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Asymmetric Synthesis of α-Alkylidene-β-hydroxy-γ-butyrolactones via Enantioselective Tandem Michael−Aldol Reaction

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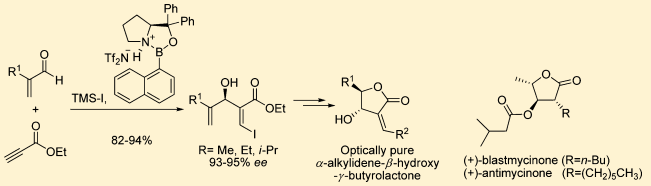
Supporting Information

ABSTRACT: A simple and efficient method for the asymmetric synthesis of α-alkylidene-β-hydroxy-γ-butyrolactones and related natural products was developed on the basis of the catalytic asymmetric tandem Michael−aldol reaction and simple transformations. The synthetic utility of this method was illustrated by the facile synthesis of trisubstituted γ-butyrolactone natural products.



α-Alkylidene-γ-butyrolactones have a rich history across the fields of natural product chemistry, biology, pharmacology, and synthetic organic chemistry. (*Z*)-α-Alkylidene-β-hydroxy-γ-butyrolactone represents an important core structure in many biologically active natural products (Figure 1).[1] Because of its

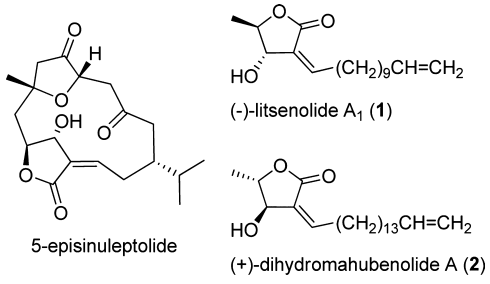


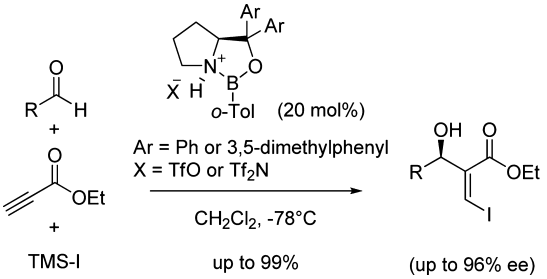
Figure 1. (*Z*)-α-Alkylidene-β-hydroxy-γ-butyrolactones in natural products.

interesting biological activities, such as antitumor and antibiotic properties, synthetic methods for chiral (*Z*)-α-alkylidene-β-hydroxy-γ-butyrolactones have received considerable attention during the past few decades.[2] Among them, catalytic enantioselective methods using Sharpless dihydroxylation[2c] and Corey−Bakshi−Shibata reduction[2d] have been developed.

We recently reported a highly enantioselective and (*Z*)-stereocontrolled Michael−aldol tandem reaction of α,β-acetylenic esters, aldehydes, and trimethylsilyl iodide (TMSI) using chiral cationic oxazaborolidinium catalysts.[3] The reaction provides optically active (*Z*)-β-iodo Morita−Baylis−Hillman (MBH) esters with good to excellent yield and enantioselectivity in a straightforward manner (Scheme 1).[4]

We anticipated that the optically active (*Z*)-β-iodo MBH esters would be suitable precursors for producing various chiral (*Z*)-α-alkylidene-β-hydroxy-γ-butyrolactones through simple transformations. Herein, we introduce a general procedure for producing optically pure (*Z*)-α-alkylidene-β-hydroxy-γ-butyrolactones via a highly enantioselective tandem Michael−aldol reaction and its applications to total synthesis of naturally occurring γ-butyrolactones (Scheme 2).

Scheme 1. Oxazaborolidinium Ion Catalyzed Asymmetric Synthesis of (*Z*)-β-Iodo Morita−Baylis−Hillman (MBH) Ester



Methacrolein **4a** was selected for the initial optimization. Surprisingly, tandem Michael−aldol reactions of α,β-unsaturated aldehyde with oxazaborolidinium catalyst **3a** and **3e** (Figure 2), which successfully catalyzed aromatic and aliphatic aldehydes, afforded only a trace amount of β-iodo MBH ester (Table 1, entry 1 and 2). Replacement of the R group by a smaller methyl group (**3b**) under similar conditions produced the desired product with poor yield and enantioselectivity (Table 1, entry 3). Oxazaborolidinium catalyst has a more sterically demanding 9-phenanthrenyl group (**3c**) and did not activate the aldehyde (Table 1, entry 4). During our investigation, oxazaborolidinium catalyst **3d**[3d,e] was the most suitable for tandem Michael−aldol reaction of methacrolein (Table 1, entry 5). This catalyst furnished (*R*)-β-iodo MBH ester in moderate yield and with excellent enantioselectivity. To improve the yield further, we changed focus to the workup procedure. Unlike the reaction with aromatic aldehydes,

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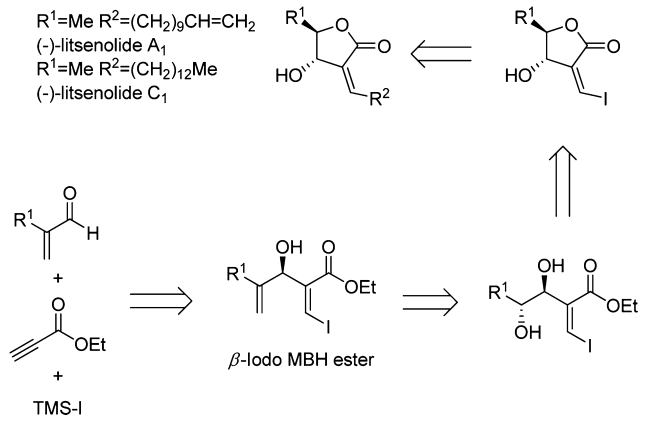
Scheme 2. Retrosynthetic Analysis of Various (*Z*)-α-Alkylidene-β-hydroxy-γ-butyrolactones via β-Iodo MBH Ester



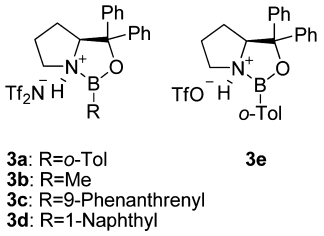
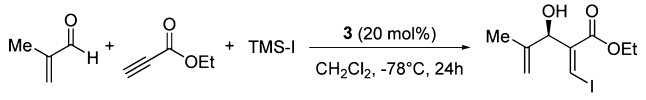


Figure 2. Structure of oxazaborolidinium ion.

