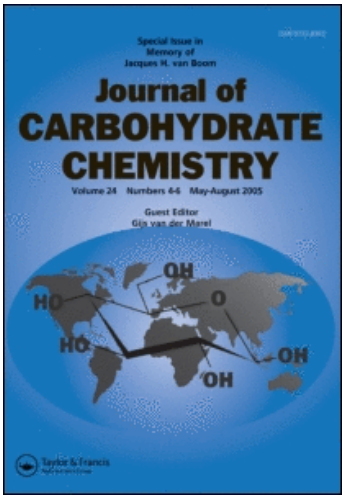

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STUDIES ON THE SYNTHESIS OF THE *C*-GLYCOSIDIC PART OF NOGALAMYCIN, PART 2

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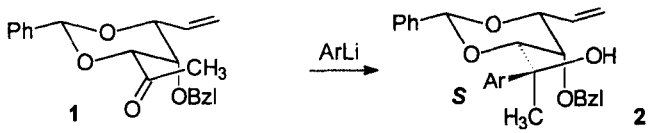
ABSTRACT

The stereochemistry of the addition of metalloaryls **11w-z** to the methyl ketones **10a-e** was studied in connection with the construction of the nogalamycin *C*-glycoside. Excellent selectivities towards the (*S*)-isomer **13a** were observed in the β-chelate model **B** in the reaction of the benzyl ethers **10a** with the cerium reagent **11y** and the titanium reagent **11z** or the alcohol **10c** with the lithium compound **11w**. A moderate 3:1 selectivity in favor of the desired (*R*)-isomer was observed in the reaction of the silyl ether **10d** with **11w**. A reversal of the addition sequence (reaction of **15a** with MeMgI) led exclusively to **13a** whereas the alcohol **15c** gave a 5:3 mixture of **12c**:**13c**.

INTRODUCTION

In studies aimed at the generation of the *C*-glycosidic bond of the nogalamycin family of antitumor antibiotics it was shown that the addition of ArLi to ketone **1** predominantly formed the wrong (*S*)-isomer (Scheme 1).[1]



Scheme 1

In the present paper we present extended work on the stereochemical outcome of the addition of a variety of metalated aryls **11w–11z** to the 4-acetyl-1,3-dioxanes **10a,c,d,e** with **inverted** configuration of the oxygen function at C-5 as compared to that in **1**. We investigated how the inversion at C-5 influenced the stereochemistry of the addition of the metalated dimethoxybenzene to the acetyl side chain of the 1,3-dioxane system.

RESULTS AND DISCUSSION

The metal in the metalaryl compounds **11** was systematically changed [M=Li (**11w**), MgBr (**11x**), $CeCl_2$ (**11y**), $Ti(OiPr)_3$ (**11z**)] as well as the oxygen functionality at C-5 of the substrates [R=Bzl (**10a**), H (**10c**), $SiMe_3$, (**10d**) and Si-*t*-$BuMe_2$ (**10e**)] to cover the entire range of possible transition states from chelate controlled to the non-chelated ones.

The stereochemistry at C-5 of the 1,3-dioxane in **10** required the inversion of configuration at C-3 if D-glucose was used as the starting material. The transformation was achieved in the usual way by borohydride reduction of 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofurano-3-ulose to the allofuranose as described by Fleet et al.[2] The required dimesylate **3a** was obtained by benzylation, selective acetal cleavage and mesylation as decribed in the literature.[3] The corresponding *p*-methoxybenzyl ether (MPM ether) **3b** was obtained in a similar way from the known 1,2-*O*-isopropylidene-3-*O*-(4-methoxybenzyl)-α-D-allofuranose.[4] The *p*-methoxybenzyl ether protecting group was introduced to enable selective deprotection of 5-OH in presence of the double bond in **10b** (see below). The introduction of the double bond in **4a,b** was achieved by treatment of

3a,b with an excess of sodium iodide in butanone.[5] Cleavage of this double bond served to create the requisite aldehyde group of the sugar as exemplified in the preceding paper.[1]

