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Synthesis of Chiral 3*E*,5*E*-Octadiene-1,2*R*,7*R*,8-tetraol Frameworks by Means of Palladium(II)-Promoted Hetero-Claisen Rearrangement: Mechanistic Aspect

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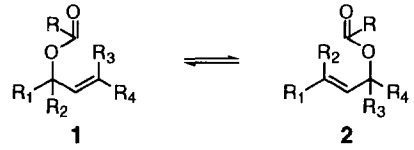
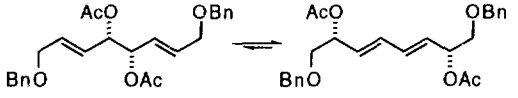
Abstract: A plausible mechanism has been proposed for the exclusive formation of symmetrical dienediol such as 1,6-bis(acetoxy)-2,4-diene in palladium(II)-promoted [3,3]sigmatropic rearrangement of 3,4-bis(acetoxy)-1,5-diene system. This mechanism referred to as migration-induced intramolecular dioxanium ion switching (MIDIS) process can reasonably explain why the vicinal acetoxy groups move from 3,4-position not to 5,6- but two-directionally to 1,6-position.

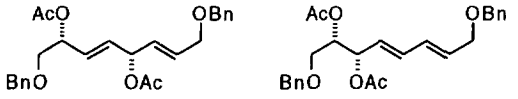
The hetero-Claisen rearrangement [eq. (1)], since its discovery,[1] has been playing an important role in introducing, in many cases, allylic functionality involving a secondary hydroxyl group in which the absolute configuration of the allylic stereogenic center is established as desired.[2] The [3,3]sigmatropic rearrangement of this class can be recognized as a thermodynamically-controlled process.[2] Accordingly, in order to employ this process for the preparation of **2** from **1**, for instance, the equilibrium should be shifted on the right hand side with a large equilibrium constant (i.e. $K \geq 10^2$) for some reason.



1 **2** (1)



3a **4a** (2)



5 **6**

In line with this issue we succeeded in performing palladium(II)-promoted two-directional [3,3]sigmatropic rearrangement of tartrate-based 4,5-bis(acetoxy)-2*E*,6*E*-octadiene system (**3a**) leading to 2,7-bis(acetoxy)-3*E*,5*E*-octadiene backbone (**4a**), while the stereogenic centers of **3** were transposed onto the migration termini in a totally retentive manner (eq 2).[3] Thus, this process provided a novel route to a chiral C_2-symmetrical C_8-chain 3,5-octadiene-1,2,7,8-tetraol framework for which the formation of a rather stable conjugated diene unit must be responsible. In fact, for this reaction, a possible isomer such as **5** was never detected at all even when the reaction was discontinued at an early stage of the reaction. Furthermore, although **6** would be one of

possible stable diene systems derivable from **3a** probably via **5**, it was not detected either, for which, however, no rationalization has been provided.

In order to gain more insights into this point we have carried out systematic studies on this two-hold [3,3]sigmatropic rearrangement, from which we have drawn a piece of conclusion that could unveil the mechanism of this bis(acetoxy)diene rearrangement.

Results and Discussion

Previous results. Palladium(II)-catalyzed [3,3]sigmatropic rearrangements employing 3-acetoxy-1,4-diene systems have been reported to give dienes as shown in Chart 1.[4] In our own efforts related to these works, when optically pure **3a**, prepared from **7** available via a two-step synthesis employing diisopropyl L-2,3-*O*-isopropylidenetartrate,[3,5] was treated with $PdCl_2(CH_3CN)_2$ (20 mol%) in CH_2Cl_2 at room temperature for 40 minutes, **4a** was obtained in 88% yield as a single product (Chart 2).[3] The structure of **4a** was confirmed on the basis of NMR spectroscopy and an appropriate chemical correlation with known compound **11**[6] as indicated below (Chart 2). Careful diagnosis revealed that other possible products such as **5** and/or **6** were not formed under the given reaction conditions. Hence, the first question arises whether the rearrangement of **3a** involves **5** as the initial rearranged product or not.

Chart 1.

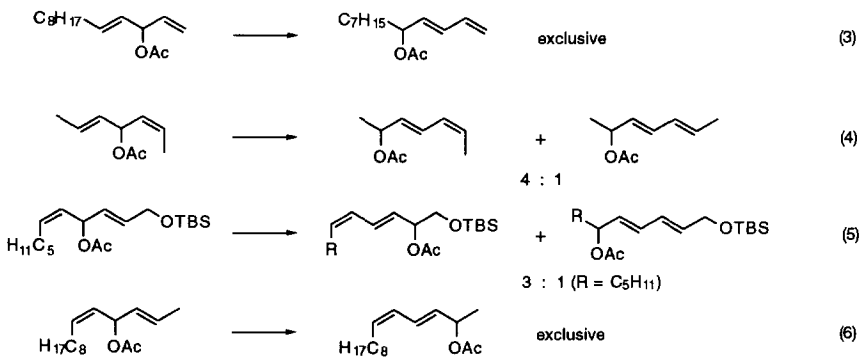
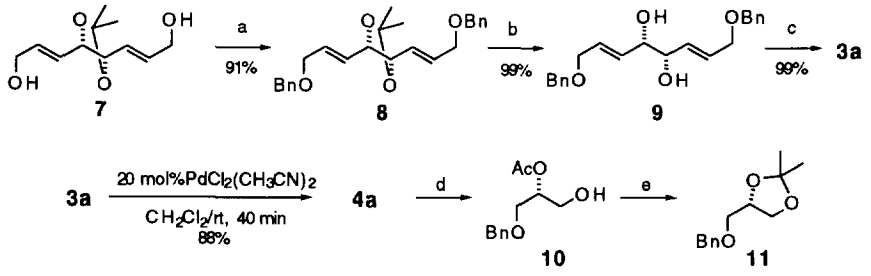


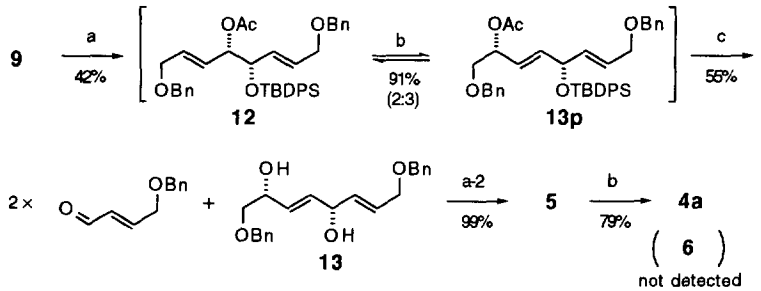
Chart 2.



a) BnBr/NaH/DMF/rt, 3 h; b) 2N-HCl/MeOH/80 °C, 6 h; c) Ac_2O/DMAP/CH_2Cl_2/rt, 2 h; d) 1. O_3/MeOH/−78°C/$(CH_3)_2S$; 2. $NaBH_4$/MeOH; e) 1.LAH/THF/−50°C, 2. $(CH_3O)_2C(CH_3)_2$/acetone/H^+.

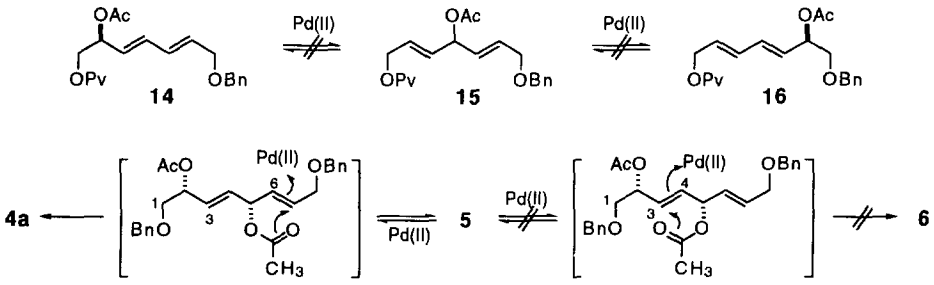
Synthesis of 5 and its Pd(II)-promoted rearrangement. In order to answer to the first question we have prepared **5** as outlined below (Chart 3). One of the hydroxyl groups of dienediol **9** was protected as a TBDPS ether followed by acetylation of a remaining hydroxyl group to give allylic acetate **12**. Treatment of **12** with 20 mol% $PdCl_2(MeCN)_2$ in CH_2Cl_2 at rt for 2 h led to an equilibrated mixture of **12** and **13p** (2:3). The mixture was successively treated with TBAF in THF, K_2CO_3 in $MeOH/H_2O$, and $NaIO_4$, which converted **12** to 4-benzyloxy-2-butenal, and **13p** to diol **13**, respectively. Much polar product **13** was separated by means of silica gel column chromatography and acetylated to give the desired bis(acetoxy)diene **5**. Its structure was determined by NMR spectroscopy including a COSY spectrum.