Table 1. Oxazaborolidinium Catalyst Screening for Asymmetric (*Z*)-Selective Michael–Aldol Tandem Reaction With Methacrolein



4a 5a

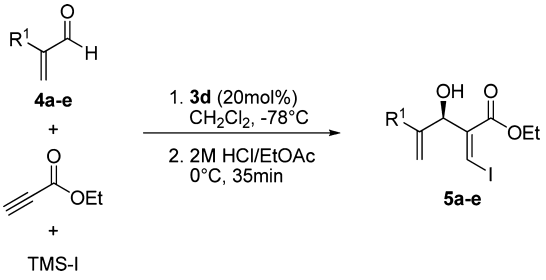
entry	catalyst	yield[a] (%)	ee[b] (%)	*Z*/*E*[c]
1	**3a**	<10	93	
2	**3e**	0		
3	**3b**	29	5	>99/1
4	**3c**	0		
5	**3d**	63	94	>99/1
6[d]	**3d**	81	94	>99/1
7[e]	**3d**	94	94	>99/1

[a]Isolated yield. [b]The ee was determined by chiral GC analysis. [c]Only (*Z*)-isomer was observed. [d]Reaction was quenched with 2 M aq HCl/EtOAc (1:1) and stirred for 20 min at rt. [e]Reaction was quenched with 2 M aq HCl/EtOAc (1:1) and stirred for 35 min at 0 °C.

tandem Michael–aldol reactions with α,β-unsaturated aldehyde afforded a mixture of alcohol **5a** and corresponding trimethylsilyl (TMS) ether. Acidic workup with 2 M HCl at room temperature successfully removed the TMS group and gave the desired product with improved yield (81%) and without loss of enantiopurity (Table 1, entry 6). Careful deprotection at 0 °C furnished (*R*)-(*Z*)-β-iodo MBH ester with excellent yield and enantioselectivity (Table 1, entry 7).

After optimizing reaction conditions for the asymmetric (*Z*)-selective Michael–aldol tandem reaction, the reaction's scope was investigated using α-substituted acrolein. Excellent yields, enantiomeric excess values, and *Z*/*E* selectivities were obtained in all cases regardless of steric congestion at the α-position (Table 2).

Table 2. Result of Asymmetric (*Z*)-Selective Michael–Aldol Tandem Reaction with α-Substituted Acroleins



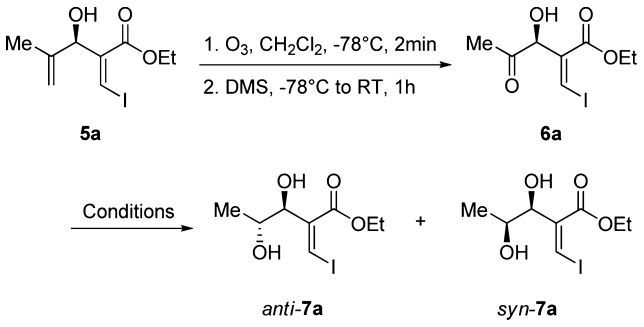
entry		R[1]	time (h)	yield[a] (%)	ee[b] (%)	*Z*/*E*
1	**a**	Me	24	94	94	>99/1
2	**b**	Et	48	84	90	>99/1
3	**c**	*i*-Pr	48	82	95	98/2[c]
4	**d**	*c*-Hex	48	87	95	>99/1
5	**e**	*n*-C_5H_{11}	48	72	85	>99/1

[a]Isolated yield. [b]The ee was determined by chiral GC or HPLC analysis. [c]Determined by isolation.

For the synthesis of (*Z*)-α-alkylidene-β-hydroxy-γ-butyrolactones, oxidative cleavage of (*Z*)-β-iodo MBH ester **5** was carried out with ozone furnished by hydroxy ketone **6**. Unfortunately, silica gel chromatographic separation of the resulting mixture induced partial alcohol racemization. To prevent loss of enantiopurity, crude ketone **6** was used for stereoselective reduction.

To control the relative stereochemistry of diol **7**, several kinds of reducing agent and solvent were tested. We anticipated that high *anti* stereoselectivity would be achieved by strong metal chelation between ketone and alcohol. Initial attemps with $LiBH_4$ and DIBAl-H were unfruitful (Table 3, entry 1 and 2). Under ethereal solvents, $Zn(BH_4)_2$ yielded vicinal diol with

Table 3. Optimization of the *Anti*-Selective Reduction of Ketone (6a)



entry	conditions[a]	yield[b] (%)	*anti*-**7a**/*syn*-**7a**[c]
1	$LiBH_4$, THF, −78 °C	0	
2	DIBAl-H, THF, −78 °C	55	6/1
3	$Zn(BH_4)_2$, Et_2O, −78 °C	50	9/1
4	$Zn(BH_4)_2$, Et_2O, −30 °C	68	12/1
5	$Zn(BH_4)_2$, THF, −78 °C	46	2/1
6	$Zn(BH_4)_2$, THF, −30 °C	72	20/1

[a]The reaction was performed using 1.0 equiv of reducing agent. [b]Isolated yield. [c]The *anti*/*syn* ratio was determined by ^1H NMR analysis.

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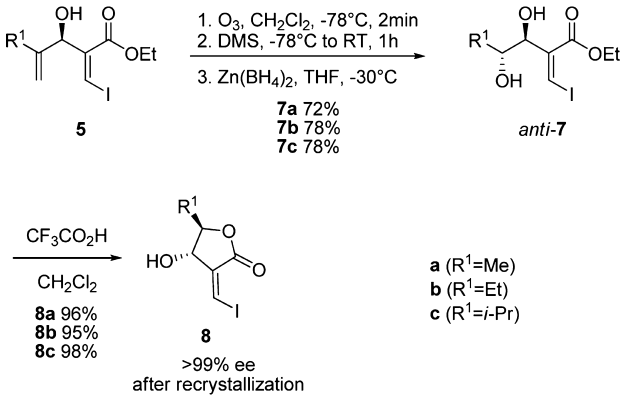
high *anti* selectivity (Table 3, entry 4 and 6).[5] Surprisingly, higher *anti* selectivity was obtained at a higher temperature (−30 °C) rather than at −78 °C (Table 3, entry 3 and 5).

Diol *anti*-**7a** was then converted to (*Z*)-α-iodomethylene-β-hydroxy-γ-lactone **8a** by a trifluoroacetic acid catalyzed intramolecular cyclization with 96% yield. (*Z*)-β-iodo MBH esters **5b** and **5c** subjected to a similar oxidation−reduction−cyclization process gave (Z)-α-alkylidene-β-hydroxy-γ-butyrolactones with excellent overall yields and selectivity. Optically pure and fully functionalized γ-butyrolactones were obtained after one recrystallization (Scheme 3).

