Plant Bioregulators, 2[+]

Syntheses of (±)- and (+)-Sorgolactone, the Germination Stimulant from *Sorghum bicolor*

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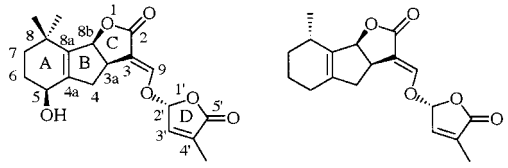
Syntheses of (±)-**2a**, the racemate of the structure proposed for sorgolactone, and its three racemic stereoisomers have been accomplished with confirmation of the stereostructures of the intermediate (±)-**10** and the final product (±)-**2a** by X-ray analysis. Its optically active form, (3a*R*,8*S*,8b*S*,2′*R*)-(+)-**2a**, has also been prepared from (*S*)-(–)-citronellal by employing radical cyclization of **18** to **19** as the key step. Spectroscopic properties of the synthetic products are compared with those reported for natural sorgolactone. Bioassays using clover broomrape (*Orobanche minor*) seeds have revealed that all the stereoisomers strongly stimulate their germination.

Parasitic weeds of the genera *Striga*, commonly known as "witchweed", and *Orobanche* cause severe yield losses in grains and legumes in Africa, Asia, and the U.S.A.[1][2] The seeds of such weeds remain dormant in soil until exudates from their host plants induce germination. (+)-Strigol (**1**, Scheme 1) was first isolated from cotton (a non-host plant) root exudates and was shown to be a strong stimulant for the germination of such seeds.[3] It was later isolated from the host plants of *Striga*, such as maize, proso millet, and sorghum.[4] To date, four stimulants have been isolated from the host plants of the parasitic weeds[5–7] and have been given the general name strigolactones.[8]



Scheme 1. Structures of strigol and sorgolactone

Early syntheses of (±)- and (+)-strigol by Sih[9] and of (±)-strigol by Raphael[10] prompted much interest in the chemistry of germination stimulants, which culminated in the determination of the absolute configuration of naturally occurring (+)-strigol by X-ray analysis.[11] The synthetic endeavor in this area is still remarkable[12][13] and a gram-scale preparation of (+)-strigol reported in the accompanying paper[14] has heralded a new stage in research concerning the problem of parasitic weeds.

In 1992, Hauck et al. isolated a second strigolactone, namely sorgolactone, from *Sorghum bicolor*, a genuine host plant for *Striga asiatica* and *Striga hermonthica*, as the potent germination stimulant for the parasitic weeds.[5] They proposed **2a** as the structure of sorgolactone based on ^{1}H-NMR and MS analysis in combination with a comparison of its CD spectrum with that of (+)-strigol.[5][15] The extremely limited amount of material (5 μg) available at the time of isolation, coupled with the fact that the natural sample is no longer available, prompted chemists to devise a synthesis of sorgolactone. Two attempted syntheses of **2a** have been reported.[16][17] We recently reported the synthesis and biological evaluation of (±)-**2a**–(±)-**2d**[18] and the synthesis of (+)-**2a** from (*S*)-(–)-citronellal[19] as preliminary communications, while Zwanenburg and co-workers synthesized (+)-**2a** and *ent*-(–)-**2b** together with the four racemates.[20] This paper gives full accounts of the synthesis and bioassay of racemic and optically active **2a**–**2d**, as well as a detailed comparison of their spectroscopic data with those published for natural sorgolactone.

Synthesis of (±)-2a–(±)-2d

In order to check the validity of the proposed structure **2a**, we first synthesized (±)-**2a** and its three racemic stereoisomers (±)-**2b**, (±)-**2c** and (±)-**2d** as outlined in Scheme 1. Phenylselenenylation of **4**,[21] prepared by alkylation of methyl 2-oxo-1-cyclopentanecarboxylate (**3**) with methyl bromoacetate, was followed by oxidative removal of the phenylselenyl group with aqueous hydrogen peroxide to afford α,β-unsaturated ketone **5**. Following the procedure of Tõke et al.,[22] employing ethyl 1-methoxycarbonyl-2-oxocy-

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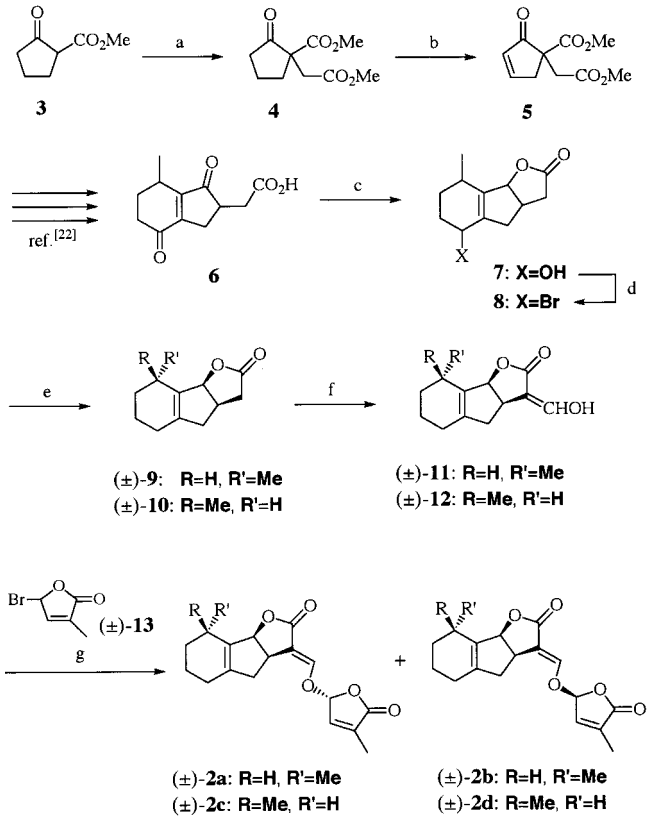
clopent-3-en-1-ylacetate, **5** was converted to a racemic and diastereomeric mixture of dioxo acid **6**. The sodium salt of **6** was reduced with sodium tetrahydroborate in the presence of cerium(III) chloride[23] to give, after acidification, a racemic and diastereomeric mixture of the hydroxylactone **7**. Treatment of **7** with carbon tetrabromide and triphenylphosphane yielded a racemic and diastereomeric mixture of the unstable bromolactone **8**, which was immediately reduced with zinc-copper couple (Zn/Cu = 91:5, Kanto Chemical Co.)[24] and acetic acid in THF to furnish a crude reduction product, presumably a stereoisomeric mixture of dienoic acids, cf. ref.[24] This was dissolved in chloroform and stirred for 60 h at room temperature in order to bring about lactone formation by 1,4-addition of the carboxyl group to the diene system.[24] The product was further purified by MPLC [Lobar LiChroprep® Si 60 (40−63 μm)] to give an oily fast-moving diastereomer and a crystalline slow-moving one. The latter (m.p. 43−46°C) was submitted to X-ray analysis, which revealed its structure to be (±)-**10**, with a *cis* relationship between the 8-methyl group and the lactone ring. Its computer-generated perspective view is shown in Figure 1. The oily lactone must therefore be (±)-**9**, which gives rise to (±)-**2a**. The ^{1}H-NMR spectrum of (±)-**9** recorded in $CDCl_3$ solution features a 1 H doublet at δ = 5.47, which is in agreement with the published data for sorgolactone (δ = 5.5),[5] whereas (±)-**10** gives a signal at δ = 5.31.

The two stereoisomeric lactones (±)-**9** and (±)-**10** were processed separately to give (±)-**2a** and its three stereoisomers. Formylation of (±)-**9** with ethyl formate and sodium hydride gave (±)-**11** (a tautomeric mixture of the aldehyde and the enol; m.p. 114−116°C). Treatment of (±)-**11** with (±)-4-bromo-2-methyl-2-buten-4-olide [(±)-**13**][10] in the presence of potassium carbonate gave a mixture of (±)-**2a** and (±)-**2b**, which could be separated by silica-gel chromatography to give two crystalline products. The structure of one of the products with m.p. 127−129°C was solved by X-ray analysis, and its perspective view is shown in Figure 1. This product was thus identified as (±)-**2a**, while the other, with m.p. 117−119°C, was evidently (±)-**2b**. Similarly, the stereoisomeric lactone (±)-**10** was converted to (±)-**2c**, m.p. 131−133°C, and (±)-**2d**, m.p. 116−118°C. The stereostructures of (±)-**2c** and (±)-**2d** were tentatively assigned on the basis of their m.p. and R_f values.[25]

The ^{1}H-NMR spectra of (±)-**2a**−(±)-**2d** were recorded in $CDCl_3$ or C_6D_6 solutions and compared with copies (sent by Dr. C. Hauck) of the spectra of the natural sorgolactone (Tables 1 and 2). Although the spectrum of (±)-**2a** was almost identical to that of the natural product, deviations in the chemical shifts of some signals were apparent (Table 2). Since Dr. Hauck's spectra of sorgolactone were unfortunately of rather poor quality due to the extremely limited amount of material available and the presence of impurities, confirmation of the validity of the proposed structure simply by comparison of the ^{1}H-NMR spectra of the synthetic products and the natural material was difficult.

The bioactivities of strigol and its stereoisomers or structural analogs as germination stimulants are known to be



Scheme 2. Synthesis of (±)-**2a**−(±)-**2d**; reagents: (a) $BrCH_2CO_2Me$, K_2CO_3, acetone (98%); (b) 1. PhSeCl, HCl, EtOAc; 2. H_2O_2, EtOAc/THF (61%); (c) NaOH, $NaBH_4$, $CeCl_3{\cdot}7H_2O$, CH_2Cl_2/H_2O (67%); (d) CBr_4, Ph_3P, CH_2Cl_2 (87%); (e) 1. Zn/Cu, AcOH, THF; 2. $CHCl_3$, stirring [40% as the mixture of (±)-**9** and (±)-**10**]; 3. MPLC separation; (f) NaH, HCO_2Et, Et_2O (quant.); (g) K_2CO_3, *N*-methylpyrrolidone; 2) SiO_2 chromatog. [42% of (±)-**2a**, 41% of (±)-**2b**, 39% of (±)-**2c** and 45% of (±)-**2d**]

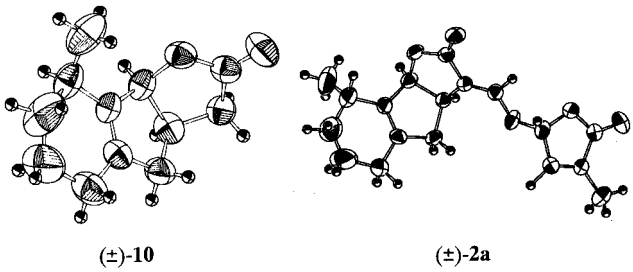


Figure 1. Perspective views of (±)-**10** and (±)-**2a**

strongly dependent on their structures, including their relative and absolute stereochemistries.[26−28] In particular, a C/D-ring moiety is considered to be essential for high activity. Bioassays of the four final racemic products were therefore carried out using seeds of clover broomrape (*Orobanche minor*) as a test parasitic weed seed[29] (Table 3). All of the four products with a C/D-ring moiety were effective in stimulating the germination of the *Orobanche minor* seeds, and the order of the stimulant activity was (±)-strigol ≈ (±)-**2b** ≥ (±)-**2d** > (±)-**2a** > (±)-**2c**.

Table 1. Comparison of the ^{1}H-NMR spectra (500 MHz, $CDCl_3$) of (±)-**2a**−(±)-**2d** with that of natural sorgolactone

	(±)-**2a**	(±)-**2b**	(±)-**2c**	(±)-**2d**	Natural sorgolactone[a]
8-Me	1.06 (3 H)	1.04 (3 H)	1.13 (3 H)	1.13 (3 H)	*1.1 (3 H)*
7-CH_2	1.24, 1.56 (2 H)	1.23, 1.55 (2 H)	1.35, 1.55 (2 H)	1.35, 1.54 (2 H)	
6-CH_2	1.70, 1.78 (2 H)	1.68, 1.77 (2 H)	1.72 (2 H)	1.74 (2 H)	
5-CH_2	1.94 (2 H)	1.93 (2 H)	1.92, 2.00 (2 H)	1.91, 2.00 (2 H)	
4′-Me	2.03 (1 H)	2.01 (1 H)	2.03 (1 H)	2.03 (1 H)	*2.02 (3 H)*
4-H	2.34 (1 H)	2.32 (1 H)	2.37 (1 H)	2.33 (1 H)	*2.37 (1 H)*
8-H	2.38 (1 H)	2.36 (1 H)	2.32 (1 H)	2.31 (1 H)	
4-H′	2.75 (1 H)	2.73 (1 H)	2.70 (1 H)	2.68 (1 H)	*2.75 (1 H)*
3a-H	3.63 (1 H)	3.60 (1 H)	3.62 (1 H)	3.60 (1 H)	*3.63 (1 H)*
8b-H	5.49 (1 H)	5.48 (1 H)	5.35 (1 H)	5.37 (1 H)	*5.51 (1 H)*
2′-H	6.15 (1 H)	6.14 (1 H)	6.14 (1 H)	6.13 (1 H)	*6.13 (1 H)*
3′-H	6.92 (1 H)	6.93 (1 H)	6.92 (1 H)	6.93 (1 H)	*6.92 (1 H)*
9-H	7.41 (1 H)	7.42 (1 H)	7.41 (1 H)	7.42 (1 H)	*7.45 (1 H)*

[a] Ref.[15], 500 MHz.