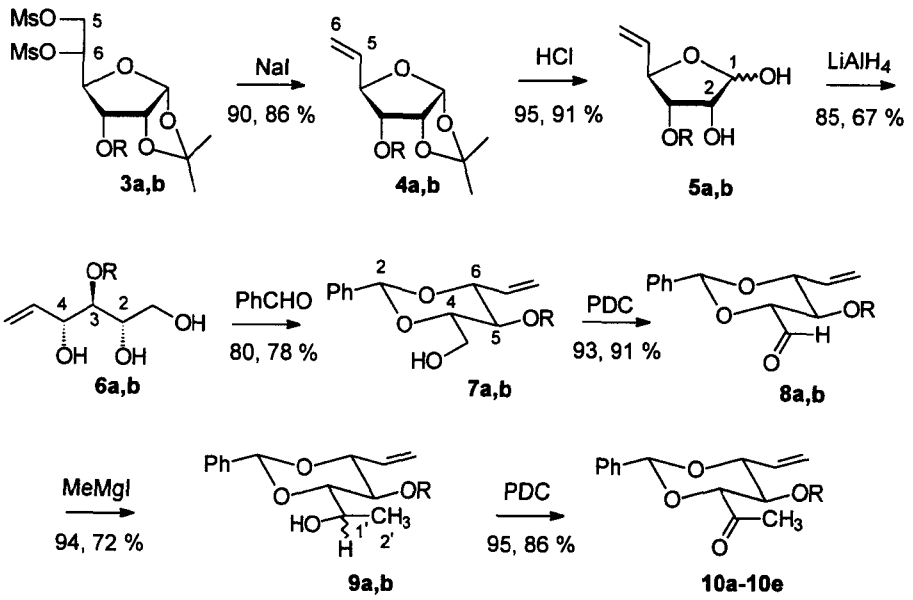
The next steps required acid-catalyzed cleavage of the acetonides **4a,b** to the anomeric mixtures of the furanoses **5a,b**. These were subjected to reduction with lithium alanate to yield the open chain triols **6a,b**. As observed with the corresponding C-3 epimer,[1] both triols **6a** and **6b** selectively formed the 1,3-dioxanes **7a** and **7b** upon treatment with benzaldehyde in a thermodynamically controlled reaction. The chain extension to the required acetyl compounds **10a** and **10b** was performed by oxidation to the aldehydes **8a,b**. Subsequent Grignard reaction with methylmagnesium iodide gave the epimeric mixtures of the secondary alcohols **9a,b** which were immediately oxidized to the ketones **10a** and **10b** with pyridinium chromate (PDC)/acetic acid anhydride (Scheme 2).

The MPM ether **10b** was cleaved selectively by treatment with dichlorodicyano benzoquinone (DDQ) to afford the alcohol **10c**. The alcohol **10c** was protected as the trimethylsilyl ether **10d** and also the sterically demanding *tert*-butyldimethylsilyl ether **10e**.

With the substrates **10a,c-e** with an equatorial oxygen substituent at C-5 in hand, the addition of the metalated dimethoxybenzenes **11w-z** was studied next (Scheme 3). The reaction of the benzyl ether **10a** with **11w-z** was examined most extensively and the results are summarized in Table 1. The addition of 2-lithio-1,4-dimethoxybenzene (**11w**) at different temperatures in THF (entries 1-3) resulted in the predominant formation of the desired (*R*)-isomer **12a** over the (*S*)-compound **13a**. The structures of the tertiary alcohols were unambigously established by X-ray structure analysis of the (*S*)-isomer **13a** (see Figure 1).

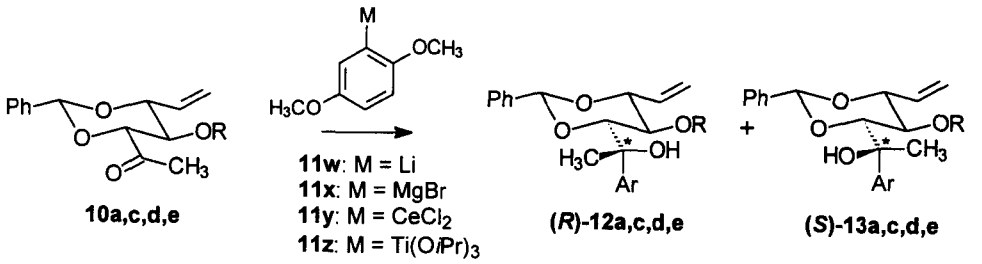
A temperature dependence with respect to the stereochemical result was not observed (Table 1, entries 1-3). However, the reaction in diethyl ether (entry 4) changed the ratio of (*R*):(*S*) from ca. 1.5:1 to 1:1.5. The addition of chelate breaking reagents such as TMEDA, HMPT or the reaction in dimethoxytetrahydrofuran (entries 5, 6 and 7) decreased the ratio of the (*R*)- to (*S*)-isomer **12a**:**13a**.