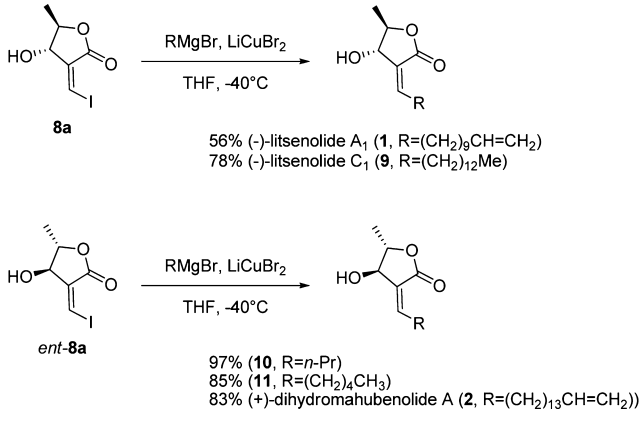
Scheme 3. Synthesis of (*Z*)-α-Iodomethylene-β-hydroxy-γ-lactone



We demonstrated that the iodine atom of β-iodo MBH ester easily converted to alkyl, aryl, and alkynyl groups through transition-metal-catalyzed cross-coupling reactions.[4,6] Thus, enantiopure α-iodomethylene-β-hydroxy-γ-lactone was chosen as a key precursor for (*Z*)-α-alkylidene-β-hydroxy-γ-butyrolactones.

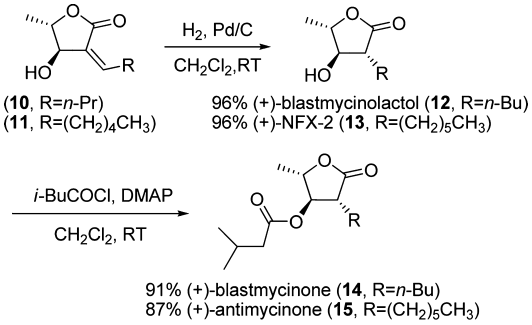
The cross-coupling of **8a** with undec-10-enylmagnesium bromide in the catalytic presence of $LiCuBr_2$ produced (−)-litsenolide A_1 (**1**)[2b,7,8] in 56% yield while coupling with *n*-tridecanylmagnesium bromide afforded (−)-litsenolide C_1 (**9**)[2b,7−9] in 78% yield without changing olefinic geometry (Scheme 4). The spectroscopic data and specific rotation of the synthetic samples of **1** and **9** (^1H, ^{13}C NMR) were in full agreement with those reported in the literature. In the same manner, the cross-coupling of *ent*-**8a** from (*S*)-β-iodo MBH ester[10] with suitable Grignard reagent produced (*Z*)-α-alkylidene butyrolactones **10**, **11**, and (+)-dihydromahubenolide (**2**)[7] in excellent yields of 97%, 85%, and 83%, respectively (Scheme 4).

Scheme 4. Synthesis of (*Z*)-α-Alkylidene-β-hydroxy-γ-butyrolactone Natural Product (−)-Litsenolide A_1, C_1, and (+)-Dihydromahubenolide A



Enantiomerically pure α-alkylidene-β-hydroxy-γ-butyrolactones are particularly useful as synthetic building blocks for trisubstituted γ-butyrolactones. Catalytic hydrogenation of **10** and **11** was achieved to give (+)-blastmycinolactol (**12**) and (+)-NFX-2 (**13**) in 96% yields with complete diastereoselectivity. Under the reported reaction conditions, alcohol acylation using isovaleryl chloride and DMAP furnished the desired natural product (+)-blastmycinone (**14**)[2b,11,12] and (+)-antimycinone (**15**)[2b,11,13] in 91% and 87% yields, respectively (Scheme 5). The spectral data are identical to those reported in the literature.

Scheme 5. Synthesis of (+)-Blastmycinone and (+)-Antimycinone



In conclusion, we suggest a simple and efficient general procedure for synthesizing optically pure (*Z*)-α-alkylidene-β-hydroxy-γ-butyrolactones and related natural products. By using (*Z*)-α-alkylidene-β-hydroxy-γ-butyrolactone as the key intermediate, we synthesized trisubstituted γ-butyrolactone natural products in short steps and with high overall yield.

EXPERIMENTAL SECTION

^1H and ^{13}C NMR were measured at 300 and 75 MHz in $CDCl_3$, respectively. HRMS were obtained on a double-focusing magnetic sector mass spectrometer

General Procedure for (*R*)-β-Iodo MBH Ester 5. A freshly prepared solution of trifluoromethanesulfonimide in CH_2Cl_2 (0.20 M solution, 1.25 mL, 0.25 mmol) was added dropwise to an (*S*)-oxazaborolidine (0.3 mmol) in 6 mL of CH_2Cl_2 at −40 °C under nitrogen. After the mixture was stirred for 15−20 min, a pale yellow homogeneous solution of (*S*)-oxazaborolidinium was obtained. α-Substituted acrolein (**4**, 1.25 mmol) was then added in one portion to the cooled (−78 °C) solution of catalyst. After 20 min of stirring at −78 °C, ethyl propiolate (6.25 mmol, 0.63 mL) and TMSI (1.5 mmol, 215 μL) were added to the mixture sequentially. After reaction completion, the reaction mixture was quenched with aq HCl (2 M, 6 mL) and ethyl acetate (6 mL) and vigorously stirred for 35 min at 0 °C. After complete removal of TMS group, the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried (Na_2SO_4), and filtered, and the solvent was removed under reduced pressure to produce the crude product. Purification by flash chromatography on silica gel (hexane/ethyl acetate = 10:1) afforded the corresponding (*R*)-(*Z*)-β-iodo MBH ester **5** as a colorless oil.

(*R*,*Z*)-Ethyl 3-Hydroxy-2-(iodomethylene)-4-methylpent-4-enoate (5a). Prepared according to the general procedure. Colorless oil, 94% yield (1.18 mmol, 348 mg). ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (t, *J* = 7.2 Hz, 3H), 1.70 (d, *J* = 0.3 Hz, 3H), 2.67 (d, *J* = 6.0 Hz,

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1H), 4.29 (q, J = 7.2 Hz, 2H), 4.88 (d, J = 6.0 Hz, 1H), 4.98−4.99(m, 1H), 5.08 (d, J = 0.6 Hz, 1H), 7.18 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ: 14.1, 18.3, 61.6, 77.7, 85.5, 113.5, 143.6, 144.4, 166.2. IR ν_{max}: 3454, 2981, 1714, 1304, 1188, 1044, 906, 738 cm^{-1}. LRMS (APCI): m/z = 297 (M + 1, 4), 279 (100), 246 (30), 152 (35), 124 (33). HRMS (EI): m/z calcd for $C_9H_{13}IO_3$ 295.9909, found 295.9906. GC: Cyclosil-B, 130 °C, flow: 3 mL/min, t_R = 44.7 min (minor) and t_R = 46.4 min (major). $[\alpha]^{20}_D$ = −10.76 (c 1.0, $CHCl_3$).