Table 2. Comparison of the ^{1}H-NMR spectra (500 MHz, C_6D_6) of (±)-**2a**−(±)-**2d** with that of natural sorgolactone

	(±)-**2a**	(±)-**2b**	(±)-**2c**	(±)-**2d**	Natural sorgolactone[a]
8-Me	0.94 (3 H)	0.95 (3 H)	1.22 (3 H)	1.22 (3 H)	*0.88 (3 H)*
7-CH_2	1.02, 1.32 (2 H)	0.99, 1.22 (2 H)	1.16, 1.27 (2 H)	1.15, 1.23 (2 H)	
4′-Me	1.35 (3 H)	1.34 (3 H)	1.30 (3 H)	1.31 (3 H)	*1.31 (3 H)*
6-H	1.44 (1 H)	1.36 (1 H)	1.48 (2 H)	1.38−1.47 (3 H)	
6′-H	1.53 (1 H)	1.43−1.56 (3 H)			
5-H	1.61 (1 H)		1.55 (1 H)		
5′-H	1.70 (1 H)		1.71 (1 H)	1.55 (1 H)	
4-H	2.27 (1 H)	2.24(1 H)	2.19 (1 H)	2.17 (1 H)	*2.13 (1 H)*
8-H	2.33 (1 H)	2.33 (1 H)	2.05 (1 H)	2.05 (1 H)	
4-H′	2.41 (1 H)	2.36 (1 H)	2.33 (1 H)	2.27 (1 H)	*2.30 (1 H)*
3a-H	3.19 (1 H)	3.24 (1 H)	3.13 (1 H)	3.19 (1 H)	*3.06 (1 H)*
8b-H	5.09 (1 H)	5.13 (1 H)	4.81 (1 H)	4.86 (1 H)	*4.93 (1 H)*
2′-H	5.31 (1 H)	5.22 (1 H)	5.01 (1 H)	4.99 (1 H)	*4.96 (1 H)*
3′-H	5.81 (1 H)	5.77 (1 H)	5.65 (1 H)	5.66 (1 H)	*5.65 (1 H)*
9-H	7.48 (1 H)	7.43 (1 H)	7.32 (1 H)	7.31 (1 H)	*7.23 (1 H)*

[a] Ref.[15], 600 MHz.

Table 3. Germination-stimulating activity of (±)-**2a**−(±)-**2d** on *Orobanche minor* seeds

Concentration	Relative germination of *Orobanche minor* seeds[a] (%) (±)-**2a**	(±)-**2b**	(±)-**2c**	(±)-**2d**	(±)-strigol
10^{-5} M	82, 90	95, 95	70, 57	92, 95	−, −
10^{-6} M	77, 65	93, 93	12, 18	90, 93	−, −
10^{-7} M	40, 51	90, 90	7, 3	87, 78	94, 94
10^{-8} M	21, 23	84, 87	3, 0	80, 70	86, 85

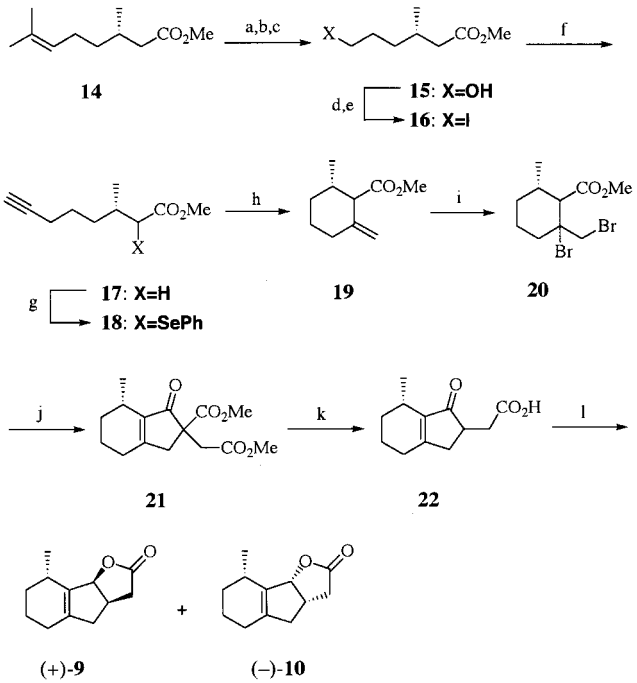
[a] Control, 2, 0%.

Synthesis of (+)-2a and Its Three Optically Active Stereoisomers

Next, (3a*R*,8*S*,8b*S*,2′*R*)-**2a** and its three optically active stereoisomers were synthesized to allow comparison of their CD spectra with that of natural sorgolactone, as well as their biological evaluation. Zwanenburg's strategy for the synthesis of **2a** involved resolution of the A/B/C-tricyclic precursor (±)-**9** with an optically active D-ring precursor corresponding to **13**.[20] Welzel and co-workers devised a similar strategy also applicable to the synthesis of **2a**.[30] Our own plan for the synthesis of (3a*R*,8*S*,8b*S*,2′*R*)-**2a** was to convert methyl (*S*)-(−)-citronellate (**14**) to the optically active (3a*R*,8*S*,8b*S*)-**9**, and then to couple this with (±)-**13** in the same manner as described for the racemate, thereby affording a separable mixture of **2a** and **2b**. As the key step, we envisaged a radical cyclization[31] of **18** to **19** to give an optically active A-ring building block.

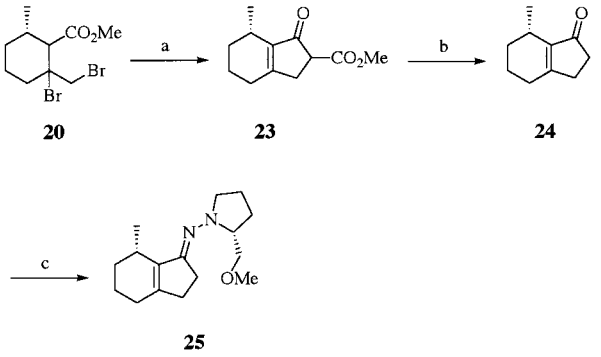
Scheme 3 summarizes the synthesis of **9** and **10**. (*S*)-(−)-Citronellal (97.0% *ee*, Takasago) was converted to methyl (*S*)-citronellate (**14**),[32] which furnished the hydroxy ester **15** after epoxidation, periodate cleavage, and reduction. The hydroxy ester **15** was converted to the corresponding iodo ester **16** in 2 steps. Ethynylation of **16** with lithium acetylide ethylenediamine complex gave the acetylenic ester **17** in moderate yield, which furnished the phenylselenenylated ester **18**. The pivotal cyclization reaction was accomplished by treatment of **18** with tri-*n*-butyltin hydride and AIBN in benzene at 80°C to generate the desired **19** as an inseparable mixture with methyl (*S*)-3-methyl-7-octenoate, an acyclic reduction product. Bromination of the mixture gave dibromide **20** (m.p. 37−39°C). Alkylation of dimethyl malonate with the allylic bromide generated in situ from **20**

was followed by Dieckmann-type cyclization, demethoxycarbonylation, and alkylation of the resulting sodium enolate of the β-oxo ester with methyl bromoacetate to give a diastereomeric mixture of diester **21**. Acid hydrolysis of **21** with concomitant decarboxylation gave oxo acid **22** as a diastereomeric mixture. Attempts to separate the mixture at this stage by means of recrystallization, asymmetric protonation of the enolate of **22**, or diastereomeric salt formation with chiral bases such as (*R*)-(+)-1-phenylethylamine, (*R*)-(+)-1-(1-naphthyl)ethylamine, cinchonine, quinine, brucine dihydrate, and (1*S*,2*R*)-(+)-2-amino-1,2-diphenylethanol, were unsuccessful. The oxo acid **22** was thus reduced under Luche conditions,[23] and the resulting hydroxy acid was lactonized. As in the case of the racemates, the mixture of **9** and **10** could be separated by MPLC [Lobar LiChroprep® Si 60 (40−63 μm)] to give pure (+)-**9** [oil, $[\alpha]_D^{24.6}$ = +3.0 (*c* = 0.60, $CHCl_3$)] and (−)-**10** [m.p. 45−47°C, $[\alpha]_D^{26.0}$ = −68.4 (*c* = 0.40, $CHCl_3$)]. The ^{1}H-NMR spectra of the products were identical to those of (±)-**9** and (±)-**10**. The matching of the NMR data was sufficient to establish the stereostructures of (+)-**9** and (−)-**10** as (±)-**10** had been submitted to X-ray analysis.



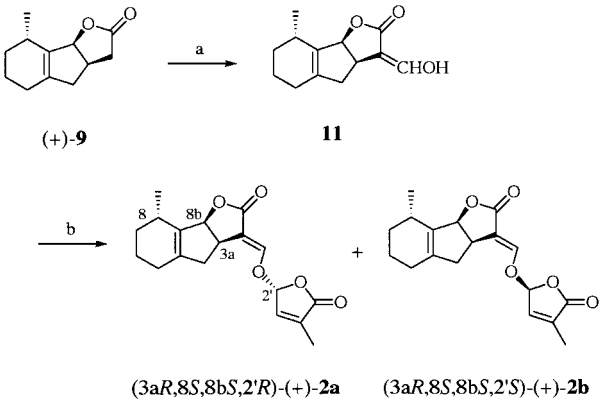
Scheme 3. Synthesis of (+)-**9** and (−)-**10**; reagents: (a) *m*CPBA, CH_2Cl_2; (b) $HIO_4 \cdot 2\ H_2O$, THF/Et_2O; (c) $NaBH_4$, MeOH (91%, 3 steps); (d) TsCl, C_5H_5N; (e) NaI, acetone (82%, 2 steps); (f) LiC≡CH·EDA, THF/DMSO (37%); (g) 1. LDA (2 equiv.), THF; 2. PhSeBr; 3. dil. HCl (69%); (h) nBu$_3$SnH, AIBN, C_6H_6; (i) $C_5H_5N{\cdot}HBr \cdot Br_2$, $CHCl_3$ (37%, 2 steps); (j) 1. NaH, $CH_2(CO_2Me)_2$, THF; 2. $BrCH_2CO_2Me$ (98%); (k) 6 N HCl, AcOH (96%); (l) 1. $NaBH_4$, $CeCl_3 \cdot 7\ H_2O$, MeOH, then dil. HCl; 2. MPLC separation [21% of (+)-**9** and 30% of (−)-**10**]

With a view to achieving a more efficient synthesis of (+)-**9**, we attempted asymmetric alkylation[33] of the α,β-unsaturated ketone **24**. The preparation of **24** is summarized in Scheme 4. Acetic acid quenching of the sodium enolate generated by treatment of **20** with sodium methoxide and dimethyl malonate afforded the β-oxo ester **23**. Hydrolysis and decarboxylation of **23** produced **24**. Attempted alkylation of its RAMP-hydrazone **25** with methyl bromoacetate or *tert*-butyl bromoacetate led to complex reaction mixtures containing **25**, a double-bond isomer of **25**, and only trace amounts of the alkylated product.



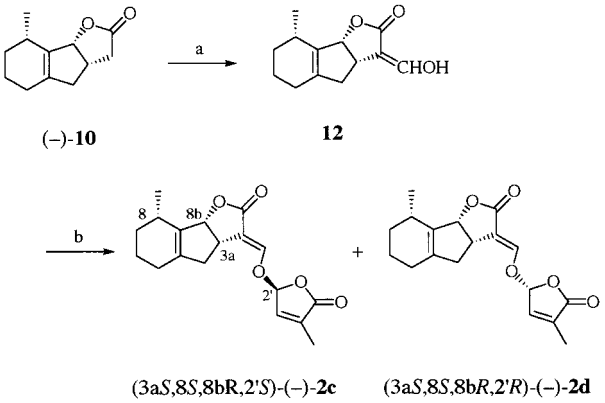
Scheme 4. Preparation of RAMP-hydrazone **25**; reagents: (a) 1. NaOMe, $CH_2(CO_2Me)_2$, MeOH; 2. AcOH (93%); (b) 6 N HCl, AcOH (72%); (c) RAMP, heating (93%)

The lactones (+)-**9** and (−)-**10** were converted to **2a**, **2b** and **2c**, **2d**, respectively (Schemes 5 and 6), the ^{1}H-NMR spectra of which were identical to those of the racemates. The final products (+)-**2a**, (−)-**2c** and (−)-**2d** were obtained as colorless crystals and recrystallization from hexane/ethyl acetate improved their enantiomeric purities to > 99.9% *ee* (as determined by HPLC, Chiralcel® OD). The enantiomeric purity of (+)-**2b**, obtained as an amorphous powder, was 99.9% *ee*. The CD spectrum of (+)-**2a** is almost identical to that of (+)-strigol[34] and the positive Cotton effect at 232 nm (Δε = 21) of (+)-**2a** is in accord with similar observations reported for the natural (236 nm)[5] and the synthetic (230 nm)[20] materials.