Chart 3.



(a) 1. TBDPSCl/Imid/THF/rt; 2. Ac_2O/TEA/DMAP/CH_2Cl_2/rt; (b) 20 mol% $PdCl_2(MeCN)_2$/ CH_2Cl_2/rt, 2 h; (c) 1. TBAF/THF, 2.K_2CO_3/MeOH·H_2O, 3. $NaIO_4$

Chart 4.



Contrary to our expectation, **5** led not to **6** at all but exclusively to **4a** on treatment with 20 mol% $PdCl_2(MeCN)_2$ in CH_2Cl_2 at rt for 1 h. In order to make it clear whether the process from **5** to **4a** was kinetically or thermodynamically controlled, acetoxydiene **14** was prepared and treated with the palladium catalyst in CH_2Cl_2 at rt for 5 h (Chart 4). And, **14** has proven to be perfectly stable under such conditions to be recovered unchanged in all respects: **14** (1-acetoxy-2,4-diene) never rearranges to **16** (5-acetoxy-1,3-diene) via **15** even if **14** involves allylic acetate moiety. The rearrangement, thus, should terminate on the formation of a conjugated 1,3-diene system. This result strongly supports that **5** led to **4a** under kinetically controlled conditions.[7]

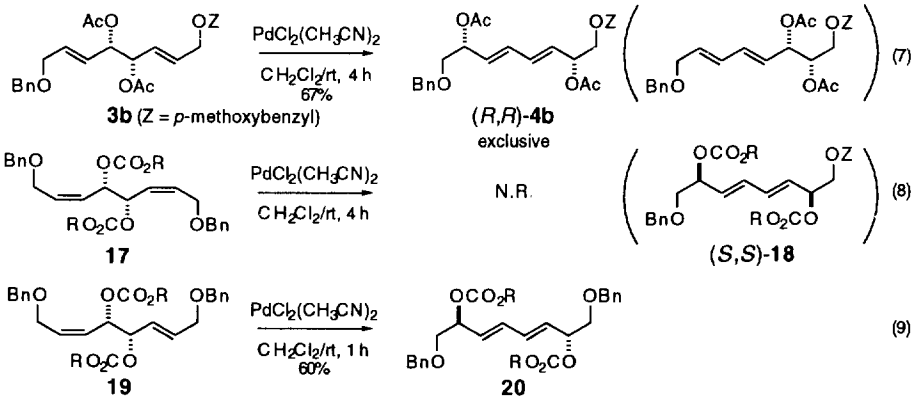
One important information obtained from this experiment was that **5** is more polar than **3a** and/or **4a** and, therefore, can be detected by means of TLC during the reaction if it is actually formed. We have reexamined the palladium(II)-promoted [3,3]sigmatropic rearrangement of **3a** while keen attention was paid on TLC

monitoring during the reaction. However, **5** was never detected at all as far as such an experiment was concerned. Hence, we tentatively concluded that the rearrangement of **3a** did not involve **5** as the initial rearranged product although it could not completely be ruled out. Thus, other rationale should be required to explain the exclusive formation of C_2-symmetrical conjugated diene **4a** from **3a.**

Additional results for bis(acetoxy)diene systems. We have carried out additional experiments employing 3,4-bis(acetoxy)-1,5-diene systems such as **3b**, **17** and **19**, which provided us with important information about the reaction mechanism [Chart 5; eqs. (7 — 9)]. Firstly, unsymmetrical substrate (**3b**) bearing differently protected hydroxyl groups at the both ends of the chain did not change the situation to exclusively give (*R,R*)-**4b** in high yield [eq (7)]. This result probably means that the rearrangement of 4,5-bis(acetoxy)-2,6-diene systems, in general, occurs in such a way that the vicinal acetoxy groups move from 4,5-position not to 2,3- but two-directionally to 2,7-position to afford 2,7-bis(acetoxy)-3,5-diene systems. It should be noted that the PMB-group of (*R,R*)-**4b** can oxidatively be deprotected and, thus, serve as a pivotal function for further manipulation.

Secondary, the expected [3,3]sigmatropic rearrangement of (Z,Z)-version (**17**)[8] did not take place to an any extent under the given reaction conditions [Chart 5; eq (8)]. In order to make this process feasible, a solution of **17** in benzene must have been heated under reflux for 24 h which indeed gave rearranged product (*S,S*)-**18**. However, the [3,3]sigmatropic rearrangement of (*E,Z*)-version (**19**) smoothly proceeded under the given reaction conditions to give symmetrical bis(carbonate)diene (**20**) with a *meso* form [eq. (9)], which is highly surprising in the light of the inertness of **17** at room temperature as just mentioned [eq (8)]. This result requires, therefore, that the mechanism which can explain the formation of the C_2-symmetrical conjugated dienes should also be able to explain the highly enhanced rate of the [3,3]sigmatropic rearrangement of (Z)-allylic carbonate part of **19**.

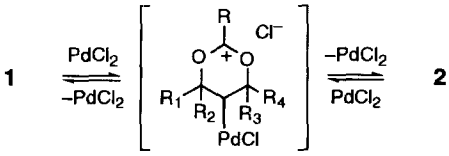
Chart 5.



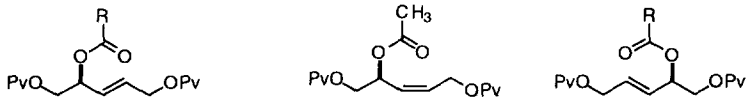
General mechanism involving 1,3-dioxanium ion intermediate and additional supporting evidence. Before discussing the mechanism of [3,3]sigmatropic rearrangement of the bisallylic system in detail, it seems important to claim that the same reaction of allylic acetates catalyzed by $PdCl_2(CH_3CN)_2$ involves a 1,3-dioxanium ion intermediate generated via oxy-palladation of the allylic carbon—carbon double bonds where the carbonyl oxygen and $PdCl_2(CH_3CN)_2$ can act as a nucleophile and an electrophile, respectively. This

mechanism is referred to as *"cyclization-induced rearrangement catalysis"* which was first suggested by Henry[9] and termed by Overmann.[10] The key observations accumulated to date are highly compatible with this mechanism.[4,10,11] In particular, the intermediate 1,3-dioxanium ion rationalizes the rate of the rearrangement of allylic esters with Pd(II) catalyst which is ranked in the order as R = NR_2 > OR > CH_3 > CF_3 reflecting the ability of R to stabilize the carbocationic center of the intermediate generated.[10] In order to accumulate further evidence in this context and to know the migratory aptitude of an acyl group of allylic esters in a practical sense, we have examined the rate of the rearrangement of **21a—c** by means of specific rotation measurement under the common reaction conditions indicated.

Chart 6.