(*R*,*Z*)-Ethyl 3-Hydroxy-2-(iodomethylene)-4-methylenehexanoate (5b). Prepared according to the general procedure. Colorless oil, 84% yield (1.05 mmol, 326 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (t, J = 7.5 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H), 1.92−2.14 (m, 2H), 2.78 (br s, 1H), 4.28 (q, J = 7.2 Hz, 2H), 4.91 (d, J = 6.3 Hz, 1H), 4.99(m, 1H), 5.11−5.12 (m, 1H), 7.19 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.1, 14.2, 24.7, 61.6, 77.3, 85.6, 111.1, 144.6, 149.6, 166.3. IR ν_{max}: 3494, 2971, 1715, 1371, 1188, 1036, 909, 736 cm^{-1}. LRMS (APCI): m/z = 310 (M + 1, 3), 295 (51), 249 (64), 166 (53), 123 (51), 93 (100), 91 (87). HRMS (FAB): m/z calcd for $C_{10}H_{16}IO_3^+$ 311.0144, found 311.0143. GC: Cyclosil-B, 150 °C, flow: 3 mL/min, t_R = 30.8 min (minor) and t_R = 31.6 min (major). $[\alpha]^{20}_D$ = 2.40 (c 0.64, $CHCl_3$).

(*R*,*Z*)-Ethyl 3-Hydroxy-2-(iodomethylene)-5-methyl-4-methylenehexanoate (5c). Prepared according to the general procedure. Colorless oil, 82% yield (1.02 mmol, 332 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (d, J = 6.9 Hz, 3H), 1.07 (t, J = 6.9 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H), 2.28 (spd, J_{AB} = 6.9 Hz, J_{AC} = 0.9 Hz, 1H), 2.55 (d, J = 6.9, 1H), 4.28 (q, J = 7.2 Hz, 2H), 4.94 (dt, J_{AB} = 6.9 Hz, J_{AC} = 0.9 Hz, 1H), 5.04 (m, 1H), 5.11 (m, 1H), 7.22 (d, J = 1.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2, 22.4, 22.8, 30.6, 61.6, 76.3, 85.9, 110.2, 114.8, 154.9, 166.3. IR: ν_{max} 3503, 2964, 2097, 1716, 1312, 1188, 1033, 951 cm^{-1}. LRMS (APCI): m/z = 325 (M + 1, 2), 295 (17), 249 (20), 180 (26), 124 (45), 107 (54), 105 (100). HRMS (EI): m/z calcd for $C_{11}H_{18}IO_3^+$ 325.0301, found 325.0302. GC: Cyclosil-B, 130 °C, flow: 3 mL/min, t_R = 49.5 min (minor) and t_R = 51.5 min (major). $[\alpha]^{20}_D$ = 21.23 (c +2.61, $CHCl_3$).

(*R*,*Z*)-Ethyl 4-Cyclohexyl-3-hydroxy-2-(iodomethylene)pent-4-enoate (5d). Prepared according to the general procedure. Colorless oil, 87% yield (1.09 mmol, 396 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.11−1.29 (m, 5H), 1.32 (t, J = 7.2 Hz, 3H), 1.67−1.77 (m, 5H), 1.88 (tt, J_{AB} = 11.1 Hz, J_{AC} = 3.0 Hz, 1H), 2.70 (d, J = 6.6, 1H), 4.27 (q, J = 7.2 Hz, 2H), 4.93 (d, J = 6.6 Hz, 1H), 5.00 (s, 1H), 5.09 (s, 1H), 7.22 (d, J = 1.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2, 26.3, 26.78, 26.83, 33.0, 33.5, 41.0, 61.5, 76.2, 85.6, 110.9, 144. 8, 154.1, 166.3. IR: ν_{max} 3486, 2925, 2852, 1714, 1447, 1310, 1281, 1131, 1033, 891 cm^{-1}. LRMS (APCI): m/z = 365 (M + 1, 3), 347 (44), 282 (77), 219 (27), 173 (36), 145 (100), 117 (45). $[\alpha]^{20}_D$ = 6.2 (c 2.05, $CHCl_3$). HRMS (FAB): m/z calcd for $C_{14}H_{22}IO_3^+$ 365.0614, found 365.0612. HPLC: Chiralcel OD-H, n-hexane/(n-hexane/2-propanol = 1:9) = 80:20, 1.0 mL/min, 256 nm UV detector, t_R = 10.3 min (major) and t_R = 11.1 min (minor).

(*R*,*Z*)-Ethyl 3-Hydroxy-2-(iodomethylene)-4-methylenenonanoate (5e). Prepared according to the general procedure. Colorless oil, 72% yield (0.90 mmol, 319 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J = 6.6 Hz, 3H), 1.24−1.35 (m, 4H), 1.33 (t, J = 7.2 Hz, 3H), 1.40−1.49 (m, 2H), 1.89−2.09 (m, 2H), 2.96 (d, J = 6.3, 1H), 4.27 (q, J = 7.2 Hz, 2H), 4.89 (d, J = 6.0 Hz, 1H), 4.98 (s, 1H), 5.10 (s, 1H), 7.18 (d, J = 0.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.11, 14.14, 22.6, 27.5, 31.6, 31.9, 61.5, 77.0, 85.5, 112.0, 144.7, 148.2, 166.3. IR: ν_{max} 3471, 2929, 1714, 1307, 1186, 1039, 908, 732 cm^{-1}. LRMS (APCI): m/z = 353 (M + 1, 2), 335 (78), 208 (44), 179 (33), 133 (100), 105 (93). $[\alpha]^{20}_D$ = 1.3 (c 1.29, $CHCl_3$). HRMS (FAB): m/z calcd for $C_{13}H_{22}IO_3^+$ 353.0614, found 353.0614. HPLC: Chiralcel OD-H, n-hexane/(n-hexane/2-propanol = 1:9) = 95:5, 1.0 mL/min, 256 nm UV detector, t_R = 28.0 min (minor) and t_R = 30.2 min (major).

General Procedure for the Synthesis of *anti*-Diol 7. To a solution of **5** (1.84 mmol) in 30 mL of HPLC-grade CH_2Cl_2 was cooled to −78 °C and ozonolyzed until color of reaction mixture converted to blue (<2 min). The resulting solution was treated with dimethyl sulfide (5 mL), stirred for 50 min at −78 °C and 10 min at rt with N_2 bubbling, and then quenched with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phase was dried over Na_2SO_4, filtered, and concentrated. Without column chromatography, the reduction was performed with crude product.