Scheme 5. Synthesis of (+)-**2a** and (+)-**2b**; reagents: (a) NaH, HCO_2Et, Et_2O (quant.); (g) 1. K_2CO_3, (±)-**13**, *N*-methylpyrrolidone; 2. SiO_2 chromatography [38% of (+)-**2a** and 46% of (+)-**2b**]

The bioactivities of the optically active stereoisomers **2a**−**2d** were evaluated in a similar manner as for the racemates (Table 4). All stereoisomers were found to exhibit strong activity, which decreased in the order **2d** > **2a** > **2b** ≈ **2c**. It should be noted that **2a** was not the strongest stimulant for *Orobanche minor* seeds.



Scheme 6. Synthesis of (−)-**2c** and (−)-**2d**; reagents: (a) NaH, HCO_2Et, Et_2O (quant.); (g) 1. K_2CO_3, (±)-**13**, *N*-methylpyrrolidone; 2) SiO_2 chromatography [33% of (−)-**2c** and 48% of (−)-**2d**]

Table 4. Germination-stimulating activity of **2a**−**2d** on *Orobanche minor* seeds

Concentration	Relative germination of *Orobanche minor* seeds[a] (%) (+)-**2a**	(+)-**2b**	(−)-**2c**	(−)-**2d**
10^{-5} M	97, 89	81, 75	98, 63	98, 98
10^{-6} M	91, 67	65, 36	62, 22	98, 95
10^{-7} M	78, 58	13, 0	7, 0	89, 87
10^{-8} M	37, 34	12, 0	3, 0	88, 72

[a] Control, 2, 0%.

In conclusion, we have accomplished syntheses of the racemate and the optically active form of the structure proposed for sorgolactone, and of their stereoisomers. Although the spectroscopic properties of (+)-**2a** are largely in agreement with those reported for natural sorgolactone, differences seen in the ^{1}H-NMR spectra do not lead us to the conclusion that the proposed structure is perfectly correct. Bioassays do not offer any clues as to the structure of sorgolactone. Since at present we have no access to the natural product itself, we conclude that reisolation of pure sorgolactone must be attempted in order to resolve this uncertainty. The isolation of sorgolactone from *Sorghum bicolor* is currently being performed by Prof. T. Yokota at Teikyo University. GC-MS analysis[7] of reisolated sorgolactone and our synthetic samples should make it clear whether the proposed structure is correct or not.

Experimental Section

General: Boiling points and melting points (Yanaco MP-S3): Uncorrected values. − IR: Shimadzu FT-IR 8100 or Jasco IRA-102. − ^{1}H NMR: Jeol JNM-EX 90A (90 MHz), Jeol JNM-EX 270L (270 MHz), Bruker DPX 300 (300 MHz), Jeol JNM-LA 400 (400 MHz), or Jeol JNM-LA 500 (500 MHz) (TMS at $\delta_H = 0.00$; $CHCl_3$ at $\delta_H = 7.26$; C_6H_6 at $\delta_H = 7.15$ as internal standards). − ^{13}C NMR: Jeol JNM-EX 270L (67.8 MHz), Bruker DPX 300 (75.5 MHz), Jeol JNM-LA 400 (100.4 MHz), or Jeol JNM-LA 500 (125.7 MHz) ($CDCl_3$ at $\delta_C = 77.0$ as internal standard). − MS: Jeol JMX-DX 303 (70 eV). − Optical rotation: Jasco DIP-1000. − CD: Jasco J-720. − CC: Merck Kieselgel 60 Art 1.07734. − TLC: 0.25 mm Merck silica gel plates (60F-254).

Methyl 1-Methoxycarbonyl-2-oxocyclopent-1-ylacetate (4): To a stirred mixture of methyl 2-oxo-1-cyclopentanecarboxylate (**3**, 2.84 g, 0.020 mol) and K_2CO_3 (13.8 g, 0.10 mol) in acetone (100 mL) was added methyl bromoacetate (3.06 g, 0.020 mol). The mixture was refluxed for 2 h and then concentrated under reduced pressure. The residue was diluted with water and extracted with diethyl ether. The combined ethereal layers were washed with brine and dried with $MgSO_4$. Evaporation of the solvent gave a crude product, which was purified by silica-gel column chromatography (hexane/ethyl acetate, 5:1) to furnish 4.02 g (98%) of the oxo diester **4**[24] as a colorless oil. An analytical sample was purified by distillation; b.p. 101−103°C/3 Torr. − IR (film): $\tilde{\nu} = 1760\ cm^{-1}$ (s, C=O), 1740 (s, C=O), 1730 (s, C=O), 1635 (w, enolic C=C), 1200 (s, C−O). − ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 1.98-2.20$ (m, 3 H, 4-CH_2 and 5-H), 2.44 (m, 2 H), 2.60 (m, 1 H), 2.80 and 2.97 (AB, 1 H each, $J_{AB} = 17.2$ Hz, $-CH_2CO_2-$), 3.65 and 3.70 (2 s, 3 H each, 2 × OMe). − ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 19.0, 32.6, 36.9, 37.3, 51.1, 52.1, 56.8, 170.1, 170.5, 213.1$.

Methyl 1-Methoxycarbonyl-2-oxocyclopent-3-en-1-ylacetate (5): To a stirred solution of the oxo diester **4** (655 mg, 3.1 mmol) in ethyl acetate (30 mL) containing a few drops of conc. HCl, phenylselenenyl chloride (703 mg, 3.7 mol) was added in one portion. After stirring for 24 h at room temperature, the resulting slightly pale-yellow solution was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with water, satd. $NaHCO_3$ solution and brine, and then dried with $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel (hexane/ethyl acetate, 9:1) to give a diastereomeric mixture of the selenide (1.01 g) as a yellowish viscous oil. This was used for the next transformation without further purification. To an ice-cooled, stirred solution of the above selenide (812 mg, 2.2 mmol) in ethyl acetate/THF (2:1, 30 mL) was slowly added ca. 35% hydrogen peroxide solution (0.64 mL, ca. 6.6 mmol). After stirring for 30 min at 0°C and for a further 1 h at room temperature, the excess oxidant was reduced with satd. $Na_2S_2O_3$ solution. The mixture was then extracted with diethyl ether, and the combined organic layers were washed with water and satd. $NaHCO_3$ solution, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/ethyl acetate, 9:1) to give 97 mg of the saturated oxo diester **4** and 254 mg (61% over 2 steps based on the consumed **4**) of the enone **5** as a colorless oil. Distillation of the oil afforded an analytical sample, b.p. 130−131°C/2.5 Torr. − $n_D^{24} = 1.4802$. − IR (film): $\tilde{\nu} = 1740\ cm^{-1}$ (s, C=O), 1735 (s, C=O), 1710 (s, C=O), 1590 (m, C=C), 1190 (s, C−O). − ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 2.59$ and 3.25 (AB, 1 H each, $J_{AB} = 17.5$ Hz, $-CH_2CO_2-$), 2.78 (dt, 1 H, $J = 19.5$, $J' = 2.3$ Hz, 5-H), 3.50 (dt, 1 H, $J = 19.5$, $J' = 2.6$ Hz, 5-H′), 3.69 and 3.71 (2 s, 3 H each, 2 × OMe), 6.21 (dt, 1 H, $J = 5.9$, $J' = 2.3$ Hz, 3-H), 7.86 (dt, 1 H, $J = 5.9$, $J' = 2.6$ Hz, 4-H). − ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 38.0, 40.3, 51.9, 53.0, 55.4, 131.2, 164.8, 169.6, 171.2, 203.7$. − $C_{10}H_{12}O_5$ (212.2): calcd. C 56.60, H 5.70; found C 56.52, H 5.80.

7-Methyl-1,4-dioxo-2,3,4,5,6,7-hexahydroinden-2-ylacetic Acid (6): According to the procedure of Tõke et al.,[22] which used ethyl 1-methoxycarbonyl-2-oxocyclopent-3-en-1-ylacetate in place of the methyl ester **5**, **5** was converted to a diastereomeric mixture of the dioxo acid **6** (54%, 3 steps). This acid **6** was unstable and aromatized in the presence of air to give an acid with the phenolic ring A.[22] It was thus used immediately for the next reaction; m.p. 135−137°C (diethyl ether) [ref.[22] 141−142°C]. − IR (KBr): $\tilde{\nu} = 3000\ cm^{-1}$ (m, O−H), 1740 (s, C=O), 1690 (s, C=O), 1685 (s, C=O), 1630 (m, C=C), 1400 (m, O−H), 1290 (m, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.25$ and 1.26 (2 d, 3 H total, $J = 7.1$ Hz,

7-Me), 1.88 (m, 1 H, 6-H), 2.22 (m, 1 H, 6-H′), 2.28−2.94 (m, 7 H), 3.00 (m, 1 H), 7.82 (s, 1 H, OH). − ^{13}C NMR (100.4 MHz, $CDCl_3$): δ (major isomer) = 17.0, 26.5, 29.7, 30.4, 34.3, 36.0, 42.4, 156.5, 157.0, 176.1, 199.1, 209.6; δ (minor isomer) = 16.9, 26.5, 29.6, 30.3, 34.6, 35.6, 42.0, 156.5, 157.2, 176.1, 199.1, 210.0.

5-Hydroxy-8-methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]-furan-2-one (7): A stirred suspension of the dioxo acid **6** (178 mg, 0.80 mmol) in water (8.5 mL) was neutralized with 1 N NaOH (0.94 mL). To the resulting orange solution, a solution of $CeCl_3 \cdot 7\ H_2O$ (298 mg, 0.80 mmol) in water (0.85 mL) was added at room temperature, followed by CH_2Cl_2 (3.4 mL). After cooling to 0°C, a solution of $NaBH_4$ (182 mg, 4.8 mmol) in water (0.85 mL) was added dropwise. The resulting mixture was stirred for 2 h at 0°C. The excess reductant was then destroyed by the addition of 6 N HCl, and the mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on silica gel (benzene/ethyl acetate, 6:1) to give 111 mg (67%) of the hydroxylactone **7** as a diastereomeric mixture of the four possible racemates, which was employed directly in the next transformation. Separation by silica-gel column chromatography (hexane/ethyl acetate, 5:1) furnished two pairs of diastereomers, the more polar isomers (R_f = 0.23, hexane/ethyl acetate, 1:2) in a ratio of ca. 3.9:1 (as determined by ^{1}H-NMR analysis) as a colorless paste, and the less polar ones (R_f = 0.29, hexane/ethyl acetate, 1:2) in a ratio of ca. 3.1:1 (^{1}H NMR) as colorless needles. − **More Polar Diastereomers:** IR (film): $\tilde{\nu}$ = 3440 cm^{-1} (m, O−H), 1760 (s, C=O), 1170 (m, C−O), 1000 (m, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ (for major isomer) = 1.09 (d, 3 H, J = 7.1 Hz, 8-Me), 1.43 (m, 1 H, 7-H), 1.67−2.00 (m, 4 H, 6-CH_2, 7-H′ and OH), 2.17 (dd, 1 H, J = 16.4, J' = 2.2 Hz, 4-H), 2.28 (dd, 1 H, J = 18.4, J' = 5.7 Hz, 3-H), 2.32 (m, 1 H, 8-H), 2.84 (dd, 1 H, J = 18.4, J' = 10.4 Hz, 3-H′), 2.98 (ddd, 1 H, J = 16.4, J' = 8.2, J'' = 2.7 Hz, 4-H′), 3.10 (m, 1 H, 3a-H), 4.17 (m, 1 H, 5-H), 5.48 (d, 1 H, J = 7.4 Hz, 8b-H), δ (characteristic signals of minor isomer) = 1.07 (d, 3 H, J = 7.0 Hz, 8-Me), 4.22 (m, 1 H, 5-H), 5.32 (d, 1 H, J = 7.1 Hz, 8b-H). − **Less Polar Diastereomers:** M.p. 109−110°C (diethyl ether). − IR (KBr): $\tilde{\nu}$ = 3420 cm^{-1} (m, O−H), 1765 (s, C=O), 1175 (m, C−O), 1010 (m, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ (major isomer) = 1.16 (d, 3 H, J = 7.1 Hz, 8-Me), 1.49 (m, 2 H, 7-CH_2), 1.68−1.86 (m, 3 H, 6-CH_2 and OH), 2.29 (m, 1 H, 8-H), 2.38 (dd, 1 H, J = 18.3, J' = 4.6 Hz, 3-H), 2.54 (m, 1 H, 4-H), 2.62 (dd, 1 H, J = 8.5, J' = 3.3 Hz, 4-H′), 2.82 (dd, 1 H, J = 18.3, J' = 10.3 Hz, 3-H′), 3.10 (m, 1 H, 3a-H), 4.13 (br. d, 1 H, J = 4.8 Hz, 5-H), 5.32 (d, 1 H, J = 7.5 Hz, 8b-H); δ (characteristic signals of minor isomer) = 1.05 (d, 3 H, J = 7.0 Hz, 8-Me), 1.30 (m, 1 H, 7-H), 1.91 and 2.05 (2 m, 1 H each, 6-CH_2), 2.33 (dd, 1 H, J = 18.4, J' = 6.0 Hz, 3-H), 2.48 (m, 1 H, 4-H), 2.68 (dd, 1 H, J = 8.7, J' = 3.5 Hz, 4-H′), 2.84 (dd, 1 H, J = 18.4, J' = 10.6 Hz, 3-H′), 5.47 (d, 1 H, J = 7.7 Hz, 8b-H). − $C_{12}H_{16}O_3$ (208.3): calcd. C 69.21, H 7.74; found C 69.27, H 7.72.