1,3-dioxanium ion



(*S*)-**21a—c**
(R: **a** = H, **b** = CH_3, **c** = $C(CH_3)_3$)

(*S*)-**21b'**

(*R*)-**21a—c**

Table 1. [3,3]Sigmatropic rearrangement of 4-acyloxy-2-pentene-1,5-diol system

(*S*)-**21a—c** $\underset{\text{THF/20 °C, 1 h}}{\overset{\text{10 mol\% } PdCl_2(MeCN)_2}{\rightleftharpoons}}$ (*R*)-**21a—c**

R	$[\alpha]_D$ (initial)	$[\alpha]_D$ (final)
H	+29.6	+21.6
CH_3	+16.3	+0.13
$C(CH_3)_3$	+13.4	+0.22

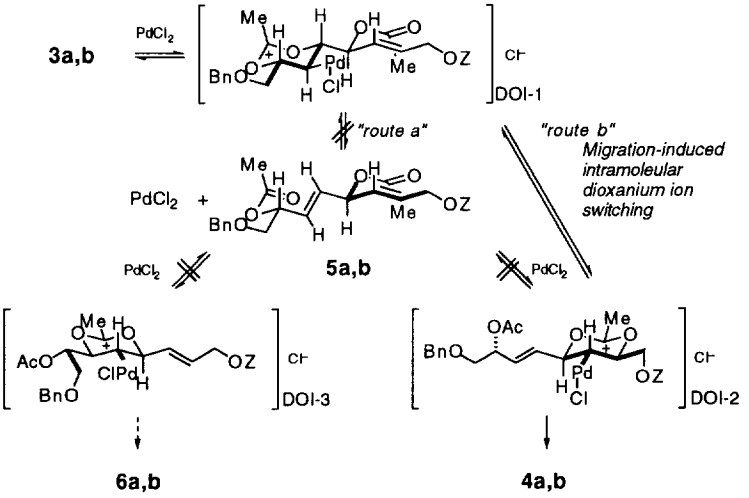
A mixture of a pure (*S*)-**21a—c** and the catalyst (10 mol% $PdCl_2(CH_3CN)_2$) in THF was stirred at 20 °C for 1 h and then the mixture was diluted with ether–hexane mixed solvent to quench the reaction. The precipitated catalyst was filtered off to leave behind **21** which, after purification with a short silica gel column,

was subjected to optical rotation measurements. The results are listed in Table 1 which again delineates that a cation destabilizing group (R = H) decelerates the reaction to result in only about 10% or more conversion under the given conditions, whereas a cation stabilizing group (R = CH_3 or $C(CH_3)_3$) accelerates the rearrangement to bring it almost completion (equilibration) under the given reaction conditions. Careful diagnosis of the reaction product by means of capillary GC or 500 MHz NMR spectroscopy confirmed that no terminal pivaloyloxy groups could migrate to the internal carbon. It also turned out that a bulky pivaloyloxy group can be employed as a migrating group in this rearrangement, which might sometimes affect the position of the equilibrium for steric reasons.

Employing the same technique, we have estimated how sluggish the palladium(II)-promoted rearrangement of simple (Z)-allylic acetate is. Thus, the progress of rearrangement of (*S*)-**21b'** (THF/10 mol% $PdCl_2(MeCN)_2$) was monitored by means of optical rotation measurement to show essentially no change within 1 hour at room temperature that has turned out to be enough conditions for the (*E*)-version **21b** to become equilibrated (Table 1). Indeed, the equilibration of **21b'** was established only when a solution of **21b'** in benzene containing the catalyst was heated at 80 °C for 24 h. The sluggishness of [3,3]sigmatropic rearrangement of (Z)-allylic acetates is indeed general.

Plausible reaction mechanism for 3,4-bis(acetoxy)-1,5-diene system. On the basis of a cyclization-induced rearrangement mechanism, a plausible mechanism which can rationalize the formation of the C_2-symmetrical conjugated diene **4a** from **3a** would be given by invoking a migration-induced intramolecular dioxanium ion switching (MIDIS) process which is outlined below (Chart 7).

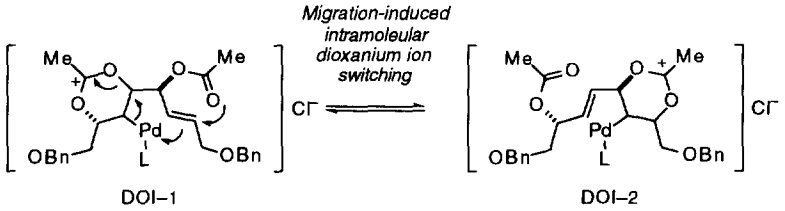
Chart 7.



The first step of this proposed mechanism involves the formation of dioxanium ion intermediate (DOI-1), which never undergoes the elimination of palladium(II) catalyst itself (*"route a"*) but rather does the coordination of a σ-palladium part to the right-hand-side carbon–carbon double bond to result in the completion of the first-stage rearrangement concomitantly with the formation of another dioxanium ion intermediate (DOI-2) (*"route b"*). More detailed picture of the latter step that is referred to as "MIDIS" is shown in Chart 8. Thus, this mechanism can reasonably explain the formation of the C_2-symmetrical

conjugated diene **4a** independent of whether [3,3]sigmatropic rearrangement starts at the right-hand side or the left-hand side allylic acetate moiety and features that the regeneration of the palladium catalyst becomes possible only at the stage of the formation of **4a**.

Chart 8.



The exclusive formation of **4b** from **3b** can also be explained by this MIDIS mechanism. Although **3b** initially leads to two DOI-1 type intermediates depending on which C=C-bond is attacked by the catalyst, the expected MIDIS processes thereof can converge to **4b**.

Unusual rate acceleration of the sigmatropic rearrangement of (*Z*)-allylic ester moiety observed for **19** can be rationalized as follows. The rearrangement initially takes place at its (*E*)-allylic ester site to give a DOI-1 type intermediate followed by a MIDIS process which makes the formation of a DOI-2 type intermediate much easier energetically (entropically) because of its intramolecular nature.

Concluding remarks: The palladium(II)-promoted hetero-Claisen rearrangement of chiral 4,5-di-*O*-acetyl-2*E*,6*E*-octadiene-1,4,5,8-tetraol exclusively led to a symmetrical 2,7-di-*O*-acetyl-3*E*,5*E*-octadiene-1,2,7,8-tetraol framework. It has been proposed that such a process probably involves an intramolecular palladium 1,4-migration which is referred to as a migration-induced intramolecular dioxanium ion switching (MIDIS) mechanism. This idea can reasonably explain other important observations: (1) no intervention of 2,5-di-*O*-acetoxy-3*E*,6*E*-octadiene-1,2,5,8-tetraol structure (**5**), though it can be a precursor for **4a**, as the initial product of [3,3]sigmatropic rearangement of **3a**; (2) no change in the mode of rearrangement even if the 1,ω-hydroxyl groups are differently protected (**3b**); (3) unexpectedly high rate of (*Z*)-allylic carbonate moiety involved in the 4,5-di-*O*-ethoxycarbonyl-2*E*,6*Z*-octadiene-1,4,5,8-tetraol system (**19**).

Synthetic applications of the chiral dienes **4a** or **4b** to asymmetric inter- or intramolecular asymmetric Diels–Alder reactions are interesting. Symmetrical chiral diene **4a** will provide various dienophiles with a homotopic π-face in intermolecular Diels–Alder reactions. On the other hand, unsymmetrical chiral diene **4b** will serve as a chiral diene unit in intramolecular Diels–Alder reactions which can be linked to appropriate dienophiles using the terminal hydroxyl group to be generated by the deprotection of the *p*-methoxybenzyl group. These topics are recently under active investigations in our laboratory and the results will be reported in due course.

Experimental

General Methods. IR spectra were obtained with a Hitachi 215 grating infrared spectrophotometer or a Horiba fourier transform infrared spectrophotometer Model FT-210 instrument, and only the major absorptions are cited. The ^{1}H-NMR (500 or 200 MHz) and ^{13}C-NMR (126 or 50 MHz) spectra were recorded on a Varian VXR-500 or VXR-200 instrument with $CDCl_3$ as a solvent. The chemical shifts are given in δ

units relative to internal $CHCl_3$ (7.26 ppm for ^1H) or $CDCl_3$ (77 ppm for ^{13}C). Splitting patterns are abbreviated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Optical rotations were measured on a JASCO DIP-4 or a Horiba SEPA-300 digital polarimeter using a 3.5 mm × 0.5 dm Pyrex cell. Mass spectra were obtained on a JEOL JMS-DX303 instrument operated either in the electron impact (EI) mode relying on a JMA-DA5000 mass data system.