From the literature[6–10] it was known that the stereochemistry of the addition of lithium alkyls and aryls on chiral alkoxycarbonyl compounds can be rationalized by the cyclic Cram model.[6,11] However, in our system the formation of competing α- and β-



a: R=Bzl; **b:** R=MPM; **c:** R=H; **d:** R=$SiMe_3$; **e:** R=Si*t*-BuMe_2

Scheme 2



a: R=Bzl; **c:** R=H; **d:** R=$SiMe_3$; **e:** R=Si*t*-BuMe_2

Scheme 3

Table 1. Reaction of the metal aryls **11w–11z** with the ketones **10a,c,d,e**

Entry	Temp.	Educt	Reagent	Solvent	**12a**:**13a**	Yield **12a**	Yield **13a**
1	–50 °C	**10a**	**11w**	THF	1.6 : 1	52 %	35 %
2	–10 °C	**10a**	**11w**	THF	1.5 : 1	58 %	34 %
3	0 °C	**10a**	**11w**	THF	1.8 : 1	58 %	32 %
4	–40 °C	**10a**	**11w**	Et_2O	1 : 1.5	35 %	53 %
5	–50 °C	**10a**	**11w**	THF, TMEDA	1 : 1	43 %	42 %
6	–70 °C	**10a**	**11w**	THF, HMPT	1 : 1	45 %	46 %
7	–25 °C	**10a**	**11w**	2,5-di-OMe-THF	1 : 1	40 %	41 %
8	–40 °C	**10a**	**11x**	THF	1 : 1.5	34 %	51 %
9	0 °C	**10a**	**11x**	THF	1 : 1.5	35 %	53 %
10	–40 °C	**10a**	**11x**	Et_2O	1 : 1.5	33 %	49 %
11	–78 °C	**10a**	**11y**	THF	1 : 70	2 %	91 %
12	0 °C	**10a**	**11z**	THF	-	0 %	75 %
13	–20 °C	**10c**	**11w**	THF	-	0 %	81 %
14	–20 °C	**10d**	**11w**	THF	3 : 1	64 %	19 %
15	–20 °C	**10e**	**11w**	THF	1.3 : 1	both 53 %	

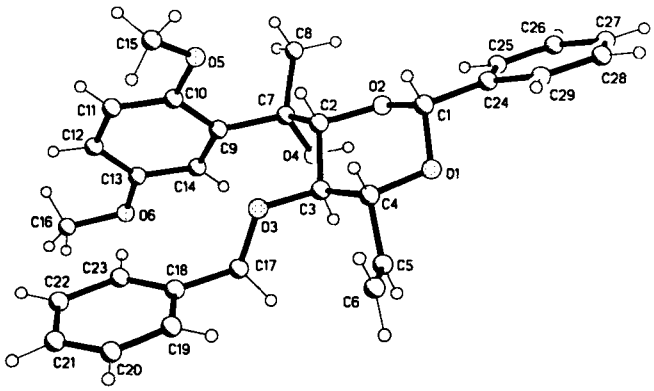
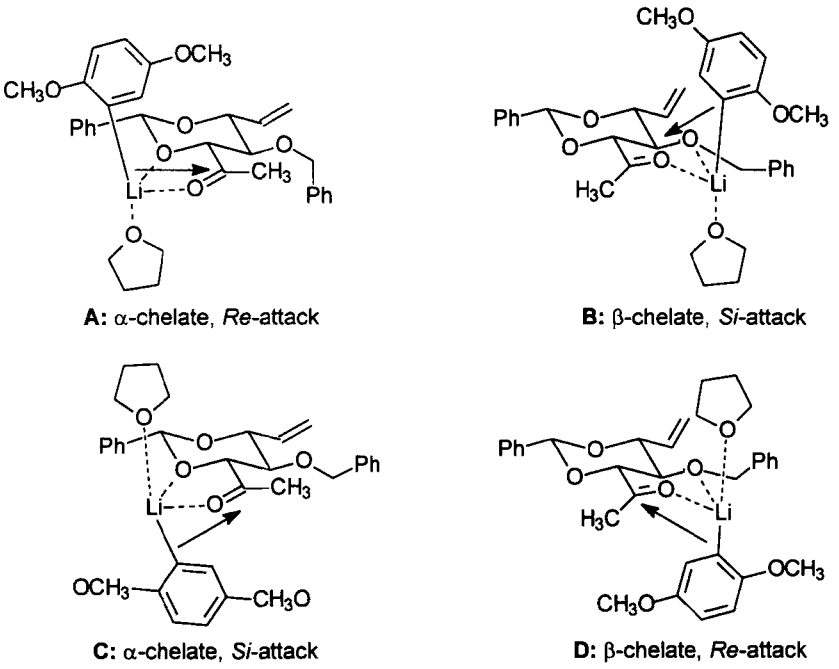