5-Bromo-8-methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one (8): To a stirred solution of the hydroxylactone **7** (156 mg, 0.75 mmol) in dry CH_2Cl_2 (5.0 mL) were added solutions of triphenylphosphane (354 mg, 1.35 mmol) in dry CH_2Cl_2 (10 mL) and of carbon tetrabromide (672 mg, 2.03 mmol) in dry CH_2Cl_2 (10 mL). The resulting mixture was stirred for 15 min at room temperature and then concentrated under reduced pressure. The yellowish residue was chromatographed on silica gel (hexane/ethyl acetate, 4:1) to give 205 mg (quant.) of a diastereomeric mixture of the bromolactone **8** as an almost colorless oil [three spots upon TLC analysis (hexane/ethyl acetate, 1:1), R_f = 0.64, 0.57 and 0.49]. Although the mixture was separated by silica-gel column chromatography (hexane/ethyl acetate, 5:1), the individual isomers could not be characterized since they quickly epimerized and then decomposed. − IR (film): $\tilde{\nu}$ = 1770 cm^{-1} (s, C=O), 1170 (s, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 1.12, 1.15 and 1.20 (3 d, 3 H total, J = 6.8 Hz, 8-Me), 1.46−1.88 (m, 2 H, 7-CH_2), 1.94−3.30 (m, 8 H), 4.72 (m, 1 H, 5-H), 5.31 and 5.50 (2 d, 1 H total, J = 7.3, 7.0 Hz, 8b-H).

(±)-(3a*R,8*S**,8b*S**)- and (±)-(3a*S**,8*S**,8b*R**)-8-Methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one [(±)-9 and (±)-10]:** To zinc-copper couple (Zn/Cu = 91:5, Kanto Chemical Co., 2.13 g, 32 mmol) at room temperature under argon, a solution of the bromolactone **8** (867 mg, 3.2 mmol) in dry THF (50 mL) was added, followed by acetic acid (0.17 mL). The mixture was stirred for 1 h at room temperature, and then the excess zinc-copper couple was filtered off. The residue obtained upon evaporation of the solvent under reduced pressure was redissolved in $CHCl_3$ (100 mL). The resulting colorless solution was stirred for 60 h at room temperature, then diluted with water and extracted with $CHCl_3$. The organic layer was washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. The slightly pale-yellow residue was chromatographed on silica gel (hexane/ethyl acetate, 8:1) to give a ca. 1:1 mixture (as determined by HPLC, silica gel) of the debrominated lactones (±)-**9** and (±)-**10** (247 mg, 40%). The mixture was separated by medium-pressure liquid chromatography [Lobar LiChroprep® Si 60 (40−63 mm), hexane/*i*PrOH, 49:1] to furnish a fast-moving diastereomer (±)-**9** as a pale-yellow oil and a slow-moving one (±)-**10** as a white solid. The latter was recrystallized from hexane to afford colorless crystals suitable for X-ray analysis. − **The Oily Lactone (±)-9:** n_D^{20} = 1.5088. − IR (film): $\tilde{\nu}$ = 1765 cm^{-1} (s, C=O), 1670 (w, C=C), 1170 (s, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (d, 3 H, J = 7.0 Hz, 8-Me), 1.25 (m, 1 H, 7-H), 1.50−1.85 (m, 3 H, 6-CH_2 and 7-H′), 1.96 (m, 2 H, 5-CH_2), 2.13 (d, 1 H, J = 16.6 Hz, 4-H), 2.29 (dd, 1 H, J = 18.3, J' = 5.7 Hz, 3-H), 2.36 (m, 1 H, 8-H), 2.66 (ddd, 1 H, J = 16.5, J' = 8.2, J'' = 1.5 Hz, 4-H′), 2.82 (dd, 1 H, J = 18.3, J' = 10.6 Hz, 3-H′), 3.05 (m, 1 H, 3a-H), 5.47 (d, 1 H, J = 7.4 Hz, 8b-H). − MS (EI, 70 eV): *m/z* (%) = 192 (71) [M$^+$], 177 (31), 148 (39), 133 (100), 131 (66), 117 (32), 105 (72), 91 (72). − HRMS: calcd. for $C_{12}H_{16}O_2$: 192.1150; found 192.1159. − **The Crystalline Lactone (±)-10:** M.p. 43−46°C (hexane). − IR (KBr): $\tilde{\nu}$ = 1755 cm^{-1} (s, C=O), 1170 (m, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (d, 3 H, J = 7.1 Hz, 8-Me), 1.34 and 1.57 (2 m, 1 H each, 7-CH_2), 1.75 (m, 2 H, 6-CH_2), 1.97 (m, 2 H, 5-CH_2), 2.17 (dt, 1 H, J = 16.6, J' = 1.7 Hz, 4-H), 2.31 (m, 1 H, 8-H), 2.34 (dd, 1 H, J = 18.2, J' = 4.4 Hz, 3-H), 2.61 (ddt, 1 H, J = 16.6, J' = 8.7, J'' = 1.5 Hz, 4-H′), 2.80 (dd, 1 H, J = 18.2, J' = 10.3 Hz, 3-H′), 3.03 (m, 1 H, 3a-H), 5.31 (d, 1 H, J = 7.1 Hz, 8b-H). − $C_{12}H_{16}O_2$ (192.3): calcd. C 74.97, H 8.39; found C 74.70, H 8.39.

(±)-(3a*R,8*S**,8b*S**)-3-Hydroxymethylene-8-methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one [(±)-11]:** To a stirred suspension of NaH (ca. 60% oil suspension, 31 mg, ca. 0.78 mmol) in dry diethyl ether (2.0 mL) at room temperature under argon, was added a solution of the lactone (±)-**9** (50 mg, 0.26 mmol) in dry diethyl ether (2.0 mL), followed by ethyl formate (0.25 mL, ca. 3 mmol). After stirring for 24 h, the mixture was acidified with 1 N HCl and then extracted with ethyl acetate. The combined organic layers were washed with water (twice) and brine, and dried with $MgSO_4$. Evaporation of the solvent left a pale-yellow solid, which was washed several times with ice-cooled diethyl ether to give 57 mg (quant.) of the formylated lactone (±)-**11** as a tautomeric mixture of the enol and the aldehyde (ca. 2.4:1, as determined by ^{1}H-NMR analysis), which was used directly in the subsequent transformation without further purification; m.p. 114−116°C. −

IR (KBr): $\tilde{\nu}$ = 3500−2800 cm^{-1} (m, O−H), 2750 (m, OC−H), 1715 (s, C=O), 1690 (s, C=O), 1635 (s, C=C), 1385 (m, OC−H), 1205 (s, C−O), 1080 (s, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ (for the enol) = 1.06 (d, 3 H, *J* = 7.1 Hz, 8-Me), 1.28 (m, 1 H, 7-H), 1.49−1.85 (m, 3 H, 6-CH_2 and 7-H′), 1.95 (m, 2 H, 5-CH_2), 2.20 (d, 1 H, *J* = 17.2 Hz, 4-H), 2.48 (m, 1 H, 8-H), 2.70 (dd, 1 H, *J* = 17.2, *J*′ = 8.4 Hz, 4-H′), 3.57 (m, 1 H, 3a-H), 5.58 (dd, 1 H, *J* = 7.8, *J*′ = 1.2 Hz, 8b-H), 7.07 (s, 1 H, 9-H), 10.41 (br s, 1 H, OH); δ (characteristic signals of the aldehyde) = 2.12 (d, 1 H, *J* = 16.8 Hz, 4-H), 3.38 (d, 1 H, *J* = 6.6 Hz, 3-H), 3.50 (m, 1 H, 3a-H), 5.48 (d, 1 H, *J* = 7.4, 8b-H), 9.86 (s, 1 H, CHO).

(±)-(3a*S,8*S**,8b*R**)-3-Hydroxymethylene-8-methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one [(±)-12]:** In the same manner as described for (±)-**11**, the lactone (±)-**10** (50 mg, 0.26 mmol) was formylated using NaH (ca. 60% oil suspension, 50 mg, ca. 0.26 mmol) and ethyl formate (0.25 mL, ca. 3 mol) in dry diethyl ether (4.0 mL) to afford 58 mg (quant.) of the formylated lactone (±)-**12** as a tautomeric mixture of the enol and the aldehyde (ca. 2.0:1, as determined by ^{1}H-NMR analysis). Again, this was employed without purification in the next step. White solid, m.p. 118−119°C. − IR (KBr): $\tilde{\nu}$ = 3600−2800 cm^{-1} (m, O−H), 2740 (m, OC−H), 2680 (m, OC−H), 1710 (s, C=O), 1660 (s, C=O), 1600 (m, C=C), 1380 (m, OC−H), 1355 (m, OC−H), 1200 (s, C−O) 1100 (m, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ (for the enol) = 1.12 (d, 3 H, *J* = 7.0 Hz, 8-Me), 1.38 (m, 1 H, 7-H), 1.50−1.83 (m, 3 H, 6-CH_2 and 7-H′), 2.00 (m, 2 H, 5-CH_2), 2.25 (d, 1 H, *J* = 17.2 Hz, 4-H), 2.32 (m, 1 H, 8-H), 2.73 (dd, 1 H, *J* = 17.2, *J*′ = 7.7 Hz, 4-H′), 3.55 (m, 1 H, 3a-H), 5.45 (d, 1 H, *J* = 8.0 Hz, 8b-H), 7.06 (s, 1 H, 9-H), 10.43 (br s, 1 H, OH); δ (characteristic signals of the aldehyde) = 1.10 (d, 3 H, *J* = 6.1 Hz, 8-Me), 2.18 (d, 1 H, *J* = 16.8 Hz, 4-H), 3.50 (m, 1 H, 3a-H), 5.34 (d, 1 H, *J* = 6.5 Hz, 8b-H), 9.84 (s, 1 H, CHO).