Usual column chromatography over SiO_2 (abbreviated as CC) was carried out with Merck silica gel 60-7743. Dichloromethane (CH_2Cl_2) and pyridine were freshly distilled from P_2O_5 under argon. Triethylamine (Et_3N) and benzene were freshly distilled from CaH_2. 4-(*N*,*N*-Dimethylamino)pyridine (DMAP) was purchased from Fluka and was used as received. All reactions were executed in flame-dried glasswares under an atmosphere of dry argon.

(4*S*,5*S*)-4,5-*O*-Isopropylidene-2*E*,6*E*-octadiene-1,4,5,8-tetraol (7). To a solution of diethyl (4*S*,5*S*)-4,5-*O*-isopropylidene-4,5-dihydroxy-2*E*,6*E*-octadienedioate[5] (2.65 g, 8.89 mmol) in THF (50 mL) precooled at –78 °C was added DIBAH (1 M/hexane: 39.1 mL) dropwise. The mixture was stirred at –78 °C for 4 h followed by the addition of EtOH (7 mL) for quenching. The mixture was allowed to warm up to room temperature and filtered through a celite pad, which was washed with ethyl acetate several times. The filtrate and washings were combined and concentrated by a rotary evaporator to give an oil, which was purified by CC to give **7** (1.65 g, 87%): $[\alpha]^{27}_D$ +19.6 (c 2.36, $CHCl_3$); ^1H-NMR (200 MHz) δ 1.36 (s, 6H), 3.30—3.65 (bs, 2H), 3.95—4.10 (m, 6H), 5.50—5.70 (m, 2H), 5.76—5.96 (m, 2H); ^{13}C-NMR (50 MHz) δ 26.6, 61.5, 81.0, 108.6, 125.5, 134.2; exact mass (EI) calcd for $C_{11}H_{18}O_4$ (M^+) 214.1205, found 214.1208.

(4*S*,5*S*)-4,5-*O*-Isopropylidene-1,8-di-*O*-benzyl-2*E*,6*E*-octadiene-1,4,5,8-tetraol (8). To a NaH (2.68 g, 66.9 mmol) suspension in DMF (20 mL) was added a solution of **7** (6.52 g, 30.4 mmol) in DMF (20 mL) at 0 °C. The mixture was stirred at that temperature for 20 min followed by the addition of BnBr (8.0 mL, 66.9 mmol) at 0 °C, stirring being continued for 3 h at 0 °C — rt. The reaction was quenched with H_2O (200 mL) and the mixture was extracted with ether (100 mL × 3). The combined ether extracts were washed (sat'd NaCl), dried (Na_2SO_4), and concentrated by a rotary evaporator to give an oil which, on CC, afforded **8** (10.9 g, 91%): $[\alpha]^{21}_D$ –11.9 (c 2.10, $CHCl_3$); ^{1}HNMR (200MHz) δ 1.45 (s, 6H), 4.05 (dd, 4H, *J* = 5.2, 1.3Hz), 4.10—4.21 (m, 2H), 4.51 (s, 4H), 5.66—5.83 (m, 2H), 5.95 (dt, *J* = 15.2, 5.2 Hz, 2H), 7.22—7.40 (m, 10H); ^{13}C-NMR (50 MHz) δ 26.7, 69.2, 71.7, 81.0, 108.5, 127.2, 127.7, 127.9, 130.9, 137.8; Anal. Calcd for $C_{25}H_{30}O_4$ (highly viscous gum): C, 76.11; H, 7.66. Found: C, 76.09; H, 7.70.

(4*S*,5*S*)-1,8-Di-*O*-benzyl-2*E*,6*E*-octadiene-1,4,5,8-tetraol (9). To a solution of **8** (0.576 g, 1.46 mmol) in MeOH (5 mL) was added aq HCl (2*N* solution; 1.75 mL) and the mixture was heated under reflux for 3 h. The mixture was cooled to rt and neutralized with Et_3N (2.5 mL), concentrated, and extracted with CH_2Cl_2 (5 mL × 3). The combined extracts were dried (Na_2SO_4) and concentrated by a rotary evaporator to give an oil, which, on CC, gave **9** (0.51 g, 99%): $[\alpha]^{17}_D$ –21.9 (c 3.10, $CHCl_3$); ^1H-NMR (200 MHz) δ 2.30—2.50 (b, 2H), 4.04 (bd, *J* = 4.3 Hz, 6H), 4.51 (s, 4H), 5.70—5.85 (m, 2H), 5.94 (dt, *J* =15.7, 5.0 Hz, 2H), 7.20—7.40 (m, 10H); ^{13}C-NMR (50 MHz) δ 69.7, 71.9, 74.7, 127.4, 127.5, 128.2, 129.0, 131.4, 137.8.

(4*S*,5*S*)-4,5-Di-*O*-acetyl-1,8-di-*O*-benzyl-2*E*,6*E*-octadiene-1,4,5,8-tetraol (3a). To a solution of **9** (1.14 g, 3.20 mmol) in CH_2Cl_2 (15 mL) were added TEA (1.16 ml, 8.32 mmol) , Ac_2O (0.73 g, 7.68 mmol) and DMAP (0.02g, 5 mol%) at 0 °C. The mixture was stirred at rt for 30 min followed by the addition of H_2O (10 mL) and extracted with CH_2Cl_2 (10 mL × 3). The combined CH_2Cl_2 extracts were dried (Na_2SO_4) and concentrated by a rotary evaporator to give an oil, which, on CC, gave **3a** (1.39 g, 99%): $[\alpha]^{29}_D$ +10.9 (c 1.58,

$CHCl_3$); ^{1}H-NMR (200 MHz) δ 2.07 (s, 6H), 4.00 (bd, J = 5.1 Hz, 4H), 4.49 (s, 4H), 5.39—5.49 (m, 2H), 5.59—5.76 (m, 2H), 5.90 (dt, J = 15.4, 5.1 Hz, 2H), 7.20—7.40 (m, 10H); ^{13}C-NMR (50 MHz) δ 20.7, 69.2, 71.9, 73.6, 125.9, 127.5, 128.2, 131.8, 137.9, 169.5. Anal. Calcd for $C_{26}H_{30}O_6$; C, 71.21; H, 6.90. Found: C, 71.02; H, 6.81.

(2*R*,7*R*)-2,7-Di-*O*-acetyl-1,8-di-*O*-benzyl-3*E*,5*E*-octadiene-1,2,7,8-tetraol (4a). To a solution of **3a** (5.76 g, 13.6 mmol) in CH_2Cl_2 (30 mL) was added $PdCl_2(CH_3CN)_2$ (0.705 g, 2.72 mmol) and the resulting orange solution was stirred at rt for 40 min. The mixture was diluted with ether and filtered through a florisil column (100–200 mesh), which was washed five times with ether. The combined filtrate and washings were concentrated by a rotary evaporator to give an oil, which, on CC, gave **4a** (5.22 g, 88%): $[\alpha]^{21}_D$ –43.0 (c 2.34, $CHCl_3$); ^{1}H-NMR (500 MHz) δ 2.07 (s, 6H), 3.52 (dd, J = 10.6, 4.5 Hz, 2H), 3.55 (dd, J = 10.6, 6.4 Hz, 2H), 4.52 (d, J = 12.2 Hz, 2H), 4.55 (d, J = 12.2 Hz, 2H), 5.46—5.58 (m, 2H), 5.61—5.80 (m, 2H), 6.19—6.37 (m, 2H), 7.25—7.43 (m, 5H); ^{13}C-NMR (126 MHz) δ 21.2, 71.2, 72.6, 73.2, 127.6, 127.7, 128.4, 129.4, 132.4, 137.8, 170.2.