The crude product in 15 mL of THF was cooled to −30 °C and zinc borohydride (1.0 M in THF, 1.84 mL, 1.84 mmol, 1.0 equiv) added. The reaction was monitored by TLC. The reaction mixture was quenched with ammonium chloride (5 mL) and extracted with ethyl acetate (3 × 10 mL). Purification by flash column chromatography (hexane/ethyl acetate = 2:1) afforded the desired product **7** as a colorless oil.

(3*S*,4*R*,*Z*)-Ethyl 3,4-Dihydroxy-2-(iodomethylene)-pentanoate (*anti*-7a). Prepared according to the general procedure. Colorless oil, 72% yield (1.32 mmol, 378 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.17 (d, J = 6.6 Hz, 3H), 1.38 (t, J = 7.2 Hz, 3H), 2.14 (d, J = 5.7 Hz, 1H), 2.89 (d, J = 5.7 Hz, 1H), 3.93−3.98 (m, 1H), 4.33 (q, J = 7.2 Hz, 2H), 4.33−4.38 (m, 1H), 7.17 (d, J = 0.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2, 18.0, 62.0, 69.3, 78.6, 86.2, 143.5, 167.0. IR: ν_{max} 3435, 2980, 2927, 1710, 1314, 1191, 1072, 1015 cm^{-1}. LRMS (APCI): m/z = 301 (M + 1, 1), 289 (8), 197 (7), 127 (100). HRMS (FAB): m/z calcd for $C_8H_{14}IO_4^+$ 300.9937, found 300.9939. $[\alpha]^{20}_D$ = 10.26 (c 1.0, $CHCl_3$).

(3*S*,4*R*,*Z*)-Ethyl 3,4-Dihydroxy-2-(iodomethylene)hexanoate (*anti*-7b). Prepared according to the general procedure. Colorless oil, 78% yield (1.44 mmol, 451 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.98 (t, J = 7.5 Hz, 3H), 1.38 (t, J = 7.2 Hz, 3H), 1.46−1.61 (m, 1H), 2.68 (br s, 1H), 3.47 (br d, J = 5.4 Hz, 1H), 3.60−3.66 (m, 1H), 4.32 (q, J = 7.2 Hz, 2H), 4.39 (br t, J = 4.2 Hz, 1H), 7.14 (d, J = 0.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.4, 14.2, 25.0, 62.0, 74.8, 77.8, 85.9, 144.0, 167.25. IR: ν_{max} 3444, 2968, 2935, 2878, 1708, 1306, 1019, 978, 735 cm^{-1}. LRMS (APCI): m/z = 315 (M + 1, 4), 282 (100), 251 (57), 223 (49), 205 (19), 149 (28). HRMS (FAB): m/z calcd for $C_9H_{16}IO_4^+$ 315.0093, found 315.0092. $[\alpha]^{20}_D$ = 22.9 (c 1.79, $CHCl_3$).

(3*S*,4*R*,*Z*)-Ethyl 3,4-Dihydroxy-2-(iodomethylene)-5-methylhexanoate (*anti*-7c). Prepared according to the general procedure. Colorless oil, 78% yield (1.44 mmol, 471 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94 (d, J = 6.6 Hz, 3H), 0.96 (d, J = 6.6 Hz, 3H), 1.39 (t, J = 7.2 Hz, 3H), 1.79−1.92 (m, 1H), 2.30 (d, J = 5.7 Hz, 1H), 3.15 (d, J = 6.9 Hz, 1H), 3.44 (q, J = 5.7 Hz, 1H), 4.34 (q, J = 7.2 Hz, 2H), 4.39 (t, J = 6.3 Hz, 1H), 7.12 (d, J = 0.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2, 16.8, 19.7, 29.7, 62.0, 76.8, 78.2, 85.9, 144.8, 167.7. IR: ν_{max} 3452, 2964, 2875, 1708, 1307, 1192, 1008, 734 cm^{-1}. LRMS (APCI): m/z = 329 (M + 1, 6), 318 (26), 290 (38), 282 (90), 265 (100), 209 (65), 149 (58), 109 (73). HRMS (FAB): m/z calcd for $C_{10}H_{18}IO_4^+$ 329.0250, found 329.0249. $[\alpha]^{20}_D$ = 11.0 (c 2.00, $CHCl_3$).

General Procedure for the Synthesis of (*Z*)-α-Iodomethylene-β-hydroxy-γ-butyrolactones 8. To *anti*-diol 7 (1.24 mmol) in CH_2Cl_2 (20 mL) was added a CF_3COOH (0.62 mmol). The reaction was stirred under the indicated conditions and monitored by TLC. After completion of the reaction, trifluoroacetic acid was quenched with saturated aqueous $NaHCO_3$ (5 mL), and the product was extracted with CH_2Cl_2 (3 × 5 mL) and dried with Na_2SO_4. The volatiles were evaporated, and the residue was purified on silica gel (hexane/ethyl acetate = 3:1) to give **8** as a white solid which was recrystallized from dichloromethane/hexanes to afford enantiopure **8**.

(4*S*,5*R*,*Z*)-4-Hydroxy-3-(iodomethylene)-5-methyldihydrofuran-2(3*H*)-one (8a). The reaction was refluxed for 3 h. Flash chromatography purification afforded the desired product as a white solid, 96% yield (1.19 mmol, 302 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (d, J = 6.9 Hz, 3H), 2.21 (d, J = 6.9 Hz, 1H), 4.30 (dq, J_{AB} = 6.3 Hz, J_{AC} = 4.8 Hz, 1H), 4.54 (ddd, J_{AB} = 6.9 Hz, J_{AC} = 4.8 Hz, J_{AD} = 1.8 Hz, 1H), 7.75 (d, J = 1.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.8, 78.1, 81.8, 92.8, 141.0, 168.8. IR: ν_{max} 3707, 3511, 2969, 2864, 1736, 1171, 1053 cm^{-1}. LRMS (APCI): m/z 255 (M + 1, 100), 256 (7), 237 (75), 209 (21). HRMS (EI): m/z calcd for $C_6H_7IO_3$ 253.9440, found 253.9437. Mp: 102−104 °C. $[\alpha]^{20}_D$ = 10.75 (c 1.0, MeOH). HPLC: Chiralcel AS-H column, n-hexane/2-propanol = 85:15, 1.0 mL/min, 256 nm UV detector, t_R = 12.07 min (major) and t_R = 14.23 min (minor).

