Stereoselective Routes for the Total Synthesis of (+)-Cryptocarya Diacetate

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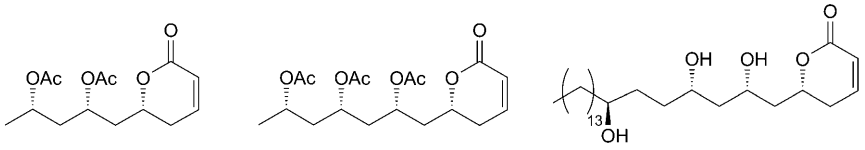
A stereoselective total synthesis of (+)-cryptocarya diacetate (**1**) was achieved by two different routes (*Schemes 2* and *3*). The sequences involve $LiAlH_4$/LiI reduction, ring-closing metathesis, *Prins* cyclization, *Wacker* oxidation, and *Wittig* olefination reactions as key steps.

Introduction. – The 1,3-diol structural unit is a common motif in many natural products. Cryptocarya diacetate (**1**) is the simplest example of such natural products. It is an α,β-unsaturated lactone isolated by *Drewes* and co-workers [1] in 1995 from the leaves and bark of the South African plant *Cryptocarya latifolia* which have been long sought after for their legendary magical and medicinal properties [2]. These properties range from the treatment of headaches and morning sickness to that of cancer, pulmonary diseases, and various bacterial and fungal infections. The structure of cryptocarya diacetate (**1**) has been unambiguously established by using NMR spectral techniques (COSY, HECTOR, DQFCOSY, HSQC, and HMBC). Other natural products containing the 1,3-diol and 5,6-dihydro-2*H*-pyran-2-one moieties [3a], such as cryptocarya triacetate (**2**) [1] and passifloricin A (**3**) [3b] having antifungal activity have also been isolated.



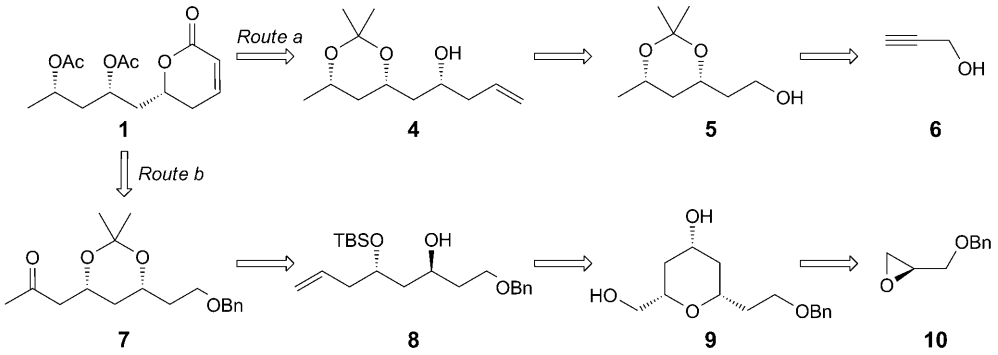
1 Cryptocarya diacetate **2** Cryptocarya triacetate **3** Passifloricin A

The preparation of 1,3-diol moieties is a challenge for the synthetic chemist. Because of its interesting structural feature and legendary medicinal properties, cryptocarya diacetate (**1**) has been the target of several syntheses. Earlier synthetic approaches for the preparation of **1** use *Sharpless* asymmetric epoxidation [4], enantio- and regioselective *Sharpless* dihydroxylation [5], an iterative *Jacobsen* hydrolytic kinetic resolution (HKR) [6], *Jacobsen*'s hydrolytic kinetic resolution of a multi-configurational synthon, and diastereoselective ketone reduction as the key steps for installing the chiral centers of the 1,3-diol system [7]. The synthesis of **1** was reported from our group [8] by an iterative *Prins* cyclization and reductive cleavage sequence.

Our ongoing project on synthesizing bioactive natural lactones [9] prompted us to explore the simple strategies for the synthesis of cryptocarya diacetate (**1**) as shown in a

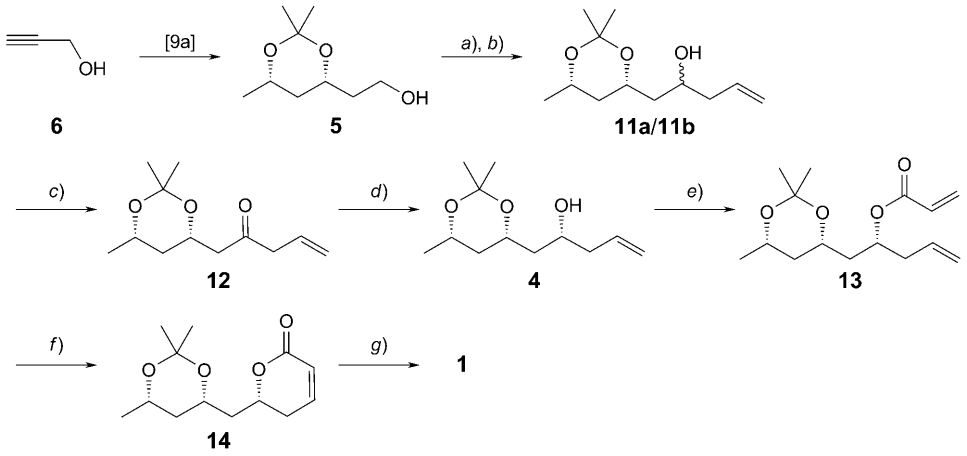
retrosynthetic plan, *i.e.*, by *Route a* from **6** *via* **5** and **4** and by *Route b* from **10** *via* **9**–**7** (*Scheme 1*).

Scheme 1. *Retrosynthetic Plan of* **1**



In *Route a*, the target molecule **1** could be synthesized from **4** through **5** *via* oxidation, allylation and diastereoselective reduction, acrylation, and ring-closing metathesis (RCM). Accordingly, the required compound **5** was prepared from commercially available propargyl alcohol (= prop-2-yn-1-ol; **6**) (*Scheme 2*) following the same procedure as that used for its enantiomer [9a]. Alcohol **5** was then oxidized to the corresponding aldehyde in 88% yield with *Dess–Martin* periodinane in CH_2Cl_2 followed by conversion into a mixture **11a**/**11b** of isomeric homoallylic alcohols under *Barbier* conditions (zinc, allyl bromide, sat. NH_4Cl in THF) in 82% yield. The diastereoisomer mixture **11** was converted into an enantiomerically enriched alcohol **4** by adopting an oxidation/selective reduction protocol. Accordingly, the mixture **11** was oxidized with *Dess–Martin* periodinane in CH_2Cl_2 at room temperature for 1 h to afford a β,γ-unsaturated ketone **12** in 88% yield. Compound **12** was subjected to '*syn*'-stereoselective reduction with 3 equiv. of $LiAlH_4$ in the presence of 3 equiv. of LiI [9a] in Et_2O at $-100°$ to provide the desired '*syn*'-alcohol **4** in 84% yield ('*syn*'/'*anti*' selectivity 95:5). Alcohol **4** was transformed into its acrylate ester **13** in 84% yield by treating with acryloyl chloride (= prop-2-enoyl chloride), catalytic amounts of DMAP (= *N*,*N*-dimethylpyridin-4-amine), and Et_3N in CH_2Cl_2. Ring-closing olefin metathesis [10] of **13** in refluxing CH_2Cl_2 for 3 h in the presence of *Grubbs*' catalyst (= benzylidenedichlorobis(tricyclohexylphosphine)ruthenium(IV); 10 mol-%) produced the isopropylidene-protected lactone **14** in 86% yield as a single diastereoisomer. Next, removal of the acetonide group was accomplished by heating **14** in 80% aqueous AcOH for 3 h at 60°. The crude diol was directly acylated after solvent removal by addition of Ac_2O in pyridine. This one pot protocol provided excellent yields of optically active cryptocarya diacetate (**1**), which had spectral data identical to that of the isolated material.