Figure 1. The molecular structure of **13a**.

chelates is possible, represented by chelate models **A** and **C** or **B** and **D** as shown in Scheme 4. Formation of the predominant (*R*)-**12a** is realized either by *Re*-attack in the α-chelate **A** or the *Si*-attack in the β-chelate **B**. In all these models, additional complexation of the lithium cation with the nucleophilic solvent THF is assumed. The stereochemical outcome is reversed by reaction in the less Lewis basic diethyl ether (entry 4). The stereoselectivity is entirely lost by addition of chelate breaking strong Lewis bases such as TMEDA, HMPT or reaction in 2,5-dimethoxytetrahydrofuran (entries 5, 6 and 7).



Scheme 4

In non-chelate controlled reactions, the open Felkin-Anh model can be applied as shown by Cohen et al.[12] and Amouroux et al.[13] On the other hand, the stereochemical result of the nucleophilic addition of alkyl or aryl Grignard reagents has also been explained by the cyclic Cram model.[8-10] The ratio of **12a**:**13a** found for the Grignard reagents **11x** was 1:1.5 (Table 1, entries 8-10). In addition, no temperature or solvent dependence was observed and it remains unclear what model can be applied to rationalize these results.

Furthermore, we investigated the less basic[14] aryl cerium compound **11y** which could be prepared from the organolithium compound **11w** by addition of anhydrous cerium trichloride (compare references 15-17). Cyclic Cram models[18,19] as well as Felkin-Anh models[20] have been discussed in the literature to explain the stereoselectivity. A very high (70:1) selectivity in the reaction with the aryl cerium reagent towards the unwanted (*S*)-isomer **13a** was observed. Assuming a β-chelate, similar to **B** (Ce instead of Li), the attack occurs from the less hindered *Si*-side.

Very strong chelates may also be formed with titanium reagents and Reetz et al. proved their existence for the first time experimentally by ^{13}C NMR spectroscopy.[21] An outstanding selectivity was observed in the reaction of $ArTi(O\text{-}i\text{-}Pr)_3$ with **10a** yielding the (*S*)-isomer **13a** exclusively.

These last two examples showed a way to achieve excellent stereoselectivity, but unfortunately in the undesired direction. Therefore, we decided to prepare the sterically more hindered silyl ethers **10d** and **10e** via the alcohol **10c** as described above (Scheme 2). Not surprisingly, the alcohol **10c** exclusively yielded the (*S*)-isomer **13c** (entry 13) in agreement with the model for a β-chelate proposed by Horton et al.[22] (see preceding paper). The structure of **13c** was confirmed by selective benzylation to **13a**. *These results indicated that β-chelation (entries 11-13) in models related to the configuration of* ***10*** *favors* ***Si****-attack to form (S)-****13*** *(model* ***B*** *in Scheme 4).*

Considering these general considerations it was interesting to see if the trimethylsilyl ether **10d** could effectively break β-chelate formation. In fact, instead of exclusive formation of (*S*)-isomer, the (*R*)-isomer **12d** was formed predominantly in a 3:1 ratio over **13d** (Table 1, entry 14). We expected that the stereoselectivity could be further increased in the reaction of the *tert*-butyldimethylsilyl ether **10e**. However, the excess of **12e** over **13e** was only 16 % (Table 1, entry 15).

In conclusion, the stereochemical results shown in Table 1 demonstrate that strong β-chelation can effectively lead to exclusive formation of the (*S*)-isomers **12**. On the other hand, the diastereofacial differentiation in the α-chelate or the non-chelated Felkin-Ank models is relatively poor.