(4*S*,5*R*,*Z*)-5-Ethyl-4-hydroxy-3-(iodomethylene)dihydrofuran-2(3*H*)-one (8b). The reaction was stirred at room temperature

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for 2.5 h. Flash chromatography purification afforded the desired product as white solid, 95% yield (1.18 mmol, 316 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (t, J = 7.2 Hz, 3H), 1.65−1.87 (m, 2H), 2.28 (br s, 1H), 4.10−4.16 (m, 1H), 4.52 (dd, J_{AB} = 4.5 Hz, J_{AC} = 1.8 Hz, 1H), 7.76 (d, J = 1.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 9.4, 26.5, 75.8, 85.3, 94.2, 139.1, 167.5. IR: ν_{max} 3427, 3050, 2970, 2937, 1742, 1623, 1165, 1081, 968, 657 cm^{-1}. LRMS (APCI): m/z 269 (M + 1, 27), 251 (93), 223 (84), 163 (51), 149 (91), 135 (100), 121 (83). HRMS (FAB): m/z calcd for $C_7H_{10}IO_3^+$ 268.9675, found 268.9675. Mp: 40 °C. $[\alpha]^{20}_D$ = 5.58 (c 1.35, $CHCl_3$). HPLC: Chiralcel AS-H column, n-hexane/2-propanol = 85:15, 1.0 mL/min, 256 nm UV detector, t_R = 11.57 min (major) and t_R = 14.97 min (minor).

(4*S*,5*R*,*Z*)-4-Hydroxy-3-(iodomethylene)-5-isopropyldihydrofuran-2(3*H*)-one (8c). The reaction was stirred at room temperature for 45 min. Flash chromatography purification afforded the desired product as white solid, 98% yield (1.21 mmol, 343 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.01 (d, J = 2.1 Hz, 3H), 1.04 (d, J = 2.1 Hz, 3H), 1.85−2.01 (m, 1H), 2.29 (br s, 1H), 3.95 (dd, J_{AB} = 6.6 Hz, J_{AC} = 4.8 Hz, 1H), 4.59 (br s, 1H), 7.77 (d, J = 1.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.7, 17.9, 31.3, 74.0, 88.7, 94.3, 139.3, 167.5. IR: ν_{max} 3445, 2966, 2876, 1741, 1622, 1165, 1004, 825, 672 cm^{-1}. LRMS (APCI): m/z 283 (M + 1, 22), 282 (89), 209 (70), 149 (100), 121 (57). HRMS (FAB): m/z calcd for $C_8H_{12}IO_3^+$ 282.9831, found 282.9834. mp: 50 °C. $[\alpha]^{20}_D$ = 7.12 (c 1.38, $CHCl_3$). HPLC: Chiralcel AS-H column, n-hexane/2-propanol = 85:15, 1.0 mL/min, 256 nm UV detector, t_R = 10.30 min (major) and t_R = 12.40 min (minor).

(*S*,*Z*)-Ethyl 3-Hydroxy-2-(iodomethylene)-4-methylpent-4-enoate (*ent*-5a). Prepared according to the general procedure for **5a**. Colorless oil, 94% yield (1.18 mmol, 348 mg). GC: Cyclosil-B, 130 °C, flow: 3 mL/min, t_R = 38.1 min (major) and t_R = 40.1 min (minor). $[\alpha]^{20}_D$ = 10.93 (c 1.16 $CHCl_3$)

(3*R*,4*S*,*Z*)-Ethyl 3,4-Dihydroxy-2-(iodomethylene)-pentanoate (*ent*-7a). Prepared according to the general procedure for **7**. Colorless oil, 72% yield (two steps). $[\alpha]^{20}_D$ = −10.5 (c 1.0 $CHCl_3$)

(4*R*,5*S*,*Z*)-4-Hydroxy-3-(iodomethylene)-5-methyldihydrofuran-2(3*H*)-one (*ent*-8a). Prepared according to the general procedure for **8**. White solid, 96% yield. $[\alpha]^{20}_D$ = −10.79 (c 1.11 $CHCl_3$).

General Procedure for the Synthesis of (*Z*)-α-Alkylidene-β-hydroxy-γ-butyrolactones. A THF solution (3 mL) of vinyl iodide (0.31 mmol) was cooled to −40 °C, $LiCuBr_2$ (0.5 M in THF, 0.13 mL, 0.065 mmol) added, and then alkylmagnesium bromide (1.0 M in THF, 0.94 mL, 0.94 mmol) slowly added dropwise. The resulting solution was quenched by addition of NH_4Cl (2 mL) and H_2O (1 mL) and stirred while the aqueous layer turned blue. The organic layer was extracted with ethyl acetate (2 mL) and CH_2Cl_2 (2 × 2 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by silica gel (hexane/ethyl acetate = 5:1) to afford the desired product.

(−)-Litsenolide A_1 (1). Prepared according to the general procedure to afford the desired product (−)-litsenolide A_1 (**1**) in 56% yield (24 mg, 0.086 mmol) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28−1.54 (br, 14H), 1.38 (d, J = 6.3 Hz, 3H), 2.04 (br q, J = 6.6 Hz, 2H), 2.38 (br, 1H), 2.75 (m, 2H), 4.3−4.4 (m, 2H), 4.93 (dq, J_{AB} = 10.2 Hz, J_{AC} = 1.2 Hz, 1H), 4.99 (m, 1H), 5.81 (ddt, J_{AB} = 17 Hz, J_{AC} = 10.2 Hz, J_{AD} = 6.6 Hz, 1H), 6.54 (td, J_{AB} = 7.8 Hz, J_{AC} = 1.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.3, 27.9, 28.96, 29.05, 29.2, 29.4, 29.5, 29.6, 33.9, 75.7, 81.5, 114.2, 128.9, 139.4, 149.6, 168.5. IR: ν_{max} 3434, 3075, 2980, 2924, 2855, 2361, 1742, 1178, 1112, 1051, 913 cm^{-1}. LRMS (APCI): m/z 281 (M + 1, 100), 282 (24), 263 (55), 217 (18), 147 (11). HRMS (EI): m/z calcd for $C_{17}H_{28}O_3$ 280.2038, found 280.2038. $[\alpha]^{20}_D$ = −15.79 (c 0.7, dioxane; lit.[7] $[\alpha]^{24}_D$ = −2.4, dioxane). HPLC: Chiralcel OD-H column, n-hexane/2-propanol =95:5, 1.0 mL/min, 256 nm UV detector, t_R = 9.97 min (major) and t_R = 14.57 min (minor).