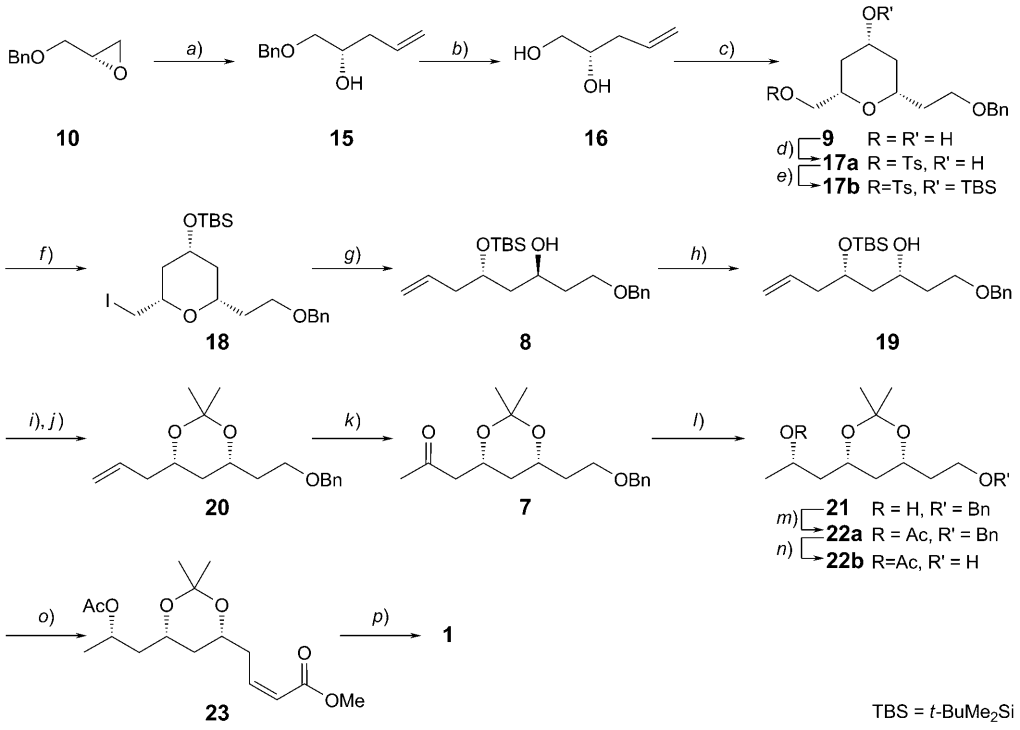
Scheme 2. *Synthesis of* **1** *from Prop-2-yn-1-ol* (**6**) (*Route a*)



a) *Dess–Martin* periodinane (=acetic acid 1,1″,1″-(3-oxo-1λ^5-1,2-benziodoxol-1(2*H*)-ylidyne) ester), CH_2Cl_2, r.t., 1 h; 88%. *b*) Allyl bromide, Zn, THF, 4 h; 82%. *c*) *Dess–Martin* periodinane, CH_2Cl_2, r.t., 1 h; 88%. *d*) $LiAlH_4$/LiI 1:1, Et_2O, $-100° \rightarrow$ r.t., 1 h; 84%. *e*) Acryloyl chloride, Et_3N, DMAP, $0° \rightarrow$ r.t., 2 h; 70%. *f*) 10 mol-% of *Grubbs*' catalyst, CH_2Cl_2, r.t., 3 h; 86%. *g*) AcOH/H_2O 4:1, 3 h, 60°, then Ac_2O/pyridine, DMAP; 76%.

In *Route b* (*Scheme 3*), the stereoselective synthesis of (+)-cryptocarya diacetate (**1**) by the *Prins*-cyclization methodology was considered. Accordingly, Cu-mediated opening of (2*S*)-2-[(benzyloxy)methyl]oxirane (**10**) [11] with vinylmagnesium bromide in THF afforded homoallylic alcohol **15**, which on treatment with lithium in liquid NH_3 underwent debenzylation to produce diol **16**. *Prins* cyclization of **16** with 3-(benzyloxy)propanal in the presence of CF_3COOH followed by hydrolysis of the resulting trifluoroacetate yielded the desired trisubstituted pyran derivative **9**. Tosylation of **9** with 1.1 equiv. of tosyl chloride (=4-methylbenzenesulfonyl chloride; TsCl) in the presence of Et_3N in CH_2Cl_2 produced the primary 4-methylbenzenesulfonate **17a** in 95% yield. Silyl protection of the secondary-alcohol function with *t*-$BuMe_2SiCl$ and 1*H*-imidazole in the presence of a catalytic amount of DMAP afforded compound **17b** in 92% yield. Compound **17b**, on exposure to NaI in refluxing acetone, was converted into the corresponding iodo derivative **18** in 24 h. The latter, on exposure to unactivated Zn in refluxing EtOH, furnished the open-chain key intermediate **8** with the '*anti*'-1,3-diol system. To get the 1,3-diol with the required '*syn*'-configuration, the OH group of **8** needed to be inverted, which was performed under standard *Mitsunobu* conditions [12] (DEAD (=diethyl diazene-1,2-dicarboxylate), Ph_3P, and 4-nitrobenzoic acid in dry THF, followed by hydrolysis of the resultant ester with K_2CO_3 in MeOH) and procured the inverted alcohol **19** in 75% yield. Desilylation of **19** with $(Bu_4N)F$ gave the 1,3-diol which was converted to acetonide **20** under conventional conditions with 2,2-dimethoxypropane in DMSO and the catalyst TsOH; the structure of '*syn*'-diol **20** was further confirmed [13] by ^{13}C-NMR spectroscopy. From **20**, methyl ketone **7** was obtained under modified *Wacker*-oxidation [14] conditions (0.1 equiv. of $PdCl_2$, 0.2 equiv. of $Cu(OAc)_2 \cdot H_2O$ in $AcNMe_2/H_2O$ 7:1) in 77% yield. '*syn*'-

Scheme 3. *Synthesis of* **1** *from 2-{(Benzyloxy)methyl]oxirane* **10** (*Route b*)



a) CH_2=CHMgBr, CuCN, $-78° \rightarrow 40°$, 4 h; 92%. *b*) Li, liq. NH_3, THF, $-30°$, 20 min, 75%. *c*) 3-(Benzyloxy)propanal, CF_3COOH, CH_2Cl_2, K_2CO_3, MeOH, r.t., 0.5 h; 65%. *d*) Et_3N, TsCl, CH_2Cl_2, $0° \rightarrow$ r.t., 3 h; 95%. *e*) *t*-$BuMe_2SiCl$, 1*H*-imidazole, DMAP (cat.), CH_2Cl_2, r.t.; 92%. *f*) NaI, acetone, reflux, 24 h; 95%. *g*) Unactivated Zn, EtOH, reflux, 1 h; 93%. *h*) 4-$NO_2C_6H_4COOH$, EtOOCN=N-COOEt, Ph_3P, THF, $0° \rightarrow$ r.t., 30 min, then K_2CO_3, MeOH, r.t., 4 h; 72%. *i*) $(Bu_4N)F$, THF, $0° \rightarrow$ r.t., 4 h; 90%. *j*) Acetone dimethyl acetal, TsOH, DMSO, 2 h; 94%. *k*) $PdCl_2$, $Cu(OAc)_2 \cdot H_2O$, O_2, DMF/H_2O 7:1, r.t., 3 to 4 h; 77%. *l*) $LiAlH_4$/LiI 1:1, Et_2O, $-100° \rightarrow$ r.t., 1 h; 84%. *m*) Ac_2O/pyridine, DMAP (cat.), CH_2Cl_2, r.t.; 94%. *n*) Pd/C, H_2, AcOEt, r.t.; 95%. *o*) 1. IBX (=1-hydroxy-1,2-benziodoxol-3-(1*H*)-one 1-oxide), DMSO, 0°, 6 h; 94%; 2. $(CF_3CH_2O)_2P(O)CH_2COOMe$, $KN(SiMe_3)_2$, THF, $-80°$, 0.5 h; 78%. *p*) 1. 0.1N HCl, MeOH; 86%; 2. $ZnCl_2$, THF, reflux; 80%; 3. Ac_2O/pyridine, CH_2Cl_2, DMAP (cat.), r.t.; 85% over three steps.