(2*S*)-1,2-*O*-Isopropylidene-3-(*O*-benzyl)glycerol (11). A stream of ozone was passed through a solution of **4a** (0.44 g, 1.02 mmol) in MeOH (10 mL) at –78°C until blue color persisted. Then, CH_3SCH_3 (0.59 mL, 8.0 mmol) was added to the reaction and the mixture was allowed to warm up to rt, stirring being continued at rt for 5 h. The mixture was again cooled to 0 °C and $NaBH_4$ (0.45 g, 12.0 mmol) was added to it, the resulting mixture being stirred at rt for 3 h followed by the addition of citric acid for quenching. The mixture was filtered through a celite pad and the filtrate was concentrated to give a crude oil, which was briefly purified by means of a short silica gel column, the column being eluted with EtOAc-hexane (1:1). The organic solution was concentrated by a rotary evaporator to give an oil (**10**), which was dissolved in THF (2 mL) and the THF solution was cooled to –50 °C followed by the addition of $LiAlH_4$ (0.076 g, 0.2 mmol). The reaction was stirred at that temperature for 2 h before quenching with EtOAc and H_2O. The mixture was taken up with EtOAc and filtered through a celite pad. The EtOAc solution was dried (Na_2SO_4) and concentrated by a rotary evaporator to give an oil, to which were added acetone (3 mL), 2,2-dimethoxypropane (1.6 mL), and *p*-TsOH (0.02 g). The mixture was stirred at rt for 10 h followed by the addition of Et_3N for quenching and partitioned between H_2O (5 mL) and CH_2Cl_2 (5 mL) and the aqueous phase was extracted with CH_2Cl_2 (5 mL × 2). The combined CH_2Cl_2 extracts were dried (Na_2SO_4) and concentrated by a rotary evaporator to give an oil, which, on CC, gave **11** (0.099 g, 44 %): $[\alpha]^{23}_D$ +20.3 (c 2.56, $CHCl_3$)[6]; ^{1}H-NMR (60 MHz) δ 1.38 (s, 3H), 1.44 (s, 3H), 3.45—4.42 (m, 5H), 4.59 (s, 2H), 7.34 (s, 5H).

(4*S*,5*S*)-4,5-Di-*O*-acetyl-1-*O*-benzyl-8-*O*-*p*-methoxybenzyl-2*E*,6*E*-octadiene-1,4,5,8-tetraol (3b). This unsymmetrical chiral diene was prepared from **7** via a series of reactions involving mono *p*-methoxybenzylation of a terminal hydroxyl group (step a), benzylation of remaining hydroxyl group (step b), deacetonidation (step c), and final di-acetylation of thus-generated diol.

(4*S*,5*S*)-4,5-*O*-Isopropylidene-1-*O*-*p*-methoxybenzyl-2*E*,6*E*-octadiene-1,4,5,8-tetraol = product of the step a: $[\alpha]^{23}_D$ +4.68 (c 8.00, $CHCl_3$); ^{1}H-NMR (200 MHz) δ 1.43 (s, 6H), 1.93-2.01 (b, 1H), 3.79 (s, 3H), 3.96—4.03 (2 × d, J = 5.2 Hz, 2H), 4.09—4.18 (m, 2H), 4.43 (s, 2H), 5.60—5.79 (m, 2H), 5.82—6.02 (m, 2H), 6.81—6.92 (m, 2H), 7.19—7.29 (m, 2H). ^{13}C-NMR (50 MHz) δ 26.4, 54.5, 61.3, 68.7, 71.2, 80.7, 80.9, 108.3, 113.1, 125.3, 127.6, 128.8, 129.4, 130.7, 134.0, 158.6.

(4*S*,5*S*)-4,5-*O*-Isopropylidene-1-*O*-*p*-methoxybenzyl-8-*O*-benzyl-2*E*,6*E*-octadiene-1,4,5,8-tetraol = product of the step b: $[\alpha]^{29}_D$ +12.7 (c 10.5, $CHCl_3$); ^{1}H-NMR (200 MHz) δ 1.47 (s, 6H), 3.82 (s, 3H), 4.02 (bt,

J = 5.5 Hz, 4H), 4.10—4.23 (m, 2H), 4.46 (s, 2H), 4.53 (s, 2H), 5.66—5.83 (m, 2H), 5.95 (ddt, J =1.9, 5.2, 15.5 Hz, 2H), 6.85—6.95 (m, 2H), 7.23—7.40 (m, 7H). ^{13}C-NMR (50 MHz) δ 26.7, 54.8, 69.0, 69.3, 71.5, 71.8, 91.1, 108.6, 113.4, 127.25, 127.31, 127.7, 127.8, 128.0, 129.0, 129.8, 131.0, 131.2, 127.8, 158.9.

(4*S*,5*S*)-1-*O*-*p*-Methoxybenzyl-8-*O*-benzyl-2*E*,6*E*-octadiene-1,4,5,8-tetraol = product of the step c: $[\alpha]^{28}_D$ +21.2 (c 8.95, $CHCl_3$); ^{1}H-NMR (200 MHz) δ 2.2—3.1 (b, 2H), 3.78 (s, 3H), 3.90—4.06 (m, 6H), 4.41 (s, 2H), 4.49 (s, 2H), 5.66—5.82 (m, 2H), 5.82—6.00 (m, 2H), 6.80—6.90 (m, 2H), 7.18—7.38 (m, 7H). ^{13}C-NMR (50 MHz) δ 55.0, 69.4, 69.7, 71.6, 71.9, 74.6, 113.5, 127.4, 127.5, 128.1, 128.9, 129.0, 129.2, 129.8, 131.5, 137.8, 138.9.

3b: $[\alpha]^{29}_D$ –10.4 (c 16.3, $CHCl_3$); ^{1}H-NMR (200 MHz) δ 2.07 (s, 6H), 3.80 (s, 3H), 4.00 (bt, J = 5.2 Hz, 4H), 4.41 (s, 2H), 4.49 (s, 2H), 5.40—5.48 (m, 2H), 5.58—5.78 (m, 2H), 5.80—5.99 (m, 2H), 6.82—6.92 (m, 2H), 7.18—7.40 (m, 7H); ^{13}C-NMR (50 MHz) δ 20.4, 54.6, 68.6, 68.9, 71.2, 71.5, 73.3, 113.2, 125.5, 125.6, 127.1, 127.9, 128.8, 129.6, 131.5, 131.6, 137.7, 158.7, 169.1. Anal. Calcd for $C_{27}H_{32}O_7$; C, 69.21; H, 6.88. Found: C, 68.95; H, 7.05.

(2*R*,7*R*)-2,7-Di-*O*-acetyl-1-*O*-benzyl-8-*O*-*p*-methoxybenzyl-3*E*,5*E*-octadiene-1,2,7,8-tetraol (4b). $[\alpha]^{28}_D$ +42.3 (c 10.1, $CHCl_3$); ^{1}H-NMR (200 MHz) δ 2.09 (s, 6H), 3.43—3.64 (m, 4H), 3.80 (s, 3H), 4.46 & 4.52 (ABq, J = 11.8 Hz, 2H), 4.53 & 4.60 (ABq, J = 12.3 Hz, 2H), 5.43—5.57 (m, 2H), 5.60—5.79 (m, 2H), 6.18—6.34 (m, 2H), 6.70—6.92 (m, 2H), 7.20—7.40 (m, 7H); ^{13}C-NMR (126 MHz) δ 20.9, 54.9, 70.5, 70.9, 72.3, 72.5, 72.8, 113.5, 127.37, 127.45, 128.1, 129.1, 129.3, 129.5, 132.0, 132.1, 137.5, 159.0, 169.8.

(2*R*,5*S*)-2,5-Di-*O*-acetyl-1,8-*O*-benzyl-3*E*,6*E*-octadiene-1,2,5,8-tetraol (5). To a solution of **9** (2.02 g, 5.69 mmol) in THF (20 mL) was added successively imidazole (0.48 g, 7.1 mmol) and *tert*-butyldiphenylsilyl chloride (1.62 mL, 6.3 mmol) at 0 °C. The mixture was stirred at rt for 1.5h at 0 °C—rt., followed by addition of H_2O for quenching the reaction. The mixture was extracted with three times with AcOEt-ether. The organic layer was dried with Na_2SO_4 and concentrated by using of a rotary evaporator to give an oil. The crude products was treated successively TEA, Ac_2O and DMAP in CH_2Cl_2 for 10 min at 0 °C. The reaction was quenched by addition of H_2O and extracted with ether (3 times). The combined organic layer was dried with $MgSO_4$ and concentrated by using of a rotary evaporator to give an oil which, on CC, gave (4*S*,5*S*)-4-*O*-acetyl-1,8-di-*O*-benzyl-5-(*O*-*tert*-butyldiphenylsilyl)-2*E*,6*E*-octadiene-1,4,5,8-tetraol (**12**) (1.51 g, 42% for 2 steps).