(±)-(3a*R,8*S**,8b*S**,2′*R**)- and (3a*R**,8*S**,8b*S**,2′*S**)-3-[(*E*)-2′,5′-Dihydro-4′-methyl-5′-oxo-2′-furanyloxymethylene]-8-methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one [(±)-Sorgolactone and (±)-2′-Episorgolactone, (±)-2a and (±)-2b]:** To a stirred mixture of the hydroxymethylene lactone (±)-**11** (55 mg, 0.25 mmol) and K_2CO_3 (69 mg, 0.50 mmol) in anhydrous *N*-methylpyrrolidone (2.0 mL) at room temperature under argon, was added (±)-4-bromo-2-methyl-2-buten-4-olide [(±)-**13**][10] (75 mg, 0.43 mmol). After stirring for 24 h at room temperature, the reaction mixture was poured into 1 N HCl (5 mL) and extracted with ethyl acetate. The organic layer was washed with water (twice) and brine, and dried with $MgSO_4$. Evaporation of the solvent under reduced pressure gave a slightly pale-yellow oil, which was chromatographed on silica gel (hexane/ethyl acetate, 6:1) to give first 33 mg (42%) of (±)-sorgolactone [(±)-**2a**] as colorless crystals (R_f = 0.41, hexane/ethyl acetate, 1:1) and then 32 mg (41%) of (±)-2′-episorgolactone [(±)-**2b**] as colorless crystals (R_f = 0.34, hexane/ethyl acetate, 1:1). The stereostructures of (±)-**2a** and (±)-**2b** were deduced from an X-ray analysis of (±)-**2a**. − **(±)-Sorgolactone [(±)-2a]:** M.p. 127−129°C (hexane/ethyl acetate). − IR (KBr): $\tilde{\nu}$ = 2930 cm^{-1} (m), 2860 (w), 1790 (s, C=O), 1745 (s, C=O), 1730 (s, C=O), 1680 (s, C=C), 1350 (m), 1340 (m), 1180 (s, C−O), 1095 (s), 1020 (s, C−O), 955 (s), 930 (w), 750 (w). − ^{1}H NMR (500 MHz): δ (in $CDCl_3$) = 1.06 (d, 3 H, *J* = 7.0 Hz, 8-Me), 1.24 and 1.56 (2 m, 1 H each, 7-CH_2), 1.70 and 1.78 (2 m, 1 H each, 6-CH_2), 1.94 (m, 2 H, 5-CH_2), 2.03 (t, 3 H, *J* = 1.5 Hz, 4′-Me), 2.34 (d, 1 H, *J* = 16.5 Hz, 4-H), 2.38 (m, 1 H, 8-H), 2.75 (dd, 1 H, *J* = 15.0, *J*′ = 9.0 Hz, 4-H′), 3.63 (m, 1 H, 3a-H), 5.49 (d, 1 H, *J* = 8.0 Hz, 8b-H), 6.15 (t, 1 H, *J* = 1.5 Hz, 2′-H), 6.92 (t, 1 H, *J* = 1.5 Hz, 3′-H), 7.41 (d, 1 H, *J* = 3.0 Hz, 9-H); δ (in C_6D_6) = 0.94 (d, 3 H, *J* = 7.0 Hz, 8-Me), 1.02 and 1.32 (2 m, 1 H each, 7-CH_2), 1.35 (t, 3 H, *J* = 1.5 Hz, 4′-Me), 1.44 and 1.53 (2 m, 1 H each, 6-CH_2), 1.61 and 1.70 (2 m, 1 H each, 5-CH_2), 2.27 (dd, 1 H, *J* = 16.5, *J*′ = 3.6 Hz, 4-H), 2.33 (m, 1 H, 8-H), 2.41 (dd, 1 H, *J* = 16.5, *J*′ = 8.5 Hz, 4-H′), 3.19 (m, 1 H, 3a-H), 5.09 (d, 1 H, *J* = 8.0 Hz, 8b-H), 5.31 (t, 1 H, *J* = 1.5 Hz, 2′-H), 5.81 (t, 1 H, *J* = 1.5 Hz, 3′-H), 7.48 (d, 1 H, *J* = 2.5 Hz, 9-H). − ^{13}C NMR (75.5 MHz): δ (in $CDCl_3$) = 10.7, 18.5, 20.6, 26.0, 27.8, 31.1, 36.4, 41.3, 88.0, 100.4, 114.3, 135.8, 137.2, 141.0, 141.3, 150.1, 170.2, 171.8; δ (in C_6D_6) = 10.2, 18.6, 21.0, 26.2, 28.2, 31.3, 36.7, 41.5, 87.3, 101.0, 114.6, 135.2, 137.9, 140.6, 140.7, 151.0, 169.9, 171.0. − MS (EI, 70 eV): *m/z* (%) 316 (50) [M^+], 219 (28), 201 (65), 191 (10), 173 (32), 159 (5), 145 (11), 131 (19), 115 (10), 105 (14), 97 (100), 91 (37), 77 (17), 69 (27). − $C_{18}H_{20}O_5$ (316.4): calcd. C 68.34, H 6.37; found C 68.12, H 6.44. − **(±)-2′-Episorgolactone [(±)-2b]:** M.p. 117−119°C (hexane/ethyl acetate). − IR (KBr): $\tilde{\nu}$ = 2940 cm^{-1} (m), 2855 (m), 1785 (s, C=O), 1745 (s, C=O), 1685 (s, C=C), 1445 (m), 1380 (m), 1335 (s), 1210 (m), 1180 (s, C−O), 1090 (s), 1025 (s, C−O), 955 (s), 930 (w), 870 (w), 750 (m), 740 (m). − ^{1}H NMR (500 MHz): δ (in $CDCl_3$) = 1.04 (d, 3 H, *J* = 7.0 Hz, 8-Me), 1.23 and 1.55 (2 m, 1 H each, 7-CH_2), 1.68 and 1.77 (2 m, 1 H each, 6-CH_2), 1.93 (m, 2 H, 5-CH_2), 2.01 (t, 3 H, *J* = 1.5 Hz, 4′-Me), 2.32 (d, 1 H, *J* = 16.5 Hz, 4-H), 2.36 (m, 1 H, 8-H), 2.73 (dd, 1 H, *J* = 15.0, *J*′ = 9.0 Hz, 4-H′), 3.60 (m, 1 H, 3a-H), 5.48 (d, 1 H, *J* = 7.5 Hz, 8b-H), 6.14 (s, 1 H, 2′-H), 6.93 (t, 1 H, *J* = 1.5 Hz, 3′-H), 7.42 (d, 1 H, *J* = 3.0 Hz, 9-H); δ (in C_6D_6) = 0.95 (d, 3 H, *J* = 7.0 Hz, 8-Me), 0.99 and 1.22 (2 m, 1 H each, 7-CH_2), 1.34 (br. s, 3 H, 4′-Me), 1.36 (m, 1 H, 6-H), 1.43−1.56 (m, 3 H, 5-CH_2 and 6-H′), 2.24 (d, 1 H, *J* = 16.5 Hz, 4-H), 2.33 (m, 1 H, 8-H), 2.36 (dd, 1 H, *J* = 16.5, *J*′ = 8.5 Hz, 4-H′), 3.24 (m, 1 H, 3a-H), 5.13 (d, 1 H, *J* = 8.0 Hz, 8b-H), 5.22 (m, 1 H, 2′-H), 5.77 (br. s, 1 H, 3′-H), 7.43 (br s, 1 H, 9-H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.7, 18.6, 20.6, 26.0, 27.8, 31.1, 36.4, 41.4, 88.0, 100.6, 114.4, 135.7, 137.1, 141.1, 141.5, 150.4, 170.3, 171.8. − $C_{18}H_{20}O_5$ (316.4): calcd. C 68.34, H 6.37; found C 68.30, H 6.42.

(±)-(3a*S,8*S**,8b*R**,2′*S**)- and (3a*S**,8*S**,8b*R**,2′*R**)-3-[(*E*)-2′,5′-Dihydro-4′-methyl-5′-oxo-2′-furanyloxymethylene]-8-methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one [(±)-8-Episorgolactone and (±)-2′,8-Diepisorgolactone, (±)-2c and (±)-2d]:** In the same manner as described for (±)-**2a** and (±)-**2b**, the hydroxymethylene lactone (±)-**12** (50 mg, 0.23 mmol) was alkylated with the bromobutenolide (±)-**13** (68 mg, 0.39 mmol) in the presence of K_2CO_3 (63 mg, 0.45 mmol) in anhydrous *N*-methylpyrrolidone (1.5 mL). Silica-gel column chromatography (hexane/ethyl acetate, 6:1) gave first 28 mg (39%) of (±)-8-episorgolactone [(±)-**2c**] as colorless crystals (R_f = 0.41, hexane/ethyl acetate, 1:1) and then 32 mg (45%) of (±)-2′,8-diepisorgolactone [(±)-**2d**] as colorless crystals (R_f = 0.33, hexane/ethyl acetate, 1:1). − **(±)-8-Episorgolactone [(±)-2c]:** M.p. 131−133°C (hexane/ethyl acetate). − IR (KBr): $\tilde{\nu}$ = 2935 cm^{-1} (m), 1790 (s, C=O), 1740 (s, C=O), 1685 (s, C=C), 1340 (m), 1210 (w), 1180 (m, C−O), 1095 (s), 1020 (s, C−O), 955 (s), 750 (w). − ^{1}H NMR (500 MHz): δ (in $CDCl_3$) = 1.13 (d, 3 H, *J* = 7.0 Hz, 8-Me), 1.35 and 1.55 (2 m, 1 H each, 7-CH_2), 1.72 (m, 2 H, 6-CH_2), 1.92 and 2.00 (2 m, 1 H each, 5-CH_2), 2.03 (t, 3 H, *J* = 1.5 Hz, 4′-Me), 2.32 (m, 1 H, 8-H), 2.37 (d, 1 H, *J* = 16.5 Hz, 4-H), 2.70 (ddd, 1 H, *J* = 16.5, *J*′ = 9.5, *J*′′ = 3.4 Hz, 4-H′), 3.62 (m, 1 H, 3a-H), 5.35 (d, 1 H, *J* = 7.5 Hz, 8b-H), 6.14 (t, 1 H, *J* = 1.5 Hz, 2′-H), 6.92 (t, 1 H, *J* = 1.5 Hz, 3′-H), 7.41 (d, 1 H, *J* = 2.5 Hz, 9-H); δ (in C_6D_6) = 1.16 (m, 1 H, 7-H), 1.22 (d, 3 H, *J* = 7.5 Hz, 8-Me), 1.27 (m, 1 H, 7-H′), 1.30 (t, 3 H, *J* = 1.5 Hz, 4′-Me), 1.48 (m, 2 H, 6-CH_2), 1.55 and 1.71 (2 m, 1 H each, 5-CH_2), 2.05 (m, 1 H, 8-H), 2.19 (d, 1 H, *J* = 16.5 Hz, 4-H), 2.33 (ddd, 1 H, *J* = 16.5, *J*′ = 8.8, *J*′′ = 3.0 Hz, 4-H′), 3.13 (m, 1 H, 3a-H), 4.81 (d, 1 H, *J* = 7.5 Hz, 8b-H), 5.01 (t, 1 H, *J* = 1.5 Hz, 2′-H), 5.65 (t, 1 H, *J* = 1.5 Hz, 3′-H), 7.32 (m, 1 H, 9-H). − ^{13}C NMR

(75.5 MHz, $CDCl_3$): δ = 10.7, 19.9, 20.2, 26.2, 30.0, 31.6, 36.8, 41.3, 90.8, 100.4, 114.4, 135.8, 136.5, 141.0, 142.8, 149.7, 170.3, 171.8. − $C_{18}H_{20}O_5$ (316.4): calcd. C 68.34, H 6.37; found C 68.42, H 6.34. − **(±)-2′,8-Diepisorgolactone [(±)-2d]:** M.p. 116−118°C (hexane/ethyl acetate). − IR (KBr): $\tilde{\nu}$ = 2930 cm^{-1} (w), 1790 (s, C=O), 1735 (s, C=O), 1730 (s, C=O), 1685 (s, C=C), 1340 (m), 1205 (w), 1180 (s, C−O), 1090 (s), 1020 (s, C−O), 955 (s), 930 (w), 870 (w), 755 (w). − ^{1}H NMR (500 MHz): δ (in $CDCl_3$) = 1.13 (d, 3 H, *J* = 7.0 Hz, 8-Me), 1.35 and 1.54 (2 m, 1 H each, 7-CH_2), 1.74 (m, 2 H, 6-CH_2), 1.91 and 2.00 (2 m, 1 H each, 5-CH_2), 2.03 (t, 3 H, *J* = 1.5 Hz, 4′-Me), 2.31 (m, 1 H, 8-H), 2.33 (d, 1 H, *J* = 16.5 Hz, 4-H), 2.68 (ddd, 1 H, *J* = 16.5, *J′* = 9.5, *J″* = 3.3 Hz, 4-H′), 3.60 (m, 1 H, 3a-H), 5.37 (d, 1 H, *J* = 7.5 Hz, 8b-H), 6.13 (t, 1 H, *J* = 1.5 Hz, 2′-H), 6.93 (t, 1 H, *J* = 1.5 Hz, 3′-H), 7.42 (d, 1 H, *J* = 2.5 Hz, 9-H); δ (in C_6D_6) = 1.15 and 1.23 (2 m, 1 H each, 7-CH_2), 1.22 (d, 3 H, *J* = 7.0 Hz, 8-Me), 1.31 (t, 3 H, *J* = 1.5 Hz, 4′-Me), 1.38−1.47 (m, 3 H, 5-H and 6-CH_2), 1.55 (m, 1 H, 5-H′), 2.05 (m, 1 H, 8-H), 2.17 (d, 1 H, *J* = 16.5 Hz, 4-H), 2.27 (ddd, 1 H, *J* = 16.5, *J′* = 9.0, *J″* = 3.0 Hz, 4-H′), 3.19 (m, 1 H, 3a-H), 4.86 (d, 1 H, *J* = 8.0 Hz, 8b-H), 4.99 (t, 1 H, *J* = 1.5 Hz, 2′-H), 5.66 (t, 1 H, *J* = 1.5 Hz, 3′-H), 7.31 (d, 1 H, *J* = 2.5 Hz, 9-H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.7, 20.0, 20.2, 26.2, 30.1, 31.6, 36.7, 41.4, 90.9, 100.6, 114.4, 135.7, 136.4, 141.1, 142.9, 150.0, 170.3, 171.8. − $C_{18}H_{20}O_5$ (316.4): calcd. C 68.34, H 6.37; found C 68.04, H 6.40.

Methyl (*S*)-Citronellate (14): Methyl (*S*)-citronellate was prepared from (*S*)-citronellal (97.0% *ee*, Takasago) by Jones′ CrO_3 oxidation and esterification with K_2CO_3 and methyl iodide (65% over the 2 steps), b.p. 104°C/24 Torr. − IR (film): $\tilde{\nu}$ = 1745 cm^{-1} (s, C=O), 1200 (m, C−O), 1160 (m, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.94 (d, 3 H, *J* = 6.4 Hz, 3-Me), 1.05−1.46 (m, 2 H, 4-CH_2), 1.59 (s, 3 H, 7-Me), 1.68 (d, 3 H, *J* = 0.9 Hz, 7-Me), 1.74−2.41 (m, 5 H, 2-CH_2, 3-H and 5-CH_2), 3.66 (s, 3 H, OMe), 5.08 (t, 1 H, *J* = 7.0 Hz, 6-H). − $[\alpha]_D^{26.0}$ = −7.6 (*c* = 2.50, $CHCl_3$) {ref.[32] $[\alpha]_D^{22}$ = −6.70 (*c* = 2.28, $CHCl_3$)}.