Stereoselective reduction of **7** with 3 equiv. of $LiAlH_4$ in the presence of 3 equiv. of LiI [9a] in Et_2O at $-100°$ provided the desired '*syn*'-compound **21** in 84% yield ('*syn*'/'*anti*' selectivity 95:5). The secondary OH group of **21** was acetylated (Ac_2O/pyridine in CH_2Cl_2 at r.t.), followed by the removal of the benzyl protecting group (Pd/C, H_2, in AcOEt at r.t.) to get alcohol **22b** in 95% yield. Oxidation of **22b** to the corresponding aldehyde in 94% was achieved with IBX (=1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide) in DMSO. For the synthesis of the δ-lactone, the connecting moiety had to be a C_2 unit with (*Z*)-configuration, which was built by a modified *Wadsworth–Emmons* reaction of the aldehyde with methyl 2-[bis(2,2,2-trifluoroethoxy)phosphinyl]acetate in

the presence of $KN(SiMe_3)_2$ in THF; thus exclusively the unsaturated (*Z*)-configurated ester **23** was obtained. After hydrolyzing the acetonide with dilute acid, the lactonization of the hydroxy ester was achieved by treating with $ZnCl_2$ in THF under reflux to give a hydroxylactone. Finally the OH group was acetylated with Ac_2O/pyridine in CH_2Cl_2 to provide the target molecule **1**.

In conclusion, two different synthetic routes were used to install the chiral centers of the 1,3-diol system of (+)-cryptocarya diacetate (**1**), thus accomplishing its stereoselective synthesis.

N. M. K. R. and *M. N. P.* thank the *CSIR*, New Delhi, for the award of fellowships.

Experimental Part

FC = Flash chromatography; CC = column chromatography. M.p.: *Büchi-R-535* apparatus; uncorrected. Optical rotations: *Jasco DIP-370* polarimeter; at 20°. IR Spectra: *Perkin-Elmer FTIR-240-c* spectrophotometer; KBr optics; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Varian Unity-200* and *Bruker 300* spectrometer; in $CDCl_3$ with $SiMe_4$ as internal standard; δ in ppm, *J* in Hz. MS: *Finnigan MAT-1020* mass spectrometer; at 70 eV; in *m*/*z*.

*1-[(4*R*,6*S*)-2,2,6-Trimethyl-1,3-dioxan-4-yl]pent-4-en-2-ol* (=*(4*R*,6*S*)-2,2,6-Trimethyl-α-(prop-2-en-1-yl)-1,3-dioxane-4-ethanol*; **11a**/**11b**). To a soln. of *Dess–Martin* periodinane (1.95 g, 4.59 mmol) in CH_2Cl_2 (4 ml) at r.t. was added a soln. of alcohol **5** (500 mg, 2.87 mmol) in CH_2Cl_2 (4 ml). After 1 h stirring, the mixture was diluted with Et_2O (10 ml) and washed once with 10% $Na_2S_2O_3$/sat. aq. $NaHCO_3$ soln. 1:1. The aq. layer was extracted with Et_2O (3 × 15 ml), the combined org. extract washed once with brine, dried ($MgSO_4$), and concentrated, and the residue purified by FC (10% AcOEt/hexane) to give the corresponding aldehyde (439 mg, 88%) as a colorless oil. To a stirred soln. of this aldehyde (225 mg, 1.30 mmol) in THF (10 ml) at 0° was added activated Zn (171 mg, 2.61 mmol) and dropwise allyl bromide (0.22 ml, 2.61 mmol). After stirring at r.t. for 1 h, the mixture was quenched with sat. NH_4Cl soln. (5 ml), and the org. compound was extracted into AcOEt (3 × 20 ml). The combined org. phase was washed with H_2O (1 × 20 ml) and brine (1 × 20 ml), dried (Na_2SO_4), and concentrated and the crude product purified by CC (SiO_2 (60–120 mesh), AcOEt/hexane 1:9): **11a**/**11b** (182 mg, 82%). Colorless liquid. IR (KBr): 3455, 3040, 2969, 2912, 1482, 1340, 1120, 725. ^1H-NMR ($CDCl_3$, 200 MHz): 5.88–5.71 (*m*, 1 H); 5.20–5.0 (*m*, 2 H); 4.20–4.04 (*m*, 1 H); 4.02–3.62 (*m*, 2 H); 2.25–2.11 (*m*, 2 H); 1.59–1.50 (*m*, 2 H); 1.44 (*s*, 3 H); 1.36 (*s*, 3 H); 1.30–1.19 (*m*, 2 H); 1.17–1.11 (*m*, 3 H). LC-MS: 237 ($[M+Na]^+$).

*1-[(4*S*,6*S*)-2,2,6-Trimethyl-1,3-dioxan-4-yl]pent-4-en-2-one* (**12**). To a soln. of *Dess–Martin* periodinane (541 mg, 1.27 mmol) in CH_2Cl_2 (4 ml) at r.t. was added a soln. of **11a**/**11b** (182 mg, 0.85 mmol) in CH_2Cl_2 (4 ml). After 1 h stirring, the mixture was diluted with Et_2O (10 ml) and washed once with 10% $Na_2S_2O_3$/sat. aq. $NaHCO_3$ soln. 1:1. The aq. layer was extracted with Et_2O (3 × 15 ml), the combined org. extract washed once with brine, dried ($MgSO_4$), and concentrated, and the residue purified by FC (10% AcOEt/hexane): **12** (158 mg, 88%). Colorless oil. $[\alpha]_D^{25} = +12.3$ ($c = 0.024$, $CHCl_3$). IR (neat): 1716, 1378, 1260, 830. ^1H-NMR ($CDCl_3$, 300 MHz): 5.99–5.84 (*m*, 1 H); 5.23–5.10 (*m*, 2 H); 4.35–4.24 (*m*, 1 H); 4.05–3.93 (*m*, 1 H); 3.18 (*d*, *J* = 6.8, 2 H); 2.68 (*dd*, *J* = 6.7, 15.8, 2 H); 2.41 (*dd*, *J* = 6.04, 15.86, 2 H); 1.61–1.54 (*m*, 1 H); 1.45 (*s*, 3 H); 1.35 (*s*, 3 H); 1.30–1.03 (*m*, 1 H); 1.16 (*d*, *J* = 6.0, 3 H). ^{13}C-NMR (300 MHz, $CDCl_3$): 206.6; 130.2; 118.8; 98.6; 65.5; 64.8; 48.6; 38.3; 30.0; 21.9; 19.6.