This allylic acetate was equilibrated on exposure to $PdCl_2(CH_3CN)_2$ catalyst (20 mol%) in CH_2Cl_2 at rt for 2 h to give a mixture of **12** and **13p** in 91% yield with a ratio of 2:3. The mixture was then treated successively with *n*-Bu_4NF in THF and with K_2CO_3 in MeOH·H_2O to deprotect TBDPS groups (79%) and acetyl groups, respectively, to furnish the corresponding mixture of 2,5- and 4,5-diols (70%), which was treated with $NaIO_4$. The unchanged 3,6-diene-2,5-diol (**13**) under such oxidative conditions was separated by CC. **13**: ^{1}H-NMR (500 MHz) δ 1.56 (s, 3H), 1.63 (d, J = 4.3 Hz, 1H), 2.45 (d, J = 3.1 Hz, 1H), 3.37 (dd, J = 8.2, 9.5 Hz, 1H), 3.53 (dd, J = 3.1, 9.5 Hz, 1H), 4.03 (d, J = 4.9 Hz, 2H), 4.34—4.40 (m, 1H), 4.51 (s, 2H), 4.58 (s, 2H), 4.68 (q, J = 5.2 Hz, 1H), 5.71 (ddd, J = 1.1, 5.8, 15.6 Hz, 1H), 5.75—5.89 (m, 3H), 7.25—7.38 (m, 10H).

The diol **13** was acetylated as usual to give the desired 2,5-*O*-acetyl derivative (**5**) in almost quantitative yield. **5**: $[\alpha]^{29}_D$ +10.1 (c 0.51, $CHCl_3$); ^{1}H-NMR (500 MHz) δ 2.07 (s, 3H), 2.10 (s, 3H), 3.5—3.6 (m, 2H), 4.02 (d, J = 5.2 Hz, 2H), 4.51 (s, 2H), 4.52 & 4.58 (ABq, J = 12.2 Hz, 2H), 5.51 (bq, J = 5.2 Hz, 1H), 5.7—5.8 (m, 4H), 5.84 (dt, J = 5.2, 14.7 Hz, 1H), 7.20—7.40 (m, 10H); ^{13}C-NMR (50 MHz) δ 21.1, 21.2, 69.6,

71.1, 72.0, 72.4, 73.1, 127.6, 127.7, 127.75, 128.3, 128.4, 129.0, 130.3, 137.9, 138.0, 169.7, 170.0. Anal. Calcd for $C_{26}H_{30}O_6$; C, 71.21; H, 6.90. Found: C, 71.04; H, 6.88.

Pd(II)-catalyzed equilibration of 5. A mixture of **5** (0.38 g) and $PdCl_2(CH_3CN)_2$ catalyst (0.045 g) in CH_2Cl_2 (3 mL) was stirred at rt for 2 h to give less polar product in 79% yield as an only isolable one, whose ^{1}H-NMR spectrum and specific rotation were completely consistent with those of **4a** in all respects.

(4*S*,5*S*)-4,5-Di-*O*-ethoxycarbonyl-1,8-di-*O*-benzyl-2*Z*,6*Z*-octadiene-1,4,5,8-tetraol (17). To a solution of diisopropyl L-2,3-*O*-isopropylidenetartrate (1.13 g, 4.11 mmol) in toluene (12 mL) cooled at –78 °C was added slowly DIBAH (2M hexane solution; 2.0 mol eq). The mixture was stirred at that temperature for 4 h followed by the slow addition of a solution of ethoxycarbonylmethylenetriphenylphosphorane (2 mol eq) in EtOH at –78 °C. The mixture was allowed to warm up to 0 °C and stirred at that temperature for 5.5 h. EtOH was added to the mixture at 0 °C and the mixture was allowed to warm up to rt followed by the successive addition of CH_2Cl_2 and H_2O. The mixture was filtered through a celite pad, concentrated, and purified by CC to give diethyl (4*S*,5*S*)-4,5-*O*-isopropylidene-4,5-dihydroxy-2*Z*,6*Z*-octadienedioate (1.00 g, 84%): $[\alpha]^{19}_D$ +242 (c 4.00, $CHCl_3$); ^{1}H-NMR (200 MHz) δ 1.23 (t, *J* = 7.0 Hz, 6H), 1.42 (s, 6H), 4.09 (q, *J* = 7.0 Hz, 4H), 5.35—5.47 (m, 2H), 5.87 (d, *J* = 11.7 Hz, 2H), 6.14—6.31 (m, 2H); ^{13}C-NMR (50 MHz) δ 14.0, 27.0, 60.2, 75.6, 110.2, 123.1, 144.1, 165.3.

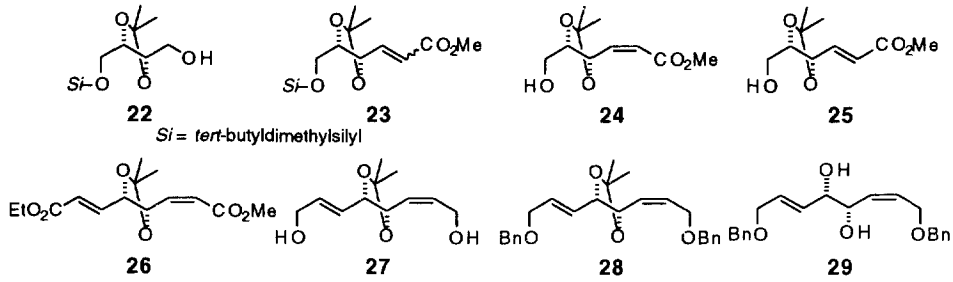
This 2*Z*,6*Z*-dienedioate was led to (4*S*,5*S*)-1,8-di-*O*-benzyl-2*Z*,6*Z*-octadiene-1,4,5,8-tetraol ($[\alpha]^{19}_D$ +102 (c 3.40, $CHCl_3$) after the same sequence of reactions executed for the synthesis of **3a** (**7** → **8** → **9**) involving DIBAH reduction of the 2*Z*,6*Z*-dienedioate to 1,ω-diol [$[\alpha]^{20}_D$ +84.0 (c 3.20, $CHCl_3$)], etherification of the diol with BnBr and deacetonidation; exact mass (EI) calcd for $C_{22}H_{28}O_4$ (M^+) 354.1831, found 354.1830.

To a solution of 1,8-bis(benzyloxy)-2*Z*,6*Z*-diene-4,5-diol (0.174, 0.49 mmol) in CH_2Cl_2 (1.5 mL) were added DMAP (6.0 mg), C_5H_5N (0.12 mL), and $ClCO_2Et$ (0.14 mL). The mixture was stirred at rt for 24 h and partitioned between H_2O and CH_2Cl_2. The organic phase was dried (Na_2SO_4) and concentrated by a rotary evaporator to give an oil, which, on CC, gave **17** (0.214 g, 88%). **17**: $[\alpha]^{22}_D$ +0.44 (c 3.40, $CHCl_3$); ^{1}H-NMR (500 MHz) δ 1.28 (t, *J* = 7.2 Hz, 6H), 4.10—4.25 (m, 8H), 4.48 and 4.51 (ABq, *J* = 11.7 Hz, 2H), 5.38—5.54 (m, 4H), 5.79—5.96 (m, 2H), 7.20—7.40 (m, 10H); ^{13}C-NMR (50 MHz) δ 13.9, 63.9, 66.0, 72.2, 73.6, 124.8, 127.39, 127.45, 128.1, 133.6, 137.8, 154.0.