(-)-Litsenolide C_1 (9). Prepared according to the general procedure to afford of the desired product (−)-litsenolide C_1 (**9**) in 78% yield (28 mg, 0.092 mmol) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, J = 6.3 Hz, 3H), 1.18−1.36 (br, 20H), 1.38 (d, J = 6.3 Hz, 3H), 1.42−1.51 (m, 1H), 1.51−1.62 (m, 1H), 2.26 (br, 1H), 2.75 (m, 2H), 3.64(m, 1H), 4.3−4.4 (br, 1H), 6.54 (td, J_{AB} = 7.5 Hz, J_{AC} = 1.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 19.5, 23.0, 28.2, 29.2, 29.6, 29.7, 29.8, 29.9, 29.98 (×2), 30.01 (×2), 32.2, 75.9, 81.7, 129.1, 149.7, 168.7. IR: ν_{max} 3708, 3455, 2918, 2851, 1730, 1256, 1055 cm^{-1}. LRMS (APCI): m/z 311 (M + 1, 100), 312 (14), 294(4), 293 (22), 247 (5). HRMS (EI): m/z calcd for $C_{19}H_{34}O_3$ 310.2508, found 310.2507. $[\alpha]^{20}_D$ = −9.70 (c 0.5, dioxane; lit.[7] $[\alpha]^{24}_D$ = −9.4, dioxane). Mp: 160−162 °C.

(4*R*,5*S*,*Z*)-3-Butylidene-4-hydroxy-5-methyldihydrofuran-2(3*H*)-one (10). Prepared according to the general procedure to afford of the desired product **10** in 97% yield (30 mg, 0.179 mmol) as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (t, J = 7.5 Hz, 3H), 1.39 (d, J = 6.3 Hz, 3H), 1.50 (qt, J_{AB} = 7.5 Hz, J_{AC} = 7.5 Hz, 2H), 2.6−2.84 (m, 2H), 3.07 (d, J = 4.5 Hz, 1H) 4.37 (br, 2H), 6.56 (td, J_{AB} = 7.8 Hz, J_{AC} = 1.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 19.2, 22.2, 75.5, 81.6, 129.0, 149.4, 168.9. IR: ν_{max} 3432, 2929, 1741, 1673, 1373, 1195, 1124, 1046, 931 cm^{-1}. LRMS (APCI): m/z 170 (M + 1, 17), 153 (74), 149 (39), 135 (30), 125 (41). HRMS (FAB): m/z calcd for $C_9H_{15}O_3$ 171.1021, found 171.1024. HPLC: Chiralcel OD-H column, n-hexane/2-propanol = 9:1, 1.0 mL/min, 256 nm UV detector, T_R = 8.13 min (major) and t_R = 7.43 min (minor). $[\alpha]^{20}_D$ = 18.19 (c 1.18, $CHCl_3$).

(4*R*,5*S*,*Z*)-3-Hexylidene-4-hydroxy-5-methyldihydrofuran-2(3*H*)-one (11). Prepared according to the general procedure to afford of the desired product **11** in 85% yield (72 mg, 0.36 mmol) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J = 6.9 Hz, 3H), 1.35 (br m, 6H), 1.38 (d, J = 6.3 Hz, 3H), 1.42−1.56 (m, 2H), 2.11 (s, 1H), 2.72 (m, 2H), 4.35 (br m, 2H), 6.56 (td, J_{AB} = 7.8 Hz, J_{AC} = 1.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 19.2, 22.5, 27.8, 28.6, 31.4, 75.6, 81.4, 128.8, 149.5, 168.3. IR: ν_{max} 3847, 3449, 2958, 2925, 2858, 1737, 1673, 1184, 1051 cm^{-1}. LRMS (APCI): m/z 197 (M − 1, 100), 198 (17), 181 (17), 153 (9), 138 (11). HRMS (EI): m/z calcd for $C_{11}H_{18}O_3$ 198.1256, found 198.1258. HPLC: Chiralcel OD-H column, n-hexane/2-propanol = 9:1, 1.0 mL/min, 256 nm UV detector, t_R = 13.60 min (major) and t_R = 10.77 min (minor). $[\alpha]^{20}_D$ = −20.14 (c 0.7, $CHCl_3$).

(+)-Dihydromahubenolide (2). Prepared according to the general procedure to afford the desired product (+)-dihydromahubenolide (**2**) in 83% yield (88 mg, 0.26 mmol) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, J = 6.8 Hz, 3H), 1.25 (br m, 18H), 1.39 (d, J = 6.3 Hz, 3H), 1.40−1.52 (m, 2H), 2.04 (m, 1H), 2.16 (br s, 1H), 2.75(q, 7.5 Hz, 2H), 4.36 (m, 2H), 4.96 (m, 2H), 5.82 (ddt, J_{AB} = 17 Hz, J_{AC} = 10.2 Hz, J_{AD}= 6.6 Hz, 1H). 6.55 (dt, J_{AB} = 7.8 Hz, J_{AC} = 1.2 Hz, 1H) ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.3, 28.0, 29.0, 29.1, 29.3, 29.4, 29.55, 29.65, 29.68 (×2), 29.76 (×2), 29.79, 34.0, 75.7, 81.5, 114.2, 128.9, 139.4, 149.6, 168.4. IR: ν_{max} 3454, 2917, 2849, 1730, 1208, 1055 cm^{-1}. LRMS (APCI): m/z 337 (M + 1, 100), 338 (30), 320 (23), 319 (68). HRMS (FAB): m/z calcd for $C_{21}H_{37}O_3$ 337.2743, found 337.2742. $[\alpha]^{20}_D$ = 8.51 (c 0.66, dioxane; lit.[7] $[\alpha]^{24}_D$ = 8.5, dioxane).

(+)-Blastmycinolactol (12). To a dichloromethane solution (2 mL) of **10** (20 mg, 0.115 mmol) was added 10% Pd/C (12 mg, 0.012 mmol) and the flask sealed with a hydrogen balloon. The solution was stirred for 3 h at room temperature. The resulting solution was filtered with a Celite bed and concentrated. The crude product was purified by silica gel (hexane/ethyl acetate = 2:1) to afford the (+)-blastmycinolactol (**12**) in 96% yield (19 mg, 0.11 mmol) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (t, J = 7.2 Hz, 3H), 1.3−1.56 (m, 4H), 1.45 (d, J = 6.3 Hz, 3H), 1.56−1.68 (m, 1H), 1.78−1.92 (m, 1H), 2.57 (ddd, J_{AB} = 8.7 Hz, J_{AC} = 7.4 Hz, J_{AD} = 6.0 Hz, 1H), 2.78 (d, J = 5.1 Hz, 1H), 3.78−3.91 (br m, 1H), 4.22 (dq, J_{AB} = 7.1 Hz, J_{AC} = 6.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 18.5, 22.9, 28.4, 29.1, 48.8, 79.1, 80.4, 176.8. IR: ν_{max} 3472, 2946, 2863, 1733, 1186, 1057 cm^{-1}. LRMS (APCI): m/z 173 (M + 1, 29), 155 (57), 149 (28), 109 (100), 69 (26). HRMS: (FAB) m/z calcd for $C_9H_{16}O_3$ 172.1099, found 172.1095. Mp: 49−51 °C. $[\alpha]^{20}_D$ = −25.43 (c 1.08, $CHCl_3$; lit.[11a] $[\alpha]^{25}_D$ = −19.4, c = 1.01, $CDCl_3$).