*(2*R*)-1-[(4*R*,6*S*)-2,2,6-Trimethyl-1,3-dioxan-4-yl]pent-4-en-2-ol* (=*(α*R*,4*R*,6*S*)-2,2,6-Trimethyl-α-(prop-2-en-1-yl)-1,3-dioxane-4-ethanol*; **4**). To a soln. of **12** (150 mg, 0.70 mmol) in dry Et_2O (10 ml) at r.t. under N_2 was added LiI (293 mg, 2.19 mmol), and the mixture was stirred at −40° for 30 min. The resulting mixture was then cooled to −100°, $LiAlH_4$ (80 mg, 2.12 mmol) was added, and the mixture was stirred for 30 min. The mixture was then cooled to 0°, diluted with Et_2O, and quenched by dropwise addition of sat. aq. Na_2SO_4 soln. (10 ml). The solid material was filtered and washed several times thoroughly with hot AcOEt. The combined org. phase was dried (Na_2SO_4) and concentrated, and the residue purified by CC (SiO_2): **4** (127 mg, 84%). Clear liquid. $[\alpha]_D^{25} = +9.48$ ($c = 0.065$, $CHCl_3$). IR (KBr): 3450, 3050, 2974, 2912, 1497, 1339. ^1H-NMR ($CDCl_3$, 200 MHz): 5.95–5.71 (*m*, 1 H); 5.16–5.03

(*m*, 2 H); 4.19–3.78 (*m*, 3 H); 3.54–3.41 (br. *s*, 1 H); 2.35–2.09 (*m*, 2 H); 1.66–1.51 (*m*, 1 H); 1.48 (*s*, 3 H); 1.30–1.20 (*m*, 1 H); 1.16 (*d*, $J = 5.5$, 3 H). ^{13}C-NMR ($CDCl_3$, 300 MHz): 134.8; 117.2; 98.6; 70.9; 70.1; 65.0; 42.3; 41.9; 38.8; 30.2; 22.1; 19.9. LC-MS: 237 ($[M+Na]^+$).

*(1*R*)-1-{[(4*S*,6*S*)-2,2,6-Trimethyl-1,3-dioxan-4-yl]methyl}but-3-en-1-yl Prop-2-enoate* (**13**). Prop-2-enoyl chloride (0.096 ml, 1.19 mmol) was added dropwise under N_2 to a soln. of **4** (170 mg, 0.79 mmol), Et_3N (0.221 ml, 1.58 mmol), and DMAP (5 mg) in dry CH_2Cl_2. The mixture was stirred at r.t. for 1 h. After completion of the reaction, the mixture was diluted with CH_2Cl_2, washed with brine, and extracted twice with CH_2Cl_2. The org. phases were washed with 1M aq. HCl and brine, dried (Na_2SO_4), and concentrated. The crude product was purified by CC (SiO_2 (60–120 mesh)): pure **13** (178 mg, 84%). Liquid. IR (KBr): 3071, 2974, 2856, 1724, 1638, 1453. ^{1}H-NMR ($CDCl_3$, 200 MHz): 6.37 (*td*, $J = 1.6$, 17.1, 1 H); 6.15–5.99 (*m*, 1 H); 5.84–5.60 (*m*, 2 H); 5.28–4.98 (*m*, 3 H); 3.99–3.70 (*m*, 2 H); 2.43–2.28 (*m*, 2 H); 1.70–1.44 (*m*, 2 H); 1.30 (*s*, 3 H); 1.40–1.19 (*m*, 2 H); 1.12 (*d*, $J = 6.2$, 3 H). LC-MS: 271 ($[M+Na]^+$).

*(6*R*)-5,6-Dihydro-6-{[(4*S*,6*S*)-2,2,6-trimethyl-1,3-dioxan-4-yl]methyl}-2*H*-pyran-2-one* (**14**). *Grubbs*' catalyst (37 mg, 0.063 mmol, 10 mol-%) was dissolved in CH_2Cl_2 (10 ml) and added dropwise to a refluxing soln. of **13** (170 mg, 0.63 mmol) in CH_2Cl_2 (100 ml). Refluxing was continued for 3 h by which time all of the starting material was consumed (TLC). The solvent was evaporated and the crude product purified by CC (SiO_2, hexane/AcOEt 70:30): **14** (130 mg, 86%). IR (KBr): 2975, 1728, 1440, 1250, 1032, 944, 810, 753. ^{1}H-NMR ($CDCl_3$, 300 MHz): 6.89–6.80 (*m*, 1 H); 6.03–5.97 (*m*, 1 H); 4.69–4.52 (*m*, 1 H); 4.22–4.05 (*m*, 1 H); 4.03–3.89 (*m*, 1 H); 2.52–2.26 (*m*, 2 H); 2.07–1.97 (*m*, 1 H); 1.87–1.23 (*m*, 3 H); 1.44 (*s*, 3 H); 1.34 (*s*, 3 H); 1.34 (*s*, 3 H); 1.16 (*d*, $J = 6.1$, 3 H). LC-MS: 263 ($[M+Na]^+$).

Cryptocarya Diacetate (*= (6*R*)-6-[(2*S*,4*S*)-2,4-Bis(acetyloxy)pentyl]-5,6-dihydro-2*H*-pyran-2-one*; **1**). To AcOH/H_2O 4:1 (10 ml), **14** (100 mg, 0.41 mmol) was added, and the mixture was heated to 60°. After 3 h, the solvent was evaporated, and the resulting diol was added to CH_2Cl_2 (10 ml), Ac_2O (0.5 ml, 6.66 mmol), pyridine (0.5 ml), and a cat. amount of DMAP. The mixture was stirred for 1 h. Then, sat. $NaHCO_3$ soln. (1 ml) was added. The aq. layer was extracted with Et_2O (3×10 ml), the combined org. phase dried (Na_2SO_4), the solvent evaporated, and the crude product purified by CC (SiO_2, hexane/AcOEt 4:1): **1** (88 mg, 75%). Colorless liquid. $[\alpha]_D^{25} = +54.6$ ($c = 0.3$, $CHCl_3$) ([1]: $[\alpha]_D^{25} = +55.8$ ($c = 1.06$, $CHCl_3$)). IR (neat): 2970, 1735, 1430, 1365, 1235, 1042, 981, 755. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.88 (*ddd*, $J = 3.0$, 6.8, 9.8, 1 H); 6.03 (*ddd*, $J = 0.7$, 3, 9.8, 1 H); 5.11 (*dddd*, $J = 4.6$, 6, 7.2, 9.1, 1 H); 5.02–4.95 (*m*, 1 H); 4.5 (*ddd*, $J = 3.7$, 6.8, 11, 1 H); 2.5 (*ddd*, $J = 1$, 5, 18, 1 H); 2.39–2.25 (*m*, 1 H); 2.16 (*ddd*, $J = 1$, 4.2, 6, 1 H); 2.07 (*s*, 3 H); 2.04 (*s*, 3 H); 2.00 (*ddd*, $J = 6$, 8, 14.1, 1 H); 1.96 (*ddd*, $J = 4$, 6.6, 14.1, 1 H); 1.79 (*ddd*, $J = 6$, 8, 14.3, 1 H); 1.27 (*d*, $J = 6.8$, 3 H). ^{13}C-NMR (300 MHz, $CDCl_3$): 20.1; 21.0; 29.3; 39.2; 40.5; 67.6; 67.8; 74.9; 121.4; 144.6; 163.7; 170.5; 170.6. LC-MS: 307 ($[M+Na]^+$).