Pd(II)-catalyzed equilibration of 17. A mixture of **17** (0.057 g) and $PdCl_2(CH_3CN)_2$ catalyst (8.4 mg) in benzene (2 mL) was heated at 85 °C for 24 h. The mixture was filtered through a florisil pad, concentrated by a rotary evaporator, and chromatographed over SiO_2 to give (*S*,*S*)-**18** in 26 % yield, while unchanged **19** was recovered in 59%. (*S*,*S*)-**18**: $[\alpha]^{21}_D$ +23.6 (c 1.54, $CHCl_3$); ^{1}H-NMR (500 MHz) δ 1.31 (t, *J* = 7.2 Hz, 6H), 3.56 (dd, *J* = 4.3, 10.7 Hz, 2H), 3.60 (dd, *J* = 6.9, 10.7 Hz, 2H), 4.19 (q, 4H), 4.56 (s, 4H), 5.28—5.42 (m, 2H), 5.54—5.88 (m, 2H), 6.20—6.43 (m, 2H), 7.20—7.42 (m, 10H). To a solution of **4a** in MeOH was added an aqueous solution of K_2CO_3 and the mixture was stirred at rt for 1 h to give the corresponding deacylated product (diol). The diol was again acylated with methyl chlorocarbonate, DMAP, and pyridine in CH_2Cl_2 to lead to the corresponding dicarbonate (*R*,*R*)-**18** with specific rotation as $[\alpha]^{21}_D$ –23.3 (c 1.54, $CHCl_3$), the ^{1}H-NMR (500 MHz) of which was completely identical with that of (*S*,*S*)-**18**.

(4*S*,5*S*)-4,5-Di-*O*-ethoxycarbonyl-1,8-di-*O*-benzyl-2*E*,6*Z*-octadiene-1,4,5,8-tetraol (19). The (*E*,*Z*)-isomer (**19**) was prepared through intermediates (**23**—**29**) starting from **22**.[12] A solution of 1-*O*-*t*-butyldimethylsilyl-2,3-*O*-isopropylidene-L-threitol (**22**; 5.80 g, 21 mmol) in CH_2Cl_2 (10 mL) was treated successively with Swern reagent prepared from $(COCl)_2$ (4.4 mL, 50 mmol) and DMSO (7.1 mL, 108 mmol)

in CH_2Cl_2 (20 mL) and Et_3N (40 mL) at -78 °C to afford the corresponding aldehyde. To a solution of the crude aldehyde in MeOH (20 mL) was added powdered $Ph_3P{=}CHCO_2Me$ (8.4 g, 25 mmol) in one portion, and the mixture was stirred at 40 °C for 1.5 h. Evaporation of the MeOH gave an oil, from which triphenylphosphin oxide was removed by passing through a short SiO_2 column to give rise to the condensation product (**23**). This crude enoate was dissolved in MeOH (10 mL) and to this solution was added a solution of pyridinium *p*-toluenesulfonate (1.2 eq) in MeOH, the mixture being stirred at 40 °C for 4 h. The reaction was diluted with H_2O (5 mL) and extracted with Et_2O (25 ml x 3). The combined ether extracts were dried ($MgSO_4$) and concentrated to afford an oil, from which, on careful column chromatography (SiO_2; 60 g), pure (*Z*)-enoate (**24**) was obtained in 49% yield (2.2 g) together with the (*E*)-isomer (**25**; 0.75 g, 16% yield).

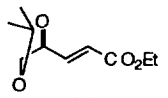


The (*Z*)-isomer (651 mg, 3 mmol) was oxidized with Swern reagent to afford the corresponding aldehyde, which was condensed with $(i\text{-PrO})_2P(O)\text{-}C(Na)HCO_2Et$ (0.28 mmol) in THF at -78 °C for 3 h, giving rise to pure (*E,Z*)-bis-enoate (**26**; 551 mg, 80% yield based on consumed aldehyde; 95 mg of the aldehyde, recovered) after purification by SiO_2 column chromatography. **26**: $[\alpha]^{20}_D$ +39.1 (c 3.30, $CHCl_3$); ^{1}H-NMR (200 MHz) δ 1.28 (t, *J* = 7.1 Hz, 3H), 1.44—1.50 (s x 2, 6H), 3.70 (s, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.15—4.31 (m, 3H), 5.40 (dt, *J* = 1.1, 8.1 Hz, 1H), 5.97 (dd, *J* = 1.1, 11.7 Hz, 1H), 6.08 (dd, *J* = 1.5, 15.7 Hz, 1H), 6.21 (dd, *J* = 8.1, 11.7 Hz, 1H), 6.94 (dd, *J* = 5.4, 15.7 Hz, 1H); ^{13}C-NMR (50 MHz) δ 14.0, 26.6, 26.9, 51.4, 60.2, 76.1, 79.8, 110.5, 122.1, 123.0, 143.1, 144.0, 165.3, 165.6. A series of routine reactions involving DIBAH reduction (**27**: $[\alpha]^{20}_D$ +52.5 (c 1.73, $CHCl_3$)), benzylation to **28**, deacetonidation to **29** ($[\alpha]^{21}_D$ +22.4 (c 2.66, $CHCl_3$)), and acylation of thus-generated diol, led to **19**: $[\alpha]^{20}_D$ +5.83 (c 1.80, $CHCl_3$); ^{1}H-NMR (500 MHz) δ 1.28 (t, *J* = 7.2 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 3.99 (bd, *J* = 5.1 Hz, 4H), 4.1—4.3 (m, 6H), 4.46 (s, 2H), 4.50 (s, 2H), 5.19—5.30 (m, 1H), 5.4—5.6 (m, 2H), 5.60—5.70 (m, 1H), 5.84—6.02 (m, 2H), 7.20—7.40 (m, 10H); ^{13}C-NMR (50 MHz) δ 14.1, 64.2, 66.3, 69.3, 72.1, 72.5, 73.7, 125.0, 127.6, 127.7, 128.3, 132.9, 133.8, 137.9, 154.1. Anal. Calcd for $C_{28}H_{34}O_8$; C, 67.45; H, 6.87. Found: C, 67.28; H, 6.81.

Pd(II)-catalyzed equilibration of 19. A mixture of **19** (0.062 g) and $PdCl_2(CH_3CN)_2$ catalyst (13 mg) in CH_2Cl_2 (1 mL) was stirred at rt for 1 h. The mixture was filtered through a florisil pad, concentrated by a rotary evaporator, and chromatographed over SiO_2 to give **20** in 60 % yield. **20**: $[\alpha]^{21}_D$ 0 (c 1.54, $CHCl_3$); ^{1}H-NMR (200 MHz) δ 1.31 (t, 6H), 3.56 (dd, *J* = 4.7, 10.7 Hz, 2H), 3.60 (dd, *J* = 6.5, 10.7 Hz, 2H), 4.19 (q, 4H), 4.56 (s, 4H), 5.28—5.39 (m, 2H), 5.64—5.78 (m, 2H), 6.24—6.40 (m, 2H), 7.20—7.40 (m, 10H). ^{13}C-NMR (50 MHz) δ 14.2, 30.9, 64.0, 71.1, 73.2, 127.6, 128.3, 129.0, 132.7, 137.7, 154.4.

(2*S*)-2-*O*-Acetyl-7-*O*-benzyl-1-*O*-pivaloyl-3*E*,5*E*-heptadiene-1,2,7-triol (14). This dienetriol derivative was prepared via intermediates (**31**—**37**) starting from **30**.[13] Among them **33**—**37** and **14** were accompanied by the corresponding geometric isomers as a minor component (5:1). Accordingly, only a proton NMR data

with regard to **14** (the major isomer of final product, (*E*,*E*)-diene) are listed: **14**: ^{1}H-NMR (500 MHz) δ 1.19 (s, 9H), 2.07 (s, 3H), 4.05—4.15 (m, 3H), 4.22 (dd, *J* = 3.9, 11.6 Hz, 1H), 4.52 (s, 2H), 5.53—5.64 (m, 2H), 5.86 (dt, *J* = 6.7, 15.1 Hz, 1H), 6.25 (dd, *J* = 10.6, 15.1 Hz, 1H), 6.35 (dd, *J* = 10.6, 14.7 Hz, 1H), 7.26—7.38 (m, 5H); exact mass (EI) calcd for $C_{21}H_{28}O_5$ (M^+) 360.1937, found 360.1935.