Inversion of addition sequence

If stereocontrol was excellent in some β-chelate models towards the formation of the (*S*)-isomers **13**, a reversal of the addition sequence of the organometallic reagents M-Me and M-Ar might lead to the corresponding (*R*)-isomers **12**. Therefore, the arylketones **15a** and **15c** were prepared by reaction of the aldehydes **8a** and **8b** with 2-lithio-2,4-dimethoxybenzene (**11w**) to yield the benzyl ethers **14a** and the dimethoxybenzyl ethers **14b** both as the usual mixture of diastereoisomers. The alcohols **14a** and **14b** were oxidized to the corresponding arylketones **15a** and **15b** without further purification using

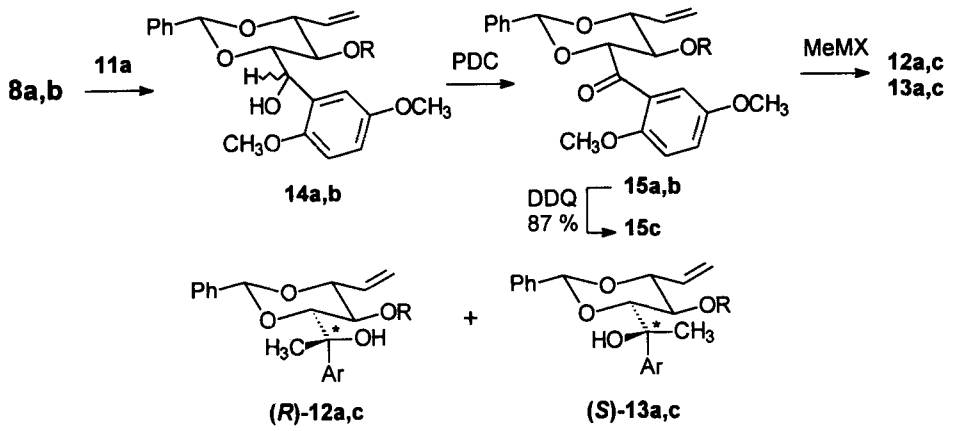
PDC/Ac_2O in 88 and 87 % yield, respectively. The MPM ether **15b** was then oxidatively cleaved using DDQ to afford the alcohol **15c** in 93 % yield (Scheme 5).

The addition of $MeCeCl_2$ on **15a** in THF exclusively afforded the (*S*)-isomer **13a** in excellent yield (95 %, Table 2, entry 1). The same result was obtained in the reaction of **15a** with MeMgBr in diethyl ether (Table 2, entry 2) (92 % of **12a**). The alcohol **15c** was also treated with MeMgBr in diethyl ether. In this case a 5:3 ratio of the adducts **12c** and **13c** were formed. These results show that a reversal of the reaction sequence did not result in a reversal of the stereochemical outcome as assumed. Evidently, the conformation and diastereofacial differentiation of the aryl ketones **15** differ from those of the methyl ketones **10**. In addition, the smaller methyl Grignard reagent may differentiate less effectively between the diastereofacial sides on **10** than the more bulky aryl reagents. The important role of the size of the incoming nucleophile is demonstrated also in the following paper.[23]

EXPERIMENTAL

For general procedures and instrumentation see reference 24.The compounds are oils if not otherwise indicated.

3-*O*-Benzyl-1,2-*O*-isopropylidene-5,6-dideoxy-α-D-*ribo*-hex-5-enofuranose (4a). A solution of dimesylate **3a**[3] (45.11 g, 0.097 mol) in dry butanone (600 mL) was treated with NaI (72.51 g, 0.483 mol) and the mixture was refluxed for 12 h (TLC control). A saturated aqueous solution of $Na_2S_2O_3$ (200 mL) was then added with stirring, the mixture diluted with CH_2Cl_2 (200 mL) and the organic phase separated. The aqueous phase was extracted with CH_2Cl_2 (200 mL), washed with water (200 mL), dried (Na_2SO_4), filtered and concentrated to yield **4a** (24.02 g, 90 %) as a yellow oil; $[\alpha]_D^{20}$ +65.1 (*c* 1.3, $CHCl_3$); IR (CH_2Cl_2) 3020 cm^{-1}, 2930, 2840, 1618, 1602, 1584, 1522, 1455, 1332, 1247, 1024; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36, 1.62 (s, 6 H, 2 x CH_3), 3.50 (dd, $J_{3,4}$ = 8.8 Hz, $J_{2,3}$ = 4.3 Hz, 1 H, 3-H), 4.47 (dd, $J_{3,4}$ = 8.8 Hz, $J_{4,5}$ = 6.9 Hz, 1 H, 4-H), 4.56 (t, J = 4.0 Hz, 1 H, 2-H), 4.62 and 4.75 (AB-signal, $J_{A,B}$ = 12.3 Hz, 2 H, OCH_2Ph), 5.26 (dt, $J_{5,6cis}$ = 10.4 Hz, J = 1.1 Hz, 1 H, CH=CH_2 (H_{cis})), 5.45 (dt, $J_{5,6trans}$ = 17.2 Hz, J = 1.2 Hz, 1 H, CH=CH_2 (H_{trans})), 5.73 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 5.81