(+)-Blastmycinone (14). To a CH_2Cl_2 solution (2 mL) of (+)-blastmycinolactol (**12**) (21 mg, 0.122 mmol) were added DMAP

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(59 mg, 0.488 mmol) and isovaleryl chloride (0.096 mL, 0.732 mmol). The mixture was stirred for 24 h at room temperature. The resulting solution was quenched by addition of $NaHCO_3$ (2 mL). The organic layer was extracted with CH_2Cl_2 (3 × 2 mL), and the combined organic layer were dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by silica gel (hexane/ethyl acetate = 10:1) to afford the desired product (+)-blastmycinone (**14**) in 91% yield (28 mg, 0.111 mmol) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (t, J = 7.2 Hz, 3H), 0.97 (d, J = 6.6 Hz, 6H), 1.25−1.45(m, 4H), 1.47(d, J = 6.6 Hz, 3H), 1.65 (m, 1H), 1.86 (m, 1H), 2.12 (m, 1H), 2.23 (d, J = 6.9 Hz, 2H), 2.69 (dt, J_{AB} = 8.1 Hz, J_{AC} = 6.0 Hz, 1H), 4.37 (qd, J_{AB} = 6.6 Hz, J_{AC} = 4.5 Hz, 1H), 4.95 (dd, J_{AB} = 5.7 Hz, J_{AC} = 4.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 19.4, 22.29, 22.33, 22.36, 25.7, 28.9, 29.0, 43.1, 46.4, 78.4, 79.4, 172.5, 176.0. IR: ν_{max} 2959, 2866, 1783, 1740, 1175, 1114, 1036, 752 cm^{-1}. LRMS (APCI): m/z 257 (M + 1, 20), 155 (100), 109 (25). HRMS (FAB): m/z calcd for $C_{14}H_{25}O_4$ 257.1753, found 257.1755. $[\alpha]^{20}_D$ = 11.21 (c 0.7, $CHCl_3$; lit.[11a] $[\alpha]^{25}_D$ = 11.3, c = 1.18, $CHCl_3$).

NFX-2 (13). To a dichloromethane solution (2 mL) of compound **11** (23 mg, 0.115 mmol) was added 10% Pd/C (12 mg, 0.012 mmol) and the flask sealed with a hydrogen balloon. The solution was stirred for 3 h at room temperature. The resulting solution was filtered with a Celite bed and concentrated. The crude product was purified by silica gel (hexane/ethyl acetate = 2:1) to afford the desired product NFX-2 (**13**) in 96% yield (22 mg, 0.11 mmol) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J = 6.9 Hz, 3H), 1.2−1.56 (m, 8H), 1.45 (d, J = 6.3 Hz, 3H), 1.56−1.67 (m, 1H), 1.8−1.92 (m, 1H), 2.49 (d, J = 5.4 Hz, 1H), 2.56 (ddd, J_{AB} = 8.1 Hz, J_{AC} = 7.3 Hz, J_{AD} = 5.6 Hz, 1H), 3.84 (ddd, J_{AB} = 8.1 Hz, J_{AC} = 7.2 Hz, J_{AD} = 5.4 Hz, 1H), 4.21 (dq, J_{AB} = 7.2 Hz, J_{AC} = 6.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 18.2, 22.6, 26.7, 28.5, 29.2, 31.6, 48.6, 79.0, 80.0, 176.3. IR: ν_{max} 3469, 2921, 2857, 1732, 1299, 1186, 1058 cm^{-1}. LRMS (APCI): m/z 201 (M + 1, 100), 183 (91), 165 (40), 149 (39), 137 (86), 95 (46). HRMS: m/z calcd for $C_{11}H_{20}O_3$: 200.1412, found: 200.1410. mp 56−58 °C. $[\alpha]^{20}_D$ = −16.19 (c 1.3, $CHCl_3$; lit.[11a] $[\alpha]^{25}_D$ = −15.1, c 1.20, MeOH).

(+)-Antimycinone (15). To a CH_2Cl_2 solution (2 mL) of NFX-2 (**13**) (22 mg, 0.11 mmol) were added DMAP (54 mg, 0.44 mmol) and isovaleryl chloride (0.08 mL, 0.67 mmol). The mixture was stirred for 24 h at room temperature. The resulting solution was quenched by adding $NaHCO_3$ (2 mL). The organic layer was extracted with CH_2Cl_2 (3 × 2 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by silica gel (hexane/ethyl acetate = 5:1) to afford the desired product (+)-antimycinone (**15**) in 87% yield (27 mg, 0.096 mmol) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, J = 6.6 Hz, 3H), 0.97 (d, J = 6.3 Hz, 6H), 1.22−1.44(m, 8H), 1.47(d, J = 6.6 Hz, 3H), 1.64 (m, 1H), 1.86 (m, 1H), 2.11 (m, 1H), 2.23 (d, J = 6.6 Hz, 2H), 2.69 (dt, J_{AB} = 8.1 Hz, J_{AC} = 5.7 Hz, 1H), 4.37 (qd, J_{AB} = 6.6 Hz, J_{AC} = 4.5 Hz, 1H), 4.95 (dd, J_{AB} = 5.7 Hz, J_{AC} = 4.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2, 19.6, 22.5, 22.7, 25.9, 27.0, 29.1, 29.5, 31.7, 43.3, 46.6, 78.6, 79.6, 172.6, 176.1. IR: ν_{max} 2954, 2866, 1784, 1741, 1175, 1112, 1037 cm^{-1}. LRMS (APCI): m/z 285 (M + 1, 56), 286 (12), 231 (12), 184 (15), 183 (100), 137(18). HRMS (FAB): m/z calcd for $C_{16}H_{29}O_4$ 285.2066, found 285.2064. $[\alpha]^{20}_D$ = 10.64 (c 1.0, $CHCl_3$; lit.[11a] $[\alpha]^{25}_D$ = 10.8, c 0.50, $CHCl_3$).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Chiral GC data for compounds **5**; chiral HPLC data for compounds **1**, **8**; NMR spectra for compounds **1**, **2**, **5**, and **7**−**15**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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