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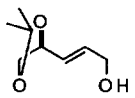

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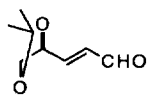
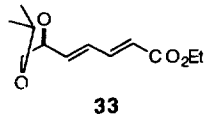


32



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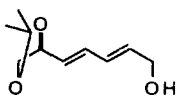

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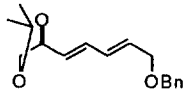

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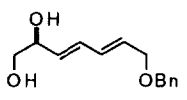

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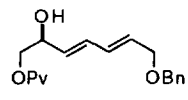

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(2*S*)-2-*O*-Acyl-1,5-di-*O*-pivaloyl-3*E*-penten-1,2,5-triol (21a—c). To a solution of **30** (0.284 g, 1.80 mmol) in EtOH (3.5 mL) was added hydrochloric acid (2*N*; 1.75 mL) and the mixture was heated at 70 °C for 15 min. The mixture was cooled to rt, neutralized with an aqueous NaOH solution, and extracted several times with CH_2Cl_2. The combined CH_2Cl_2 extracts were dried (Na_2SO_4) and concentrated by a rotary evaporator to give an oil, which, on CC, gave the corresponding triol in quantitative yield, which was dissolved in CH_2Cl_2 (6 mL). To this solution were added pyridine (4 mL) and pivaloyl chloride (0.51 mL, 2.3 mol eq) at 0 °C and the mixture was stirred at rt for 4 h followed by the addition of H_2O for quenching. The mixture was extracted several times with CH_2Cl_2. The combined CH_2Cl_2 extracts were dried (Na_2SO_4) and concentrated by a rotary evaporator to give an oil, which, on CC, gave (2*S*)-1,5-di-*O*-pivaloyl-3*E*-penten-1,2,5-triol (0.339 g, 66%).

To a solution of this 1,5-*O*-protected triol (0.051 g, 0.18 mmol) in CH_2Cl_2 (3 mL) were added DMAP (0.042 g, 1.9 eq) and acetic formic anhydride (0.03 mL, 2.3 eq) and the mixture was stirred at rt for 0.5 h followed by the addition of H_2O for quenching. The mixture was extracted several times with CH_2Cl_2. The combined CH_2Cl_2 extracts were dried (Na_2SO_4) and concentrated by a rotary evaporator to give an oil, which, on CC, gave (2*S*)-2-*O*-formyl-1,5-di-*O*-pivaloyl-3*E*-penten-1,2,5-triol (**21a**) (0.056 g, 99%). **21a**: $[\alpha]^{20}_D$ +29.6 (c 1.65, $CHCl_3$); ^{1}H-NMR (500 MHz) δ 1.19 (s, 9H), 1.21 (s, 9H), 4.13 (dd, *J* = 12.1, 6.9 Hz, 1H), 4.26 (dd, *J* = 12.1, 3.7 Hz, 1H), 4.57 (d, *J* = 5.4 Hz, 2H), 5.63—5.68 (m, 1H), 5.71 (dd, *J* = 15.4, 6.6 Hz, 1H), 5.94 (dt, *J* = 15.0, 5.4 Hz, 1H), 8.09 (s, 1H). Anal. Calcd for $C_{16}H_{26}O_6$; C, 61.13; H, 8.59. Found: C, 61.02; H, 8.65.

Acetate (**21b**) and pivaloate (**21c**) were prepared in the similar manner as described above. (2*S*)-2-*O*-acetyl-1,5-di-*O*-pivaloyl-3*E*-penten-1,2,5-triol (**21b**): $[\alpha]^{20}_D$ +16.3 (c 1.84, $CHCl_3$); ^{1}H-NMR (500 MHz) δ 1.18 (s, 9H), 1.20 (s, 9H), 2.07 (s, 3H), 4.08 (dd, *J* = 11.7, 6.8 Hz, 1H), 4.23 (dd, *J* = 11.7, 3.9 Hz, 1H), 4.56 (d, *J* = 5.3 Hz, 2H), 5.51—5.56 (m, 1H), 5.70 (ddt, *J* = 15.6, 6.4, 1.5 Hz, 1H), 5.89 (dtd, *J* = 15.6, 5.4, 1.5 Hz, 1H). Anal. Calcd for $C_{17}H_{28}O_6$; C, 62.18; H, 8.59. Found: C, 62.30; H, 8.65.

(2*S*)-1,2,5-tri-*O*-pivaloyl-3*E*-penten-1,2,5-triol (**21c**): $[\alpha]^{20}_D$ +13.4 (c 2.92, $CHCl_3$); ^{1}H-NMR (500 MHz) δ 1.18 (s, 9H), 1.197 (s, 9H), 1.202 (s, 9H), 4.07 (dd, *J* = 11.7, 7.0 Hz, 1H), 4.25 (dd, *J* = 11.8, 3.6 Hz, 1H), 4.55 (d, *J* = 5.5 Hz, 2H), 5.48—5.53 (m, 1H), 5.70 (ddt, *J* = 15.7, 6.0, 1.5 Hz, 1H), 5.87 (dtd *J* = 15.6, 5.4, 1.5 Hz, 1H). Anal. Calcd for $C_{20}H_{34}O_6$; C, 62.56; H, 8.03. Found: C, 62.48; H, 7.98.

(2*S*)-2-*O*-Acetyl-1,5-di-*O*-pivaloyl-3*Z*-penten-1,2,5-triol (21b'). This substrate was prepared from ethyl (4*S*)-4,5-*O*-isopropylidene-4,5-dihydroxy-2*Z*-pentenoate through a series of reactions as shown above in the

synthesis of **21b**. **21b'**: $[\alpha]^{20}_{D}$ –15.0 (c 2.05, $CHCl_3$); ^{1}H-NMR (500 MHz) δ 1.181 (s, 9H), 1.184 (s, 9H), 2.04 (s, 3H), 4.11 (dd, *J* = 11.7, 7.2 Hz, 1H), 4.17 (dd, *J* = 11.7, 4.2 Hz, 1H), 4.71 (ddd, *J* = 13.6, 6.6, 1.5 Hz, 1H), 4.76 (ddd, *J* = 18.4, 6.5, 1.6 Hz, 1H), 5.52 (ddt, *J* = 11.1, 9.0, 1.5 Hz, 1H), 5.72—5.82 (m, 2H). Anal. Calcd for $C_{17}H_{28}O_6$; C, 62.18; H, 8.59. Found: C, 62.01; H, 8.39; exact mass (EI) calcd for $C_{17}H_{28}O_6$ (M^+) 326.1729, found 327.1728.

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(6) The antipodes of **11** was prepared by benzylation of (*R*)-1,2-*O*-isopropylideneglycerol obtained after a literature procedure (A.-Hakim, A. H.; Haines, A. H.; Morley, C. *Synthesis*. **1985**, 207–209; (*R*)-1,2-*O*-isopropylidene-3-(*O'*-benzyl)glycerol: $[\alpha]^{27}_{D}$ –21.2 (c 4.33, $CHCl_3$).

(7) If this is the case, it should be pointed out that the palladium catalyst attacked a double bond not at C(4) but at C(6) of **5**. Thus, the $\Delta^{3(4)}$ double bond seems to be much less nucleophilic than the $\Delta^{6(7)}$ one for which the effect of an electron withdrawing AcO-group at C(2) and more sterically congested nature of the $\Delta^{3(4)}$ double bond than the $\Delta^{6(7)}$ one must be responsible. The similar effect has been proposed for the rearrangements of 3-acetoxy-(1*E*,4*Z*)-dienes shown in eq (5): the rate of rearrangement involving (*E*)-allylic acetate moiety might be decelerated because of the π–σ* hyperconjugative electron withdrawing inductive effect of a TBSO-group attached to it (ref. 4(c)).

(8) The carbonates gave much better results as compared with those obtained in the case of acetates in terms of the amount of byproducts and chemical yield.

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