*(2*S*)-2-[(Benzyloxy)methyl]oxirane* (*= Benzyl (*S*)-Glycidyl Ether*; **10**). To the (*R*,*R*)-(salen)cobalt-(II) precatalyst (151 mg, 0.250 mmol, 0.5 mol-%), sequentially (±)-benzyl glycidyl ether ((±)-**10**; 8.20 g, 50.0 mmol) and AcOH (57 µl, 1.0 mmol, 0.02 equiv.) were added. After the mixture turned from a red suspension to a dark brown soln., it was cooled to 0°, and THF (0.5 ml) followed by H_2O (495 µl, 27.5 mmol, 0.55 equiv.) were added. The mixture was allowed to warm to r.t. over 2 h and stirred for an additional 20 h. Distillation of the mixture at 75°/11 Torr gave unreacted **10** (3.77 g, 46%). Colorless oil. TLC (SiO_2, 20% AcOEt/hexane): R_f 0.6. $[\alpha]_D^{25} = -5.2$ ($c = 2.0$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.35–7.28 (*m*, 5 H); 4.60 (*d*, $J = 12.0$, 1 H); 4.55 (*d*, $J = 12.0$, 1 H); 3.76 (*dd*, $J = 11.2$, 2.8, 1 H); 3.42 (*dd*, $J = 11.2$, 5.8, 1 H); 3.18 (*m*, 1 H); 2.78 (*dd*, $J = 4.5$, 4.2, 1 H); 2.60 (*dd*, $J = 4.5$, 2.5, 1 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 140.0; 128.5; 127.8; 73.3; 70.9; 50.9; 44.3. LC-MS: 165 ($[M+H]^+$).

*(2*S*)-1-(Benzyloxy)pent-4-en-2-ol* (**15**). To Mg (1.18 g, 48.78 mmol) in dry THF (35 ml) at r.t. was sequentially added 1,2-dibromoethane (3 drops) and, dropwise, freshly prepared vinyl bromide (3.45 ml, 48.78 mmol). After 0.5 h stirring, CuCN (10.9 mg, 5 mol-%) was added. Then, the mixture was cooled to −78°, **10** (4.0 g, 24.39 mmol) in THF (6 ml) was added, and the mixture was warmed to −40° and stirred for 4 h. After quenching with sat. NH_4Cl soln. (30 ml) and extraction with AcOEt (2×30 ml), the combined org. phase was washed with brine (20 ml), dried (Na_2SO_4), and concentrated. Purification by CC afforded **15** (4.30 g, 92%). Colorless liquid. TLC (SiO_2, 20% AcOEt/hexane): R_f 0.45. $[\alpha]_D^{25} = -2.32$ ($c = 1.2$, $CHCl_3$). IR (neat): 3360, 3021, 1637, 1494, 1450. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.31 (*m*, 5 H); 5.91–5.69 (*m*, 1 H); 5.20–4.93 (*m*, 2 H); 4.52 (*s*, 2 H); 4.00–3.63 (*m*, 1 H); 3.49 (*dd*, $J = 9.5$, 3.7, 1 H);

3.32 (*dd*, $J = 9.5$, 6.5, 1 H); 2.48 (br. *s*, 1 H); 2.23 (*t*, $J = 6.7$, 2 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 138.3; 134.2; 128.5; 127.9; 127.7; 117.7; 73.8; 73.4; 69.7; 37.9. LC-MS: 215 ($[M + Na]^+$).

(2S)-Pent-4-ene-1,2-diol (**16**). To a soln. of Li (3.72 g, 104.1 mmol) in liq. NH_3 (25 ml) was added **15** (4.0 g, 20.8 mmol) in dry THF (8 ml). The mixture was stirred for 20 min and quenched with solid NH_4Cl (5.5 g). Ammonia was allowed to evaporate, and to the residual mixture, Et_2O was added. The mixture was filtered through *Celite*, the filtrate dried (Na_2SO_4) and concentrated, and the residue purified by CC: **16** (1.59 g, 75%). Colorless oil. TLC (SiO_2, 80% AcOEt/hexane): R_f 0.25. $[\alpha]_D^{25} = +3.6$ ($c = 2.8$, $CHCl_3$). IR (neat): 3388, 2927, 1645, 1440, 1075. ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.91–5.63 (*m*, 1 H); 5.13–5.04 (*m*, 2 H); 3.75–3.55 (*m*, 2 H); 3.38 (*dd*, $J = 11.0$, 7.6, 1 H); 3.16 (br. *s*, 2 H); 2.18 (*t*, $J = 6.0$, 2 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 135.1; 117.2; 71.3; 66.0; 37.5. LC-MS: 125 ($[M + Na]^+$).

3-(Benzyloxy)propan-1-ol. Under N_2, a 60% dispersion of NaH in mineral oil (10.7 g, 447.3 mmol) was washed thoroughly with dry hexane. Then DMF (600 ml) was added and the mixture cooled to 0°. To the formed suspension was added dropwise within 15 min the soln. of propane-1,3-diol (20 g, 263.1 mmol) in dry DMF (40 ml). After the addition, the temp. of the mixture was raised to r.t. and kept at r.t. for 4 h. Then, at 0°, cat. amounts of $(Bu_4N)I$ followed by benzyl bromide (31.25 ml, 263.1 mmol) within 10 min were added, and the mixture was stirred at r.t. for 4 h. Thereafter, cold H_2O (60 ml) was added cautiously, and the aq. phase was extracted with AcOEt (3×60). The combined org. extract was washed with H_2O and brine and concentrated, and the residue subjected to CC: pure 3-(benzyloxy)propan-1-ol (34.9 g, 80%). Colorless liquid. TLC (SiO_2, 50% AcOEt/hexane): R_f 0.5. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.43–7.13 (*m*, 5 H); 4.50 (*s*, 2 H); 3.75 (*t*, $J = 5.5$, 2 H); 3.63 (*t*, $J = 5.5$, 2 H); 1.78 (*m*, 2 H). LC-MS: 189 ($[M + Na]^+$).

3-(Benzyloxy)propanal. To a soln. of 3-(benzyloxy)propan-1-ol (30 g, 182.9 mmol) in dry CH_2Cl_2 (300 ml) at 0° was added *Celite* and then portionwise pyridinium chlorochromate (PCC; 78.86 g, 365.8 mmol). The mixture was brought to r.t., stirred for 2.5 h, diluted with Et_2O, and filtered through a pad of *Celite*, which was washed with excess of Et_2O. The filtrate was concentrated and the residue purified by CC: 3-(benzyloxy)propanal (23.1 g, 78%). Colorless liquid. TLC (SiO_2, 20% AcOEt/hexane): R_f 0.4. IR (neat): 2858, 1722, 1098, 740, 698. ^{1}H-NMR ($CDCl_3$, 300 MHz): 9.78 (*s*, 1 H); 7.40–7.20 (*m*, 5 H); 4.44 (*s*, 2 H); 3.70 (*dt*, $J = 7.0$, 1.3, 2 H); 2.65–2.50 (*m*, 2 H).

