 6.9 Hz, 1 H), 1.84 (ddd, *J* = 13.7, 8.7, 7.8 Hz, 1 H), 1.97 (m, 2 H), 2.61 (m, 4 H), 5.08 (tq, *J* = 6.9, 1.4 Hz, 1 H), 5.12 (d, *J* = 11.0 Hz, 1 H), 5.15 (d, *J* = 17.9 Hz, 1 H), 5.96 (dd, *J* = 17.9, 11.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.5, 22.3, 23.5, 25.6, 28.9, 29.8, 39.8, 83.6, 113.2, 123.7, 131.8, 141.5, 170.9, 173.8.

IR (neat): ν = 2977, 2935, 1733, 1717, 1647, 1413, 1374 cm^{-1}.

HRMS (FAB, M + Na^+): *m*/*z* calcd for $C_{14}H_{22}O_4Na$ 277.1416, found 277.1415.

Succinic Acid Mono-[1-methyl-1-(4-methylcyclohex-3-enyl)ethyl] Ester (23)

Following the typical procedure for the preparation of **32**, the hemisuccinate **23** was formed from **21** (26.8 mg, 0.1 mmol) and **22** (29.4 mg, 0.1 mmol) as a colorless oil in 96% and 96% yields, respectively (Table 2, entries 3,4); R_f 0.30 (hexane–EtOAc–AcOH, 50:25:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (s, 3 H), 1.44 (s, 3 H), 1.64 (br s, 3 H), 1.75–2.08 (m, 7 H), 2.52–2.64 (m, 4 H), 5.36 (br s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.1, 23.3, 23.3, 23.8, 26.3, 29.1, 30.1, 37.3, 42.6, 85.8, 120.2, 133.9, 171.3, 178.2.

IR (neat): ν = 2965, 2935, 1732, 1717, 1370 cm^{-1}.

HRMS (FAB, M + Na^+): *m*/*z* calcd for $C_{14}H_{22}O_4Na$ 277.1416, found 277.1415.

Succinic Acid (2*S*,3*R*,6*S*,8*R*,9*S*)-Mono-{3-butyl-2-[(1*E*,3*E*)-4-carboxy-3-methylbuta-1,3-dienyl]-8-(2-hydroxyethyl)-9-methyl-1,7-dioxaspiro[5.5]undec-3-yl} Ester (35)

Following the typical procedure for the preparation of **32**, the hemisuccinate **35** was formed from **34** (5.8 mg, 0.01 mmol) as a colorless oil in 88% yield; R_f 0.45 (CH_2Cl_2–MeOH, 85:15).

^{1}H NMR (500 MHz, CD_3OD): δ = 0.89 (d, *J* = 6.0 Hz, 3 H), 0.90 (t, *J* = 6.9 Hz, 3 H), 1.10–2.20 (m, 17 H), 2.33 (d, *J* = 0.9 Hz, 3 H), 2.50–2.80 (m, 4 H), 3.51 (m, 1 H), 3.70–3.80 (m, 2 H), 4.68 (d, *J* = 7.8, 1 H), 5.91 (br s, 1 H), 6.43 (dd, *J* = 15.6, 7.8 Hz, 1 H), 6.47 (d, *J* = 15.6, 1 H).

IR (neat): ν = 3500, 2958, 2935, 2855, 1733, 1717, 1610, 1514 cm^{-1}.

HRMS (FAB, M + Na^+): *m*/*z* calcd for $C_{26}H_{40}O_9Na$ 519.2570, found 519.2567.

Succinic Acid (2*S*,3*R*,6*S*,8*R*,9*S*)-Mono-{3-butyl-2-[(1*E*,3*E*)-4-carboxy-3-methylbuta-1,3-dienyl]-8-(4-hydroxy-3-methylbut-2-enyl)-9-methyl-1,7-dioxaspiro[5.5]undec-3-yl} Ester (37)

Following the typical procedure for the preparation of **32**, the hemisuccinate **37** was formed from **36** (6.2 mg, 0.01 mmol) as a colorless oil in 87% yield; R_f 0.45 (CH_2Cl_2–MeOH, 85:15).

^{1}H NMR (500 MHz, CD_3OD): δ = 0.83 (d, *J* = 6.0 Hz, 3 H), 0.89 (t, *J* = 6.9 Hz, 3 H), 1.20–1.90 (m, 16 H), 1.71 (s, 3 H), 2.05 (m, 1 H), 2.31 (d, *J* = 1.4 Hz, 3 H), 2.58–2.70 (m, 4 H), 3.48 (dt, *J* = 9.6, 4.1 Hz, 1 H), 3.97 (s, 2 H), 4.66 (d, *J* = 8.7, 1 H), 5.57 (br t, *J* = 6.4 1 H), 5.92 (br s, 1 H), 6.46 (d, *J* = 15.6 Hz, 1 H), 6.51 (dd, *J* = 15.6, 8.7 1 H).

^{13}C NMR (125 MHz, CD_3OD): δ = 14.1, 14.2, 14.5, 18.1, 23.8, 25.1, 25.5, 28.8, 29.9, 31.1, 32.2, 32.8, 34.4, 35.2, 36.8, 69.0, 76.2, 79.7, 84.2, 97.1, 121.6, 121.9, 134.3, 137.3, 139.1, 152.6, 170.2, 173.4, 175.9.