Methyl (*S*)-6-Hydroxy-3-methylhexanoate (15): To an ice-cooled mixture of the methyl ester **14** (57.0 g, 0.31 mol) and $NaHCO_3$ (28.6 g, 0.34 mol) in CH_2Cl_2 (1 L), *m*-chloroperbenzoic acid (*m*CPBA, 84.0 g, 0.34 mol) was carefully added in several portions. The resulting mixture was stirred for 30 min at 0°C, quenched by the addition of $Na_2S_2O_3$ solution, and then extracted with CH_2Cl_2. The organic layer was successively washed with satd. $NaHCO_3$ solution, water and brine, and dried with $MgSO_4$. Evaporation of the solvent gave a crude product, which was purified by silica-gel column chromatography (hexane/ethyl acetate, 20:1) to afford 62.0 g of a diastereomeric mixture of the epoxide as a colorless oil. This was used for the next transformation without further purification. − IR (film): $\tilde{\nu}$ = 2960 cm^{-1} (s, C−H), 1740 (s, C=O), 1250 (m, epoxide), 1205 (m, C−O), 1165 (m, C−O), 1120 (m, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.97 (d, 3 H, *J* = 6.4 Hz, 3-Me), 1.26 and 1.30 (2 s, 3 H each, 2 × Me), 1.47−1.67 (m, 4 H, 4-CH_2 and 5-CH_2), 1.82−2.43 (m, 3 H, 2-CH_2 and 3-H), 2.70 (t, 1 H, *J* = 6.7 Hz, 6-H), 3.67 (s, 3 H, OMe). − To an ice-cooled solution of $HIO_4 \cdot 2\,H_2O$ (74.2 g, 0.34 mol) in THF (800 mL), an ethereal solution (600 mL) of the above epoxide (ca. 0.31 mol) was added dropwise over a period of 1 h. After stirring for 30 min at 0°C, the mixture was diluted with water and extracted with diethyl ether. The combined organic layers were successively washed with water, satd. $NaHCO_3$ solution and brine, and dried with $MgSO_4$. Evaporation of the solvent gave a crude product, which was purified by silica-gel column chromatography (hexane/ethyl acetate, 15:1) to afford the aldehyde as a colorless oil. This was employed in the next transformation without further purification. − IR (film): $\tilde{\nu}$ = 2830 cm^{-1} (m, OC−H), 2730 (w, OC−H), 1740 (s, C=O), 1725 (s, C=O), 1205 (m, C−O), 1165 (m, C−O). − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (d, 3 H, *J* = 6.8 Hz, 3-Me), 1.54 and 1.71 (2 m, 1 H each, 4-CH_2), 2.00 (m, 1 H, 3-H), 2.19 (dd, 1 H, *J* = 15.1, *J′* = 7.5 Hz, 2-H), 2.31 (dd, 1 H, *J* = 15.1, *J′* = 6.3 Hz, 2-H′), 2.47 (dtd, 2 H, *J* = 8.9, *J′* = 6.2, *J″* = 1.6 Hz, 5-CH_2), 3.68 (s, 3 H, OMe), 9.78 (t, 1 H, *J* = 1.6 Hz, CHO). − To an ice-cooled solution of the above aldehyde (ca. 0.31 mol) in methanol (700 mL), $NaBH_4$ (12.5 g, 0.33 mol) was carefully added in several portions. After stirring for 1 h at 0°C, the mixture was diluted with water, concentrated to remove most of the methanol, and extracted with diethyl ether. The organic layer was washed with brine and dried with $MgSO_4$. Evaporation of the solvent gave a crude product, which was purified by silica-gel column chromatography (hexane/ethyl acetate, 10:1) to afford 43.8 g (91% from **14** over 3 steps) of the alcohol **15**[35] as a colorless oil. Distillation furnished an analytical sample, b.p. 99−100°C/24 Torr. − IR (film): $\tilde{\nu}$ = 3600−3200 cm^{-1} (m, O−H), 1735 (s, C=O), 1200 (m, C−O), 1160 (m, C−O), 1055 (m, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (d, 3 H, *J* = 6.6 Hz, 3-Me), 1.23 and 1.38 (2 m, 1 H each, 4-CH_2), 1.56 (m, 2 H, 5-CH_2), 1.91−2.03 (m, 2 H, 3-H and OH), 2.12 (dd, 1 H, *J* = 14.9, *J′* = 6.4 Hz, 2-H), 2.19 (dd, 1 H, *J* = 14.9, *J′* = 7.3 Hz, 2-H′), 3.60 (t, 2 H, *J* = 6.5 Hz, 6-CH_2), 3.64 (s, 3 H, OMe). − $[\alpha]_D^{23.0}$ = −6.6 (*c* = 2.50, $CHCl_3$).

Methyl (*S*)-6-Iodo-3-methylhexanoate (16): To a stirred, ice-cooled mixture of the alcohol **15** (51.0 g, 0.32 mol) and pyridine (50 mL) in CH_2Cl_2 (200 mL), *p*-toluenesulfonyl chloride (92 g, 0.48 mol) was added portionwise. The resulting mixture was stirred for 19 h at 5°C, then diluted with water, and poured into dilute aq. HCl. This mixture was extracted with diethyl ether and the combined organic layers were successively washed with dilute aq. HCl, satd. $NaHCO_3$ solution and brine, and dried with $MgSO_4$. Evaporation of the solvent gave a crude product, which was purified by silica-gel column chromatography (hexane/ethyl acetate, 25:1) to afford the corresponding tosylate as a colorless oil. This was used for the subsequent transformation without further purification. − IR (film): $\tilde{\nu}$ = 1740 cm^{-1} (s, C=O), 1600 (m, Ar), 1500 (w, Ar), 1360 (s, sulfonate), 1190 (s, sulfonate), 1180 (s, sulfonate), 970 (m, S−O−C), 920 (m, S−O−C), 660 (s, Ar). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.90 (d, 3 H, *J* = 6.4 Hz, 3-Me), 1.05−2.03 (m, 5 H, 3-H, 4-CH_2 and 5-CH_2), 2.05−2.38 (m, 2 H, 2-CH_2), 2.45 (s, 3 H, 3-Me), 3.65 (s, 3 H, OMe), 4.02 (t, 2 H, *J* = 6.3 Hz, 6-CH_2), 7.34 (d, 2 H, *J* = 8.4 Hz, Ar), 7.79 (d, 2 H, *J* = 8.4 Hz, Ar). − A mixture of the above tosylate (ca. 0.32 mol) and sodium iodide (62.4 g, 0.42 mol) in acetone (950 mL) was refluxed for 2 h and then diluted with water. The resulting mixture was then concentrated to remove most of the acetone and extracted with diethyl ether. The combined organic layers were successively washed with water, satd. $Na_2S_2O_3$ solution, satd. $NaHCO_3$ solution and brine, and dried with $MgSO_4$. Evaporation of the solvent gave a crude product, which was purified by silica-gel column chromatography (hexane/diethyl ether, 80:1) to afford 71.1 g (81% from **15** over 2 steps) of the iodide **16** as a colorless oil. Distillation of the oil gave an analytical sample, b.p. 109−110°C/10 Torr. − n_D^{24} = 1.4940. − IR (film): $\tilde{\nu}$ = 1745 cm^{-1} (s, C=O), 1200 (s, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.94 (d, 3 H, *J* = 6.1 Hz, 3-Me), 1.11−1.54 (m, 2 H), 1.55−2.39 (m, 5 H), 3.16 (t, 2 H, *J* = 6.8 Hz, 6-CH_2), 3.66 (s, 3 H, OMe). − $[\alpha]_D^{24.0}$ = −12.6 (*c* = 2.00, $CHCl_3$). − $C_8H_{15}IO_2$ (270.1): calcd. C 35.57, H 5.60; found C 35.54, H 5.58.

Methyl (*S*)-3-Methyl-7-octynoate (17): To a solution of the iodide **16** (21.6 g, 80 mmol) in dry THF/DMSO (2:1, 120 mL) under argon at 5°C was slowly added a suspension of ca. 90% lithium acetylide ethylenediamine complex (9.8 g, 96 mmol) in dry THF/

DMSO (2:1, 120 mL). After stirring for 15 min at 5°C, water was added to the resulting dark-orange suspension. The mixture was extracted with diethyl ether and the combined organic layers were washed with water and brine, and dried with $MgSO_4$. Evaporation of the solvent gave a crude product, which was chromatographed on silica gel (pentane/diethyl ether, 250:1) to afford 4.97 g (37%) of **17** as a colorless oil, b.p. 86−89°C/16 Torr. − n_D^{24} = 1.4411. − IR (film): $\tilde{\nu}$ = 3300 cm^{-1} (m, ≡C−H), 2130 (w, C≡C), 1740 (s, C=O), 1200 (s, C−O), 1155 (m, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (d, 3 H, *J* = 6.6 Hz, 3-Me), 1.20−1.62 (m, 4 H, 4-CH_2 and 5-CH_2), 1.92 (t, 1 H, *J* = 2.6 Hz, 8-H), 1.96 (m, 1 H, 3-H), 2.11 (dd, 1 H, *J* = 14.8, *J′* = 8.0 Hz, 2-H), 2.16 (td, 1 H, *J* = 7.0, *J′* = 2.6 Hz, 6-CH_2), 2.29 (dd, 1 H, *J* = 14.8, *J′* = 6.1 Hz, 2′-H), 3.64 (s, 3 H, OMe). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 18.4, 19.5, 25.8, 29.9, 35.6, 41.4, 51.3, 68.2, 84.2, 173.4. − MS (EI, 70 eV): *m/z* = 153 [M^+ − Me], 139, 127, 114, 109, 101, 95, 87, 81, 74, 59. − $[\alpha]_D^{25.2}$ = −10.0 (*c* = 1.10, $CHCl_3$). − Due to the high volatility of **17**, correct elemental analytical data could not be obtained.

Methyl (3*S*)-3-Methyl-2-phenylselenenyl-7-octynoate (18): To a stirred solution of lithium diisopropylamide (LDA, 7.39 mmol), prepared from diisopropylamine (1.14 mL, 8.13 mmol) and *n*-butyllithium (1.66 M hexane solution, 4.45 mL, 7.39 mmol), in dry THF (14 mL), was added a solution of the ester **17** (564 mg, 3.36 mmol) in THF (14 mL) at −78°C under argon. The resulting white suspension was stirred for 1 h at −78°C, allowed to warm to −30°C over a period of 1 h, and then cooled to −78°C once more. A solution of phenylselenenyl bromide (1.21 g, 3.86 mmol) in THF (8 mL) was added to the mixture at −78°C and stirring was continued for 1 h. The resulting dark-orange solution was slowly allowed to warm to room temperature, poured into 1 N HCl, and extracted with diethyl ether. The ethereal layer was washed with water (twice) and brine, and dried with $MgSO_4$. Evaporation of the solvent followed by silica-gel column chromatography (hexane/diethyl ether, 100:1) afforded a diastereomeric mixture of the selenide **18** (748 mg, 69%) as a yellowish oil, which was used without further purification in the next step. − IR (film): $\tilde{\nu}$ = 3250 cm^{-1} (w, ≡C−H), 2120 (vw, C≡C), 1735 (s, C=O), 1575 (m, Ar), 1210 (s, C−O), 1200 (s, C−O), 1150 (m, C−O), 740 (s, Ar). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.97 and 1.17 (2 d, 3 H total, *J* = 6.2, 6.6 Hz, 3-Me), 1.25−1.70 (m, 4 H, 4-CH_2 and 5-CH_2), 1.97 (m, 1 H, 8-H), 2.02−2.44 (m, 3 H, 3-H and 6-CH_2), 3.53 (m, 1 H, 2-H), 3.64 and 3.69 (2 s, 3 H each, 2 × OMe), 7.36 (m, 3 H, Ar), 7.64 (m, 2 H, Ar).

Methyl (2*S*)-2-Methyl-6-methylenecyclohexane-1-carboxylate (19): To a stirred mixture of the selenide **18** (3.88 g, 12 mmol) and 2,2′-azobisisobutyronitrile (AIBN) (0.20 g, 1.2 mmol) in dry benzene (400 mL) under reflux, a solution of tri-*n*-butyltin hydride (6.45 mL, 24 mmol) in dry benzene (50 mL) was added dropwise over a period of 15 min. The resulting pale-pink solution was refluxed for a further 1 h and then cooled to room temperature. Evaporation of the solvent left a dark-yellow residue, which was purified by silica-gel column chromatography (pentane/diethyl ether, 250:1) and distillation (b.p. 84−88°C/20 Torr) to afford an inseparable mixture (1.11 g) of **19** and methyl (*S*)-3-methyl-7-octenoate, the acyclic reduction product, as a colorless oil. This mixture was used directly for the next transformation. − IR (film): $\tilde{\nu}$ = 3240 cm^{-1} (w, C=C−H), 1740 (s, C=O), 1640 (m, C=C), 1200 (m, C−O), 1160 (s, C−O), 910 (m, =CH_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ (for **19**) = 0.94 (d, 3 H, *J* = 6.5 Hz, 2-Me), 1.12−1.52 (m, 3 H, 3-CH_2 and 4-H), 1.78 (m, 1 H, 4-H′), 1.91−2.10 (m, 2 H, 5-CH_2), 2.34 (m, 1 H, 2-H), 2.74 (d, 1 H, *J* = 9.6 Hz, 1-H), 3.74 (s, 3 H, OMe), 4.52 (d, 1 H, *J* = 1.2 Hz, =CH), 4.81 (s, 1 H, =CH). − MS (EI, 70 eV): *m/z* = 168 [M^+], 153, 136, 125, 109, 108, 93, 79, 67, 55.