(2S,4R,6S)-6-[2-(Benzyloxy)ethyl]tetrahydro-4-hydroxy-2H-pyran-2-methanol (**9**). CF_3COOH (37.5 ml, 490.1 mmol) was added slowly to a soln. of **16** (2.5 g, 24.5 mmol) and 3-(benzyloxy)propanal (12.0 g, 73.5 mmol) in CH_2Cl_2 (90 ml) at r.t. under N_2. The mixture was stirred for 3 h, then sat. $NaHCO_3$ soln. (200 ml) was added, and the pH was adjusted to > 7 by addition of Et_3N. The aq. layer was extracted with CH_2Cl_2 (4×70 ml) and the combined org. phase concentrated. The residue was dissolved in MeOH (40 ml) and stirred with K_2CO_3 (6.77 g) for 30 min. MeOH was then evaporated, and H_2O (30 ml) was added. The mixture was extracted with CH_2Cl_2 (3×30 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the residue purified by CC (SiO_2): **9** (3.65 g, 56%). Gummy liquid. TLC (SiO_2, 80% AcOEt/hexane): R_f 0.2. $[\alpha]_D^{25} = -12.9$ ($c = 0.04$, $CHCl_3$). IR (neat): 3410, 2922, 2854, 1736, 1453, 1368, 1244, 1096, 1029, 742, 699. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.36–7.17 (*m*, 5 H); 4.47 (*q*, $J = 12.5$, 14.7, 2 H); 4.02–3.66 (*m*, 1 H); 3.66–3.30 (*m*, 6 H); 1.98–1.59 (*m*, 3 H); 1.57–1.30 (*m*, including two OH, 3 H); 1.28–1.06 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 138.2; 128.3; 127.6; 75.9; 72.8; 72.7; 67.5; 66.5; 65.5; 40.9; 36.6; 35.9. LC-MS: 289 ($[M + Na]^+$).

{(2S,4R,6S)-6-[2-(Benzyloxy)ethyl]tetrahydro-4-hydroxy-2H-pyran-2-yl}methyl 4-Methylbenzenesulfonate (**17a**). To the soln. of **9** (2.0 g, 7.51 mmol) in dry CH_2Cl_2 (15.0 ml), Et_3N (2.09 ml, 15.0 mmol) was added at 0°. Then, 4-methylbenzenesulfonyl chloride (1.57 g, 8.27 mmol) was added over 2 h. The mixture was allowed to warm to r.t. and stirred for 3 h. Then the mixture was treated with aq. 1N HCl (10 ml) and extracted with CH_2Cl_2 (3×30 ml). The org. layers were washed with sat. $NaHCO_3$ soln. (15 ml) and H_2O (15 ml). The combined org. phase was dried (Na_2SO_4) and concentrated and the residue subjected to FC: **17a** (3.0 g, 95%). Gummy liquid. TLC (SiO_2, 80% AcOEt/hexane): R_f 0.5. $[\alpha]_D^{25} = -22.3$ ($c = 1$, $CHCl_3$). IR (neat): 3405, 2922, 2856, 1450, 1146, 973. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.74 (*d*, $J = 8.3$, 2 H); 7.34–7.19 (*m*, 7 H); 4.43 (*AB*, $J = 12.1$, 14.4, 2 H); 4.0–3.86 (*m*, 2 H); 3.70 (*tt*, $J = 3.8$, 9.8, 1 H); 3.36–3.55 (*m*, 4 H); 2.43 (*s*, 3 H); 1.85 (*dd*, $J = 3.0$, 12.8, 2 H); 1.68 (*q*, $J = 6.0$, 13.0, 2 H); 1.17–1.0 (*qd*, $J = 3.8$, 12.1, 2 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 144.6; 138.2; 132.7; 129.6; 128.1; 127.7; 127.4; 127.3; 72.7; 72.5; 71.9; 67.1; 66.2; 40.5; 36.5; 35.7; 21.4. LC-MS: 443 ($[M + Na]^+$).

*{(2*S*,4*R*,6*S*)-6-[2-(Benzyloxy)ethyl]-4-{[(*tert*-butyl)dimethylsilyl]oxy}tetrahydro-2*H*-pyran-2-yl}-methyl 4-Methylbenzenesulfonate* (**17b**). To a stirred soln. of **17a** (3.0 g, 7.1 mmol) in CH_2Cl_2 (15 ml), 1*H*-imidazole (1.45 g, 21.3 mmol) was added at 0° and stirred for 15 min. (*tert*-Butyl)chlorodimethylsilane (1.23 g, 7.8 mmol) was added to the mixture at 0° and stirred for 2 h. After completion of the reaction (TLC monitoring), the mixture was directly concentrated and the residue subjected to CC: pure **17b** (3.5 g, 92.1%). ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.79–7.71 (*m*, 2 H); 7.32–7.18 (*m*, 7 H); 4.44 (*s*, 2 H); 3.98–3.86 (*m*, 2 H); 3.77–3.66 (*m*, 1 H); 3.54–3.38 (*m*, 4 H); 2.44 (*s*, 3 H); 1.78–1.60 (*m*, 4 H); 1.40–1.22 (*m*, 2 H); 0.85 (*s*, 9 H); 0.02 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 144.5; 138.5; 133.1; 129.6; 128.3; 127.6; 127.6; 127.48; 72.9; 72.7; 72.6; 68.1; 66.3; 41.3; 37.3; 35.9; 25.7; 21.5; 18.0; −4.5; −4.6. LC-MS: 535 ([*M* + 1]$^+$).

*{(2*S*,4*R*,6*S*)-2-[2-(Benzyloxy)ethyl]tetrahydro-6-(iodomethyl)-2*H*-pyran-4-yl]oxy}(*tert*-butyl)dimethylsilane* (**18**). NaI (4.7 g, 31.5 mmol) was added to a soln. of **17** (3.4 g, 6.3 mmol) in acetone (50 ml) and heated under reflux for 24 h. The acetone was evaporated, and to the residue, H_2O (15 ml) and AcOEt (20 ml) were added. The org. layer was dried (Na_2SO_4) and concentrated, and the residue chromatographed: **18** (2.9 g, 93%). Colorless liquid. TLC (SiO_2, 10% AcOEt/hexane): R_f 0.7. IR (neat): 3360, 2935, 2850, 1146, 735. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.33–7.24 (*m*, 5 H); 4.49 (*s*, 2 H); 3.84–3.25 (*m*, 5 H); 3.11 (*d*, *J* = 6.2, 2 H); 2.07–1.93 (*m*, 1 H); 1.81–1.67 (*m*, 3 H); 1.34–1.01 (*m*, 2 H); 0.87 (*s*, 9 H); 0.04 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 138.63; 128.39; 127.7; 127.5; 75.1; 73.2; 72.6; 68.4; 66.6; 41.6; 41.3; 36.1; 25.8; 18.1; 9.20; −4.3.

*(3*S*,5*S*)-1-(Benzyloxy)-5-{[(*tert*-butyl)dimethylsilyl]oxy}oct-7-en-3-ol* (**8**). To a soln. of **18** (2.8 g, 5.7 mmol) in EtOH (30 ml), commercial Zn dust (5.4 g, 85.5 mmol) was added. The mixture was refluxed for 4 h and then cooled to 25°. Addition of solid NH_4Cl (2.0 g) and Et_2O (60 ml) followed by stirring for 5 min gave a gray suspension. The suspension was filtered through *Celite*, the filtrate concentrated, and the residue purified by FC: **8** (1.9 g, 91.3%). Colorless liquid. TLC (SiO_2, 10% AcOEt/hexane): R_f 0.4. $[\alpha]_D^{25} = -35.1$ (*c* = 1, $CHCl_3$). IR: 3358, 2860, 1428, 1105, 740, 705, 508. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.32–7.21 (*m*, 5 H); 5.81–5.66 (*m*, 1 H); 5.07–4.98 (*m*, 2 H); 4.5 (*q*, *J* = 2.2, 12.8, 2 H); 4.08–3.98 (*m*, 2 H); 3.68–3.54 (*m*, 2 H); 3.19 (br. *s*, 1 H); 2.28 (*t*, *J* = 6.7, 2 H); 1.80–1.39 (*m*, 4 H); 0.89 (*s*, 9 H); 0.09 (*s*, 3 H); 0.08 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 138.1; 134.7; 128.3; 127.5; 117.2; 73.08; 70.2; 68.2; 66.8; 42.4; 41.6; 37.4; 25.8; −4.48; −4.86. LC-MS: 387 ([*M* + Na]$^+$).