IR (neat): ν = 3500, 2957, 2935, 2853, 1733, 1715, 1610, 1510 cm^{-1}.

HRMS (FAB, M + Na^+): *m*/*z* calcd for $C_{29}H_{44}O_9Na$ 559.2883, found 559.2875.

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(15) The alcohol **7** was prepared from the known lactone **6**[13] in two steps:(1)LAH, THF, 0 °C (90%);(2)BOMCl, *i*-Pr_2NEt, CH_2Cl_2, 0 °C to r.t. (79%). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 6.7 Hz, 3 H), 1.20–1.80 (m, 10 H), 1.37 (s, 3 H), 1.42 (s, 3 H), 2.03 (s, 1 H), 3.54 (dt, *J* = 9.6, 6.3 Hz, 1 H), 3.60 (dt, *J* = 9.6, 6.3 Hz, 1 H), 3.87 (dd, *J* = 8.2, 7.8 Hz, 1 H), 3.93 (dd, *J* = 7.8, 6.1 Hz, 1 H), 4.03 (dd, *J* = 8.2, 6.1 Hz, 1 H), 4.60 (s, 2 H), 4.75 (s, 2 H), 7.25–7.40 (m, 5 H). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 14.2, 23.3, 23.5, 25.6, 25.8, 26.5, 31.0, 36.6, 64.6, 68.3, 69.3, 72.7, 79.8, 94.5, 108.7, 127.6, 127.7, 128.3, 128.4, 137.8.

(16) The alcohol **10** was prepared from the known amide **9**[13] in four steps:(1)DIBAH, Et_2O, 0 °C (90%);(2)CBr_4, Ph_3P, 2,6-lutidine, CH_2Cl_2, 0 °C (80%);(3)BuLi, THF, –78 °C to r.t. (68%);(4)MeI, $NaHCO_3$, acetone, H_2O, 60 °C (83%). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 6.7, 3 H), 1.22–1.36 (m, 4 H), 1.36 (s, 3 H), 1.42 (s, 3 H), 1.48–1.70 (m, 4 H), 1.97 (dd, *J* = 2.8, 2.8, 1 H), 2.22 (dddd, *J* = 16.6, 9.5, 7.2, 2.8, 1 H), 2.34 (dddd, *J* = 16.6, 9.2, 6.4, 2.8, 1 H), 3.87 (dd, *J* = 7.9, 7.9, 1 H), 3.97 (dd, *J* = 7.9, 6.4, 1 H), 4.06 (dd, *J* = 7.9, 6.4, 1 H). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 12.7, 14.2, 23.3, 25.5, 25.9, 26.4, 33.1, 36.2, 62.5, 64.6, 72.9, 79.4, 84.3, 108.9.

(17) The alcohol **28** was prepared from the enantiomer of the amide **9**[12] using the same procedure for the preparation of **24**[13]: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.77 (d, *J* = 6.4 Hz, 3 H), 0.92 (t, *J* = 6.9 Hz, 3 H), 1.05 (s, 9 H), 1.20–1.80 (m, 16 H), 2.00 (m, 1 H), 3.36 (ddd, *J* = 10.1, 101, 2.3 Hz, 1 H), 3.62 (ddd, *J* = 9.2, 8.7, 6.9 Hz, 1 H), 3.69 (dd, *J* = 9.6, 6.9 Hz, 1 H), 3.73 (ddd, *J* = 9.2, 9.2, 5.0 Hz, 1 H), 3.77 (s, 3 H), 3.77 (dd, *J* = 6.9, 6.0 Hz, 1 H), 3.85 (dd, *J* = 9.6, 6.9 Hz, 1 H), 4.47 (d, *J* = 11.5 Hz, 1 H), 4.52 (d, *J* = 11.5 Hz, 1 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 7.28 (d, *J* = 8.7 Hz, 2 H), 7.30–7.80 (m, 10 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 17.6, 19.1, 23.4, 24.7, 26.8, 28.0, 29.5, 30.6, 33.4, 33.7, 35.0, 35.1, 55.2, 63.6, 67.3, 71.2, 72.2, 72.8, 74.4, 95.0, 113.8, 127.8, 127.8, 129.3, 129.8, 129.9, 130.8, 132.7, 132.8, 135.6, 135.7, 159.1.

(18) The reaction of 2-methyl-1-phenylpropan-2-ol with the succinic acid monomethyl ester (**4a**, 2 equiv), DCC (2.4 equiv) and DMAP (0.1 equiv) in CH_2Cl_2 at r.t. smoothly proceeded to give the methyl succinate **30** after 4.5 h in 98% yield even under atmospheric pressure: ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.45 (s, 6 H), 2.56 (m, 4 H), 3.06 (s, 2 H), 3.68 (s, 3 H), 7.15–7.35 (m, 5 H). The allyl succinate **31** was also prepared using the succinic acid monoallyl ester (**4b**) in the same manner in 96% yield: ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.44 (s, 6 H), 2.58 (m, 4 H), 3.05 (s, 2 H), 4.59 (ddd, *J* = 5.6, 1.4, 1.4, 2 H), 5.23 (ddt, *J* = 10.6, 1.4, 1.4, 1 H), 5.32 (ddt, *J* = 17.2, 1.4, 1.4, 1 H), 5.91 (ddt, *J* = 17.2, 10.6, 5.6, 1 H), 7.15–7.35 (m, 5 H).

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