Methyl (6*S*)-2-Bromo-2-bromomethyl-6-methylcyclohexane-1-carboxylate (20): To a mixture of **19** and methyl (*S*)-3-methyl-7-octenoate (32 mg), obtained as described above, in $CHCl_3$ (1.5 mL), ca. 90% pyridinium hydrobromide perbromide (77 mg, ca. 0.22 mmol) was added portionwise at −60°C. After stirring for 3 h at this temperature, the reaction mixture was extracted with $CHCl_3$. The organic layer was washed twice with water and dried with $MgSO_4$. Evaporation of the solvent left a crude product, which was purified by silica-gel column chromatography (hexane/diethyl ether, 100:1) affording 49 mg (37% from **18**) of the dibromide **20** as colorless rods, m.p. 42−43°C (pentane). − IR (KBr): $\tilde{\nu}$ = 1735 cm^{-1} (s, C=O), 1195 (m, C−O), 1150 (s, CH_2Br). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.86−1.12 (m, 1 H), 0.93 (d, 3 H, *J* = 6.2 Hz, 6-Me), 1.64−2.35 (m, 5 H), 2.50 (d, 1 H, *J* = 10.8 Hz, 1-H), 3.75 (s, 3 H, OMe), 3.84 and 4.10 (AB, 1 H each, J_{AB} = 10.4 Hz, −CH_2Br). − $[\alpha]_D^{25.5}$ = +12.1 (*c* = 0.15, $CHCl_3$). − $C_{10}H_{16}Br_2O_2$ (328.0): calcd. C 36.61, H 4.92; found C 36.73, H 5.02.

Methyl (7*S*)-2-Methoxycarbonyl-7-methyl-1-oxo-2,3,4,5,6,7-hexahydroinden-2-ylacetate (21): To a stirred suspension of NaH (ca. 60% oil suspension, 288 mg, 7.21 mmol) in dry THF (25 mL) at −10°C under argon, was added dimethyl malonate (0.40 mL, 3.47 mmol). After stirring for 10 min at −10°C, a solution of the dibromo ester **20** (659 mg, 2.07 mmol) in dry THF (5 mL) was added dropwise. The resulting pale-yellow suspension was stirred for 28 h at room temperature and then methyl bromoacetate (665 mg, 4.35 mmol) was added. The dark-orange mixture was stirred for a further 43 h at room temperature, then quenched by the addition of water, and extracted with diethyl ether. The combined organic layers were washed with 5% Na_2CO_3 solution, water and brine, and dried with $MgSO_4$. Evaporation of the solvent left a crude product, which was chromatographed on silica gel (hexane/ethyl acetate, 11:1) to afford a diastereomeric mixture (ca. 1:1, as determined by ^{1}H-NMR analysis) of **21** (550 mg, 98%) as a yellowish viscous oil. This was used directly for the next transformation without further purification. − IR (film): $\tilde{\nu}$ = 1740 cm^{-1} (s, C=O), 1705 (s, C=O), 1645 (m, C=C), 1215 (m, C−O), 1200 (m, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 and 1.09 (2 d, 3 H total, *J* = 7.0 Hz, 7-Me), 1.43 (m, 1 H, 6-H), 1.58−1.86 (m, 3 H, 5-CH_2 and 6-H′), 2.19−2.58 (m, 3 H, 4-CH_2 and 7-H), 2.45 and 3.29 (AB, 1 H each, J_{AB} = 17.1 Hz), 2.47 and 3.24 (AB, 1 H each, J_{AB} = 17.4 Hz), 3.66 and 3.67 (2 s, 3 H total, OMe), 3.69 (s, 3 H, OMe).

(7*S*)-7-Methyl-1-oxo-2,3,4,5,6,7-hexahydroinden-2-ylacetic Acid (22): A solution of the diester **21** (28 mg, 0.10 mmol) in 6 N HCl (0.5 mL) and glacial acetic acid (0.5 mL) was refluxed for 2.5 h. It was then diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine and dried with $MgSO_4$. Evaporation of the solvent followed by silica-gel column chromatography (hexane/ethyl acetate, 2:1) afforded a diastereomeric mixture [ca. 1:1, as determined by HPLC (Chiralcel® OD)] of **22** (20 mg, 96%) as a pale-yellow paste, which was employed in the next transformation without further purification. − IR (film): $\tilde{\nu}$ = 3600−2800 cm^{-1} (m, O−H), 1730 (s, C=O), 1695 (s, C=O), 1420 (m, O−H), 1310 (m, C−O), 1205 (m, C−O), 920 (m, CO_2H). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (d, 3 H, *J* = 7.0 Hz, 7-Me), 1.45 (m, 1 H, 6-H), 1.60−1.84 (m, 3 H, 5-CH_2 and 6-H′), 2.19−2.33 (m, 3 H, 2-H and −CH_2CO_2−), 2.40 and 2.43 (2 dd, 1 H total, *J* = 16.2, *J′* = 6.6 Hz and *J* = 16.3, *J′* = 6.2 Hz, 3-H), 2.52 (m, 1 H, 7-H), 2.66−2.90 (m, 2 H, 4-CH_2), 2.86 (2 dd, 1 H total, *J* = 16.2, *J′* = 5.1 Hz and *J* = 16.3, *J′* = 5.5 Hz, 3′-H).

(3a*R*,8*S*,8b*S*)- and (3a*S*,8*S*,8b*R*)-8-Methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one (9 and 10): A mixture of the oxo acid **22** (300 mg, 1.44 mmol) and $CeCl_3 \cdot 7\ H_2O$ (1.07 g, 2.88 mmol) in methanol (22 mL) was treated with $NaBH_4$ (219 mg, 5.76 mmol) at 0°C. After stirring for 45 min at room temperature, the mixture was acidified with 20% H_2SO_4 and then extracted with ethyl acetate. The combined organic layers were washed with satd. $NaHCO_3$ solution and brine, and dried with $MgSO_4$. Evaporation of the solvent gave a crude product, which was purified by silica-gel column chromatography (hexane/ethyl acetate, 7:1) to afford a diastereomeric mixture of the tricyclic lactones **9** and **10**. The mixture was separated by medium-pressure liquid chromatography [Lobar LiChroprep® Si 60 (40−63 mm), hexane/2-propanol, 33:1] to furnish a fast-moving diastereomer **9** (59 mg, 21%) as a pale-yellow oil and a slow-moving one **10** (83 mg, 30%) as a white solid. The latter was recrystallized from hexane to afford colorless needles. − **(+)-9:** 97.2% *ee* {determined by GC [column: Chirasil-Dex CB®, 0.25 mm × 25 m, 100°C (1 min) to 210°C (5°C/min); carrier gas: He (120 kPa); detector: FID]; (−)-**9**: t_R = 21.48 min (1.4%) and (+)-**9**: t_R = 21.68 min (98.6%)}. − Its IR and ^{1}H-NMR spectra were identical to those of (±)-**9**. − n_D^{25} = 1.4991. − $[\alpha]_D^{24.6}$ = +3.0 (*c* = 0.60, $CHCl_3$). − **(−)-10:** > 99.9% *ee* {determined by GC [column: Chirasil-Dex CB®, 0.25 mm × 25 m, 100°C (1 min) to 210°C (5°C/min); carrier gas: He (120 kPa); detector: FID]; (−)-**10**: t_R = 16.55 min (> 99.9%); (+)-**10**: t_R = 16.77 min (undetectable)}; m.p. 45−47°C (hexane). − IR (KBr): $\tilde{\nu}$ = 1765 cm^{-1} (s, C=O), 1170 (s, C−O). − Its ^{1}H-NMR spectrum was identical to that of (±)-**10**. − $[\alpha]_D^{26.0}$ = −68.4 (*c* = 0.40, $CHCl_3$). − $C_{12}H_{16}O_2$ (192.3): calcd. C 74.97, H 8.39; found C 74.78, H 8.26.

Methyl (7*S*)-7-Methyl-1-oxo-2,3,4,5,6,7-hexahydroindene-2-carboxylate (23): To a solution of sodium methoxide, prepared from sodium (217 mg, 9.44 mmol) and methanol (10 mL), was added dimethyl malonate (1.31 g, 9.91 mmol). The resulting mixture was cooled in an ice bath and stirred for 15 min. At this temperature, a solution of the dibromide **20** (583 mg, 1.78 mmol) in methanol (30 mL) was added dropwise. The mixture was stirred at room temperature for 14.5 h and then refluxed for 2 h. The resulting orange solution was acidified with acetic acid and extracted with ethyl acetate. The organic layer was washed with $NaHCO_3$ solution, water and brine, and dried with $MgSO_4$. Evaporation of the solvent gave a crude product, which was chromatographed on silica gel (hexane/ethyl acetate, 16:1) to afford a diastereomeric mixture of the β-oxo ester **23** (342 mg, 93%) as a yellowish paste. This was employed in the subsequent step without further purification. − IR (film): $\tilde{\nu}$ = 1740 cm^{-1} (s, C=O), 1705 (s, C=O), 1640 (s, C=C), 1215 (m, C−O), 1160 (s, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (d, 3 H, *J* = 7.0 Hz, 7-Me), 1.45 (m, 1 H, 6-H), 1.63−1.83 (m, 3 H, 5-CH_2 and 6-H′), 2.33 (m, 2 H, 4-CH_2), 2.52 (m, 1 H, 7-H), 2.67 (dd, 1 H, *J* = 18.1, *J*′ = 5.5 Hz, 3-H), 2.88 (d, 1 H, *J* = 18.0 Hz, 3-H′), 3.40 (m, 1 H, 2-H), 3.76 (s, 3 H, OMe).

(*S*)-7-Methyl-1-oxo-2,3,4,5,6,7-hexahydroindene (24): A solution of the β-oxo ester **23** (198 mg, 0.95 mmol) in 6 N HCl/glacial acetic acid (4:1, 2.5 mL) was refluxed for 1 h under argon. The reaction mixture was then diluted with water and extracted with diethyl ether. The combined organic layers were washed with water and brine, and dried with $MgSO_4$. Evaporation of the solvent left a yellowish residue, which was chromatographed on silica gel (pentane/diethyl ether, 9:1) to afford the α,β-unsaturated ketone **24** (103 mg, 72%) as a pale-yellow oil, n_D^{24} = 1.4841. − IR (film): $\tilde{\nu}$ = 2950 cm^{-1} (s, C−H), 1695 (s, C=O), 1645 (s, C=C), 1250 (m, C−O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (d, 3 H, *J* = 7.2 Hz, 7-Me), 1.43 (m, 1 H, 6-H), 1.58−1.82 (m, 3 H, 5-CH_2 and 6-H′), 2.28 (m, 2 H), 2.35 (m, 2 H), 2.45 (m, 2 H), 2.52 (m, 1 H, 7-H). − MS (EI, 70 eV): *m/z* = 150 [M^+], 135, 122, 117, 108, 93, 79. − HRMS: calcd. for $C_{10}H_{14}O$: 150.1045; found 150.1017.

(*S*)-7-Methyl-1-oxo-2,3,4,5,6,7-hexahydroindene RAMP-Hydrazone (25): A mixture of the α,β-unsaturated ketone **24** (50 mg, 0.32 mmol) and (*R*)-(+)-1-amino-2-(methoxymethyl)pyrrolidine (RAMP, 216 mg, 1.65 mmol) was heated at 90°C for 20 h. The mixture was then diluted with CH_2Cl_2, washed with water and brine, and dried with $MgSO_4$. Evaporation of the solvent left a yellowish crude product, which was chromatographed on silica gel (hexane/diethyl ether, 9:1) to afford the RAMP-hydrazone **25** (81 mg, 93%) as a yellowish paste. This was employed in the subsequent alkylation reaction without further purification. − IR (film): $\tilde{\nu}$ = 2940 cm^{-1} (s, C−H), 1700 (m, C=N), 1645 (m, C=N), 1620 (m, C=C), 1130 (s, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 1.10 (d, 3 H, *J* = 6.8 Hz, 7-Me), 1.40−2.80 (m, 17 H), 3.05−3.62 (m, 3 H), 3.34 (s, 3 H, OMe).

(3a*R*,8*S*,8b*S*)-3-Hydroxymethylene-8-methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one (11): In the same manner as described for (±)-**11**, the lactone **9** (29 mg, 0.15 mmol) was formylated using NaH (ca. 60% oil suspension, 18 mg, ca. 0.45 mmol) and ethyl formate (0.15 mL, ca. 2 mmol) in dry diethyl ether (4.0 mL) to afford 33 mg (quant.) of the formylated lactone **11** (a tautomeric mixture of the enol and the aldehyde in a ca. 2.1:1 ratio, as determined by ^{1}H-NMR analysis) as a slightly yellow solid. This was employed in the subsequent step without further purification; m.p. 113−115°C. − IR (KBr): $\tilde{\nu}$ = 3600−3000 cm^{-1} (m, O−H), 2730 (m, OC−H), 1715 (s, C=O), 1680 (m, C=O), 1640 (m, C=C), 1415 (w, OC−H), 1200 (s, C−O), 1080 (m, C−O). − Its ^{1}H-NMR spectrum was identical to that of (±)-**11**. − $[\alpha]_D^{24.8}$ = +144.3 (*c* = 0.30, $CHCl_3$).