*(3*R*,5*S*)-1-(Benzyloxy)-5-{[(*tert*-butyl)dimethylsilyl]oxy}oct-7-en-3-ol* (**19**). To a stirred soln. of **8** (1.3 g, 10.56 mmol) in toluene (10 ml) was added triphenylphosphine (1.76 g, 6.6 mmol) and 4-nitrobenzoic acid (1.12 g, 6.6 mmol). The mixture was cooled to −78°, and slowly diethyl diazene-1,2-dicarboxylate (1.69 ml, 10.56 mmol) was added. The mixture was slowly brought to −20° and stirred for 1 h. Then, the mixture was concentrated, and MeOH (20 ml) and K_2CO_3 (1.6 g, 12 mmol) were added. After 1 h stirring, the mixture was filtered through a plug of *Celite* and washed with AcOEt. The combined org. phase was concentrated, and the residue subjected to CC: pure **19** (1.2 g, 92%). IR (neat): 3360, 2872, 1445, 758, 508. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.34–7.19 (*m*, 5 H); 5.86–5.66 (*m*, 1 H); 5.03 (*dd*, *J* = 11.8, 1.1, 2 H); 4.49 (*s*, 2 H); 4.0–3.80 (*m*, 2 H); 3.69–3.55 (*m*, 2 H); 3.22 (br. *s*, 1 H); 2.33–2.16 (*m*, 2 H); 1.74–1.51 (*m*, 4 H); 0.90 (*s*, 9 H); 0.09 (*s*, 6 H). LC-MS: 387 ([*M* + Na]$^+$).

*(3*R*,5*S*)-1-(Benzyloxy)oct-7-ene-3,5-diol*. To a stirred soln. of **19** (1.2 g, 3.1 mmol) in THF, $(Bu_4N)F$ (3.1 ml, 3.1 mmol) was added slowly at 0°. After completion of the reaction (TLC monitoring), the mixture was concentrated, and the residue subjected to CC: pure (3*R*,5*S*)-1-(benzyloxy)oct-7-ene-3,5-diol (0.8 g, 95.2%). $[\alpha]_D = -5.4$ (*c* = 1, $CHCl_3$). IR (neat): 3384, 2928, 2864, 1438, 1094. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.27 (*m*, 5 H); 5.03–5.13 (*m*, 2 H); 4.5 (*s*, 2 H); 4.05 (*m*, 1 H); 3.90–3.85 (*m*, 1 H); 3.65 (*m*, 2 H); 2.2 (*m*, 2 H); 1.52 (*m*, 4 H). LC-MS: 273 ([*M* + Na]$^+$).

*(4*R*,6*S*)-4-[2-(Benzyloxy)ethyl]-2,2-dimethyl-6-(prop-2-en-1-yl)-1,3-dioxane* (**20**). To a stirred soln. of (3*R*,5*S*)-1-(benzyloxy)oct-7-ene-3,5-diol (0.8 g, 2.7 mmol) in dry DMSO (4 ml), 2,2-dimethoxypropane (10 ml) and a cat. amount of 4-methylbenzenesulfonic acid were added and stirred at r.t. for 1 h. Then, Et_3N (1 ml) was added, the mixture stirred for 10 min and diluted with AcOEt (20 ml), the org. layer washed with H_2O (2 × 5 ml) and brine (2 × 5 ml), dried (Na_2SO_4), and concentrated, and the residue purified by CC: **20** (0.8 g, 94%). Colorless liquid. $[\alpha]_D = +5.9$ (*c* = 1.0, $CHCl_3$). IR (neat): 2935, 1620, 1455, 1239, 1180, 950, 763, 720. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.29–7.24 (*m*, 5 H); 5.8–5.68 (*m*, 1 H); 5.1–5.08 (*m*, 2 H); 4.46 (*d*, *J* = 2.3, 2 H); 4.01–3.96 (*m*, 1 H); 3.9–3.72 (*m*, 1 H); 3.6–3.4 (*m*, 2 H);

2.35–2.05 (*m*, 2 H); 1.76–1.61 (*m*, 2 H); 1.49 (*t*, *J* = 3, 1 H); 1.43 (*t*, *J* = 3.1, 1 H); 1.40 (*s*, 3 H); 1.32 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.9; 30.1; 40.7; 66.0; 66.4; 68.3; 73.0; 116.7; 127.6; 127.4; 128.3; 134.1. LC-MS: 313 ($[M+Na]^+$).

*1-{(4*R*,6*R*)-6-[2-(Benzyloxy)ethyl]-2,2-dimethyl-1,3-dioxan-4-yl}propan-2-one* (**7**). A suspension of **20** (0.8 g, 2.7 mmol), $PdCl_2$ (48 mg, 0.27 mmol), and $Cu(OAc)_2 \cdot H_2O$ (109 mg, 0.54 mmol) in $AcNMe_2$/H_2O 7:1 (6 ml) was placed under O_2 (balloon) and stirred at r.t. for 6 h. The mixture was diluted with Et_2O, washed with H_2O and brine, dried (Na_2SO_4), and concentrated. The residue was purified by FC: **7** (0.60 g, 66%). Colorless oil. IR (neat): 3085, 2935, 1724, 1436, 1055, 720. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.39–7.17 (*m*, 5 H); 4.45 (*s*, 2 H); 4.31–4.13 (*m*, 1 H); 4.05–3.86 (*m*, 1 H); 3.60–3.41 (*m*, 2 H); 2.64 (*dd*, *J* = 8.1, 15.4, 1 H); 2.38 (*dd*, *J* = 5.1, 16.1, 1 H); 2.14 (*s*, 3 H); 1.79–1.44 (*m*, 4 H); 1.31 (*s*, 3 H); 1.27 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 206.9; 138.4; 128.3; 127.6; 127.5; 98.6; 72.6; 66.1; 65.8; 65.6; 50.0; 36.7; 36.4; 31.0; 30.1; 19.7. LC-MS: 329 ($[M+Na]^+$).

*(2*S*)-1-{(4*S*,6*R*)-6-[2-(Benzyloxy)ethyl]-2,2-dimethyl-1,3-dioxan-4-yl}propan-2-ol* (=*(α*S*,4*S*,6*R*)-6-[2-(Benzyloxy)ethyl]-α,2,2-trimethyl-1,3-dioxane-4-ethanol*; **21**). To a soln. of **7** (500 mg, 1.6 mmol) in dry Et_2O (10 ml) at r.t. under N_2 was added LiI (650 mg, 4.8 mmol), and the mixture was stirred at −40° for 30 min. After cooling to −100°, $LiAlH_4$ (134 mg, 4 mmol) was added, and the mixture was stirred for 30 min. The mixture was then warmed to 0°, diluted with Et_2O, and quenched by dropwise addition of sat. aq. Na_2SO_4 soln. (6 ml). The solid material was filtered and washed thoroughly with AcOEt. The combined org. phase was dried (Na_2SO_4) and concentrated, and the residue purified by CC: **21** (450 mg, 89%). Liquid. $[\alpha]_D = +11.4$ (*c* = 1, $CHCl_3$). IR (neat): 3443, 2991, 1452, 1378, 1134, 864, 766. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.27–7.23 (*m*, 5 H); 4.43 (*s*, 2 H); 3.90–4.13 (*m*, 3 H); 3.40–3.71 (*m*, 2 H); 1.62–1.74 (*m*, 2 H); 1.44 (*s*, 3 H); 1.35 (*s*, 3 H); 1.17–1.59 (*m*, 4 H); 1.13 (*d*, *J* = 6.5, 3 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 138.6; 128.5; 127.8; 127.0; 98.8; 73.1; 67.3; 66.2; 65.2; 43.7; 37.4; 30.3; 29.8; 25.1; 23.5; 20.1. LC-MS: 308 (M^+).

*(1*S*)-2-{(4*S*,6*R*)-6-[2-(Benzyloxy)ethyl]-2,2-dimethyl-1,3-dioxan-4-yl}-1-methylethyl Acetate* (=*(α*S*,4*S*,6*R*)-6-[2-(Benzyloxy)ethyl]-α,2,2-trimethyl-1,3-dioxane-4-ethanol Acetate*; **22a**). To a stirred soln. of **21** (0.3 g, 0.95 mmol) in CH_2Cl_2 was added pyridine (1 ml), Ac_2O (0.2 ml, 2.05 mmol), and DMAP (cat.), and the mixture was stirred for 3 h. The mixture was diluted with CH_2Cl_2 (10 ml), washed with H_2O (1 × 5 ml) and brine (1 × 5 ml), dried (Na_2SO_4), and concentrated. The crude product was purified by CC (AcOEt/hexane 1:9): **22a** (0.32 g, 94%). Colorless liquid. $[\alpha]_D = +12.8$ (*c* = 1, $CHCl_3$). IR (neat): 2940, 1736, 1375, 1274, 1202, 748. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.26–7.24 (*m*, 5 H); 5.03 (*m*, 1 H); 4.45 (*s*, 2 H); 3.73–4.05 (*m*, 2 H); 3.50–3.48 (*m*, 2 H); 2.0 (*s*, 3 H); 1.64–1.89 (*m*, 2 H); 1.09–1.52 (*m*, 4 H); 1.38 (*s*, 3 H); 1.3 (*s*, 3 H); 1.2 (*d*, *J* = 6.0, 3 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 171.4; 138.1; 128.2; 127.0; 126.9; 98.4; 73.1; 67.7; 65.1; 64.2; 43.9; 36.9; 36.2; 30.0; 29.8; 20.9; 20.0; 19.1. LC-MS: 350 (M^+).

*(1*S*)-2-[(4*S*,6*R*)-6-(2-Hydroxyethyl)-2,2-dimethyl-1,3-dioxan-4-yl]-1-methylethyl Acetate* (=*(α*^{4}S*,4*S*,6*R*)-α*^{4}*,2,2-Trimethyl-1,3-dioxane-4,5-diethanol 4-Acetate*; **22b**). To a stirred soln. of **22a** (0.3 g, 0.84 mmol) in AcOEt (1 ml) was added 10% Pd/C. The mixture was stirred under H_2 for 12 h and then filtered through *Celite*. The filtrate was concentrated: **22b** (0.216 g, 95%). Colorless liquid. $[\alpha]_D = +14.2$ (*c* = 1, $CHCl_3$). IR (neat): 3453, 2985, 2943, 1730, 1375, 1230, 936, 729. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.05–5.02 (*m*, 1 H); 3.88–4.05 (*m*, 2 H); 3.72 (*ddq*, *J* = 1.4, 3.6, 6.6, 2 H); 1.69–1.66 (*m*, 1 H); 2.0 (*s*, 3 H); 1.72–1.51 (*m*, 1 H); 1.40 (*s*, 3 H); 1.36 (*s*, 3 H); 1.24–1.46 (*m*, 4 H); 1.2 (*d*, *J* = 6.6, 3 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 170.3; 98.7; 69.3; 67.5; 65.4; 60.8; 42.7; 38.0; 36.7; 30.5; 30.1; 21.3; 19.4. LC-MS: 261 ($[M+1]^+$).

*Methyl (2*Z*)-4-{(4*R*,6*S*)-6-[(2*S*)-2-(Acetyloxy)propyl]-2,2-dimethyl-1,3-dioxan-4-yl}but-2-enoate* (**23**). To a stirred soln. of **22b** (0.21 g, 0.78 mmol) in dry DMSO (1 ml) was added IBX (0.330 g, 1.2 mmol) at 0°, and the mixture was stirred for 6 h. Then the mixture was quenched with sat. $NaHCO_3$ soln. (1 ml), filtered, and washed with AcOEt (2 × 5 ml). The org. phase was washed with H_2O (1 × 10 ml) and brine (1 × 10 ml), dried (Na_2SO_4), and concentrated: aldehyde (0.19 g, 94%). The crude aldehyde was used as such without purification. To a stirred soln. of methyl 2-[bis(2,2,2-trifluoroethoxy)-phosphinyl]acetate (0.36 g, 0.9 mmol) and [18]crown-6 (0.9 g, 03.5 mmol) in dry THF (1 ml) at −78° was added potassium bis(trimethylsilyl)amide (= potassium 1,1,1,3,3,3-hexamethyldisilazanide; 1 ml, 0.6 mmol), and the mixture was stirred for 30 min at −78°. Then, the crude aldehyde (0.19 g) in dry THF (1 ml) was added, and the mixture was stirred for 30 min at −78°. The reaction was quenched by

adding sat. NH_4Cl soln. (2 ml) and stirring at r.t. for 10 min. Then, the mixture was extracted with AcOEt (2×8 ml), the combined org. phase washed with H_2O (1×10 ml) and brine (1×6 ml), dried (Na_2SO_4), and concentrated, and the residue purified by CC (SiO_2 (60–120 mesh), AcOEt/hexane 1:9): pure **23** (0.15 g, 60%). $[\alpha]_D = +29.1$ ($c = 1.0$, $CHCl_3$). IR (neat): 2935, 2859, 1722, 1650, 1455, 1340, 1160, 856, 752. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.38 (*ddd*, $J = 1.4, 2.5, 6.1$, 1 H); 5.8 (*dd*, $J = 2.1, 6.9$, 1 H); 3.77–3.95 (*m*, 2 H); 5.07–5.01 (*m*, 1 H); 3.70 (*s*, 3 H); 2.92–2.88 (*m*, 1 H); 2.6–2.65 (*m*, 1 H); 2.0 (*s*, 3 H); 1.35–1.59 (*m*, 10 H), 1.19 (*d*, $J = 6.0$, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.3; 20.0; 20.7; 21.2; 30.4; 35.7; 36.9; 42.8; 50.3; 65.4; 67.7; 67.8; 68.3; 120.5; 146.0; 145.8. LC-MS: 314 (M^+).

Cryptocarya Diacetate (**1**). A soln. of **23** (0.1 g, 0.3 mmol) in 80% AcOH/H_2O (0.6 ml) was stirred at r.t. for 4 h. The mixture was concentrated, and the residue dissolved in benzene (2 ml). Then, 4-methylbenzenesulfonic acid (cat.) was added, and the mixture stirred at r.t. for 3 h. After concentration, the crude product was dissolved in CH_2Cl_2 (3 ml), and pyridine (0.3 ml), Ac_2O (0.1 ml), and DMAP (cat.) were added. The mixture was stirred at r.t. for 2 h, then diluted with CH_2Cl_2 (4 ml), washed with H_2O (3 ml) and brine (3 ml), dried (Na_2SO_4), and concentrated. The residue was purified by CC (SiO_2 (60–120 mesh), AcOEt/hexane 3:2): **1** (81 mg, 91%). Colorless liquid. Spectral data: identical with those of the natural product.

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