(3a*S*,8*S*,8b*R*)-3-Hydroxymethylene-8-methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one (12): In the same manner as described for (±)-**11**, the lactone **10** (33 mg, 0.17 mmol) was formylated using NaH (ca. 60% oil suspension, 20 mg, ca. 0.51 mmol) and ethyl formate (0.16 mL, ca. 2 mmol) in dry diethyl ether (3.0 mL) to afford 30 mg (quant.) of the formylated lactone **12** (a tautomeric mixture of the enol and the aldehyde in a ca. 1.1:1 ratio, as determined by ^{1}H-NMR analysis) as a white solid. This was employed in the subsequent step without further purification; m.p. 143−145°C. − IR (KBr): $\tilde{\nu}$ = 3300−2800 cm^{-1} (s, O−H), 2750 (m, OC−H), 1710 (s, C=O), 1680 (m, C=O), 1600 (m, C=C), 1430 (m, OC−H), 1205 (s, C−O). − Its ^{1}H-NMR spectrum was identical to that of (±)-**12**. − $[\alpha]_D^{24.4}$ = −232.2 (*c* = 0.30, $CHCl_3$).

(3a*R*,8*S*,8b*S*,2′*R*)- and (3a*R*,8*S*,8b*S*,2′*S*)-3-[(*E*)-2′,5′-Dihydro-4′-methyl-5′-oxo-2′-furanyloxymethylene]-8-methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one (Sorgolactone and 2′-Episorgolactone, 2a and 2b): In the same manner as described for (±)-**2a** and (±)-**2b**, the hydroxymethylene lactone **11** (33 mg, 0.15 mmol) was coupled with the bromobutenolide (±)-**13** (53 mg, 0.30 mmol) in the presence of K_2CO_3 (41 mg, 0.30 mmol) in anhydrous *N*-methylpyrrolidone (2.5 mL). Silica-gel column chromatography (hexane/ethyl acetate, 6:1) gave first 18 mg (38%) of sorgolactone (**2a**) as colorless needles (R_f = 0.41, hexane/ethyl acetate, 1:1) and then 22 mg (46%) of 2′-episorgolactone (**2b**) as an amorphous powder (R_f = 0.33, hexane/ethyl acetate, 1:1). − **Sorgolactone [(+)-2a]:** > 99.9% *ee* determined by HPLC (column: Chiralcel® OD, 4.6 mm × 25 cm; solvent: hexane/2-PrOH, 4:1; flow rate: 0.5 mL/min; detector: 205 nm); (−)-**2a**: t_R = 24.7 min (undetectable); (+)-**2a**: t_R = 24.8 min (> 99.9%)]. − M.p. 145−147°C (hexane/ethyl acetate). − IR (KBr): $\tilde{\nu}$ = 2925 cm^{-1} (m), 2865 (w), 1780 (s, C=O), 1765 (s, C=O), 1740 (s, C=O), 1680 (s, C=C), 1400 (w), 1350 (m), 1335 (m), 1215 (w), 1180 (s, C−O), 1100 (s), 1055 (m), 1020

(s, C−O), 970 (s), 930 (m), 875 (m), 750 (w). − Its ^{1}H-NMR spectrum was identical to that of (±)-**2a**. − $[\alpha]_D^{24.8} = +285.2$ ($c = 0.26$, $CHCl_3$). − CD (CH_3CN, 43.4 μM): λ_{max} ($\Delta\varepsilon$) = 205 nm (−16.3), 230 (+26.8), 263 (−2.1). − $C_{18}H_{20}O_5$ (316.4): calcd. C 68.34, H 6.37; found C 68.09, H 6.18. − **2′-Episorgolactone [(+)-2b]:** 99.9% *ee* determined by HPLC (column: Chiralcel® OD, 4.6 mm × 25 cm; solvent: hexane/2-PrOH, 4:1; flow rate: 0.5 mL/min; detector: 205 nm); (+)-**2b**: t_R = 22.0 min (99.95%); (−)-**2b**: t_R = 25.7 min (0.05%)]. − IR (KBr): $\tilde{\nu}$ = 2930 cm^{-1} (m), 1780 (s, C=O), 1745 (s, C=O), 1680 (s, C=C), 1340 (m), 1210 (m), 1185 (s, C−O), 1095 (s), 1020 (s, C−O), 955 (s), 930 (w), 875 (w), 775 (w). − Its ^{1}H-NMR spectrum was identical to that of (±)-**2b**. − $[\alpha]_D^{23.4} = +109.5$ ($c = 0.10$, $CHCl_3$). − CD (CH_3CN, 31.8 μM): λ_{max} ($\Delta\varepsilon$) = 218 nm (−5.0), 245 (+4.3). − $C_{18}H_{20}O_5$ (316.4): calcd. C 68.34, H 6.37; found C 68.26, H 6.37.

(3a*S*,8*S*,8b*R*,2′*S*)- and (3a*S*,8*S*,8b*R*,2′*R*)-3-[(*E*)-2′,5′-Dihydro-4′-methyl-5′-oxo-2′-furanyloxymethylene]-8-methyl-3,3a,4,5,6,7,8,8b-octahydroindeno[1,2-*b*]furan-2-one (8-Episorgolactone and 2′,8-Diepisorgolactone, 2c and 2d): In the same manner as described for (±)-**2a** and (±)-**2b**, the hydroxymethylene lactone **12** (36 mg, 0.16 mmol) was coupled with the bromobutenolide (±)-**13** (57 mg, 0.32 mmol) in the presence of K_2CO_3 (44 mg, 0.32 mmol) in anhydrous *N*-methylpyrrolidone (2.0 mL). Silica-gel column chromatography (hexane/ethyl acetate, 6:1) gave first 17 mg (33%) of 8-episorgolactone (**2c**) as colorless crystals (R_f = 0.41, hexane/ethyl acetate, 1:1) and then 25 mg (48%) of 2′,8-diepisorgolactone (**2d**) as colorless crystals (R_f = 0.33, hexane/ethyl acetate, 1:1). − **8-Episorgolactone [(−)-2c]:** > 99.9% *ee* determined by HPLC (column: Chiralcel® OD, 4.6 mm × 25 cm; solvent: hexane/2-PrOH, 4:1; flow rate: 0.5 mL/min; detector: 205 nm); (+)-**2c**: t_R = 30.3 min (undetectable); (−)-**2c**: t_R = 39.8 min (> 99.9%)]. − m.p. 178−179°C (hexane/ethyl acetate). − IR (KBr): $\tilde{\nu}$ = 2930 cm^{-1} (m), 1780 (s, C=O), 1765 (s, C=O), 1740 (s, C=O), 1680 (s, C=C), 1400 (m), 1345 (m), 1340 (s), 1220 (w), 1183 (s, C−O), 1100 (s), 1055 (m), 1020 (s, C−O), 965 (s), 925 (w), 880 (w), 755 (w), 745 (w). − Its ^{1}H-NMR spectrum was identical to that of (±)-**2c**. − $[\alpha]_D^{24.6} = -354.8$ (c = 0.20, $CHCl_3$). − CD (CH_3CN, 40.5 μM): λ_{max} ($\Delta\varepsilon$) = 206 nm (+16.5), 229 (−26.5), 263 (+2.8). − $C_{18}H_{20}O_5$ (316.4): calcd. C 68.34, H 6.37; found C 68.24, H 6.24. − **2′,8-Diepisorgolactone [(−)-2d]:** > 99.9% *ee* determined by HPLC (column: Chiralcel® OD, 4.6 mm × 25 cm; solvent: hexane/2-PrOH, 4:1; flow rate: 0.5 mL/min; detector: 205 nm); (+)-**2d**: t_R = 26.8 min (undetectable); (−)-**2d**: t_R = 29.6 min (> 99.9%)]. − M.p. 136−137°C (hexane/ethyl acetate). − IR (KBr): $\tilde{\nu}$ = 2930 cm^{-1} (m), 1775 (s, C=O), 1750 (s, C=O), 1740 (s, C=O), 1675 (s, C=C), 1350 (m), 1340 (s), 1180 (s, C−O), 1090 (s), 1020 (s, C−O), 955 (s), 930 (w), 870 (w), 750 (w). − Its ^{1}H-NMR spectrum was identical to that of (±)-**2d**. − $[\alpha]_D^{23.4} = -185.0$ (c = 0.20, $CHCl_3$). − CD (CH_3CN, 41.1 μM): λ_{max} ($\Delta\varepsilon$) = 217 nm (+8.6), 245 (−2.9). − $C_{18}H_{20}O_5$ (316.4): calcd. C 68.34, H 6.37; found C 68.31, H 6.35.

X-ray Analysis of (±)-10: Crystal size, 0.2 × 0.5 × 0.8 mm. All data were obtained with a Rigaku AFC-5S automated four-circle diffractometer using graphite-monochromated Mo-K_α radiation. Final lattice parameters were obtained from a least-squares refinement using 25 reflections. Crystal data: $C_{12}H_{16}O_2$, M_r = 192.26, monoclinic, space group $P2_1/a$, a = 9.020(6), b = 7.494(6), c = 15.673(3) Å, β = 96.26(3)°, V = 1053.1(8) Å^3, Z = 4, D_X = 1.213 g/cm^3, F(000) = 416, μ(Mo-K_α) = 0.756 cm^{-1}. The intensities were measured using ω/2θ scans up to 45°. Three standard reflections were monitored every 150 measurements. The data were corrected for Lorentz and polarization factors. An absorption correction was applied, but not a decay correction. Of the 1521 independent reflections collected, 840 reflections with $I > 3.0\sigma(I)$ were used for the structure determination and refinement. The structure was solved by direct methods using the TEXSAN crystallographic software package.[36] All non-H atoms were located in a Fourier map. All H atoms were calculated at geometrical positions and were not refined. Atomic parameters were refined by full-matrix least-squares methods, using anisotropic temperature factors for all non-H atoms. The final refinement converged with R = 0.058 and R_w = 0.072 for 127 parameters. The minimum and maximum peaks in the final difference Fourier map were −0.27 and 0.18 eÅ^{-3}. Atomic scattering factors were taken from "International Tables for X-ray Crystallography".[37] Supplementary material available includes lists of atomic coordinates for the non-H atoms, the bond lengths and angles in (±)-**10**, with their e.s.d.s in parentheses.[38]

X-ray Analysis of (±)-2a: Crystal size, 0.3 × 0.4 × 0.5 mm. All data were obtained with a Rigaku AFC-5S automated four-circle diffractometer using graphite-monochromated Mo-K_α radiation. Final lattice parameters were obtained from a least-squares refinement using 25 reflections. Crystal data: $C_{18}H_{20}O_5$, M_r = 316.35, monoclinic, space group $P2_1/n$, a = 6.957(3), b = 17.541(3), c = 13.777(4) Å, β = 97.78(3)°, V = 1665.8(9) Å^3, Z = 4, D_X = 1.261 g/cm^3, F(000) = 672, μ(Mo-K_α) = 0.86 cm^{-1}. The intensities were measured using ω/2θ scans up to 45°. Three standard reflections were monitored every 150 measurements. The data were corrected for Lorentz and polarization factors. An absorption correction was applied, but not a decay correction. Of the 2285 independent reflections collected, 1248 reflections with $I > 3.0\ \sigma(I)$ were used for the structure determination and refinement. The structure was solved by direct methods using the TEXSAN crystallographic software package.[36] All non-H atoms were located in a Fourier map. All H atoms were calculated at geometrical positions and were not refined. Atomic parameters were refined by full-matrix least-squares methods, using anisotropic temperature factors for all non-H atoms. The final refinement converged with R = 0.056 and R_w = 0.063 for 208 parameters. The minimum and maximum peaks in the final difference Fourier map were −0.24 and 0.25 eÅ^{-3}. Atomic scattering factors were taken from "International Tables for X-ray Crystallography".[37] Supplementary material available includes lists of atomic coordinates for the non-H atoms, the bond lengths and angles in (±)-**2a**, with their e.s.d.s in parentheses.[38]

Bioassays:[29] Seeds of *Orobanche minor* were harvested at the riverside of Watarase river in Tochigi in 1994 and 1995, dried, and stored in a refrigerator. Compounds to be tested were dissolved in a 10^{-4} M solution of gibberelin A_3. For preconditioning, the seeds were spread on glass fibre filter paper (5 mm diameter), wetted with a 10^{-4} M solution of gibberelin A_3, and stored in the dark for 10 d at room temperature. The seeds were then treated with the test solutions. After incubation in the dark for 6 d, the germination rate was determined under a microscope. In each series of tests, a 10^{-4} M solution of gibberelin A_3 was used as a negative control and (±)-strigol was used as a positive control. Tests were replicated 4 times.

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