Scheme 5

Table 2. Reaction of the metalated methyls with the ketones **15a,c**

Entry	Temp.	Educt	Reagent	Solvent	12:13	Yield 12	Yield 13
1	–20 °C	**15a**	$MeCeCl_2$	THF	-	0 %	95 %
2	–20 °C	**15a**	MeMgI	Et_2O	-	0 %	92 %
3	–15 °C	**15c**	MeMgI	Et_2O	5 : 3	54 %	32 %

(ddd, $J_{5,6trans}$ = 17.2 Hz, $J_{5,6cis}$ = 10.4 Hz, $J_{4,5}$ = 6.9 Hz, 1 H, C*H*=CH_2), 7.27–7.37 (m, 5 H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.98, 26.26, (q, 2 x CH_3), 71.73 (t, OCH_2Ph), 76.25, 78.60, 81.27, (d, C-2, C-3, C-4), 103.26 (d, C-1), 112.43 (s, $C(CH_3)_2$), 118.33 (t, C-6), 127.45, 127.48, 127.95 (d, 5 C, C-Ar), 134.37 (d, 5-C), 137.03 (s, C-Ar); MS (CI / NH_3, pos.) *m/z* (%) 304 (2) [$M^+ + NH_4$], 296 (62), 160 (5), 108 (7), 91 (100) [$PhCH_2^+$].

Anal. Calcd for $C_{16}H_{20}O_4$ (276.33): C, 69.57; H, 7.25. Found: C, 69.48; H 7.31.

1,2-*O*-Isopropylidene-5,6-di-*O*-methanesulfonyl-3-*O*-(4-methoxybenzyl)-α-D-allofuranose (3b). A solution of 1,2-*O*-isopropylidene-3-*O*-(4-methoxybenzyl)-α-D-allofuranose[4] (9.53 g, 28.0 mmol) and triethylamine (7.09 g, 70.0 mmol) in dry CH_2Cl_2 (300 mL) was treated at 0 °C with methanesulfonyl chloride (7.71 g, 67.1 mmol). After 30 min (TLC control) the solution was successively washed with aqueous solutions of $NaHSO_4$, $NaHCO_3$ and brine, dried ($MgSO_4$), filtered and concentrated to yield the

dimesylate **3b** (12.89 g, 93 %) as an oil; $[\alpha]_D^{20}$ +62.1 (*c* 0.42, $CHCl_3$); IR (CH_2Cl_2) 3063 cm^{-1}, 2938, 1613, 1514; ^1H NMR (300 MHz, $CDCl_3$) δ 1.34, 1.56 (s, 6 H, 2 x CH_3 (acetonide)), 2.99, 3.02 (s, 6 H, 2 x SO_3CH_3), 3.79 (s, 3 H, OCH_3), 3.91 (dd, $J_{3,4}$ = 8.9 Hz, $J_{2,3}$ = 4.2 Hz, 1 H, 3-H), 4.17 (dd, $J_{3,4}$ = 8.9 Hz, $J_{4,5}$ = 3.1 Hz, 1 H, 4-H), 4.33–4.37 (m, 2 H, 6-H), 4.58 and 4.67 (AB-signal, $J_{A,B}$ = 11.0 Hz, 2 H, OCH_2Ar), 4.57 (t, *J* = 3.9 Hz, 1 H, 2-H), 5.04–5.08 (m, 1 H, 5-H), 5.71 (d, $J_{1,2}$ = 3.4 Hz, 1 H, 1-H), 6.88 (d, J_{ortho} = 8.4 Hz, 2 H, Ar-H), 7.30 (d, J_{ortho} = 8.4 Hz, 2 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.47, 26.85 (q, 2 x CH_3 (acetonide)), 37.70, 38.74 (q, 2 x SO_3CH_3), 55.30 (q, OCH_3), 66.71 (t, C-6), 71.88 (t, OCH_2Ar), 76.65, 77.01, 77.49, 77.68 (C-2, C-3, C-4, C-5), 104.21 (d, C-1), 113.64 (s, $C(CH_3)_2$), 113.97 (d, 2 x C-Ar), 128.75 (s, C-Ar), 130.12 (d, 2 x C-Ar), 159.69 (s, C-Ar); MS (EI) *m/z* (%) 496 (2) [M^+], 365 (3), 242 (7), 152 (12), 136 (18), 123 (100), 109 (6), 85 (10), 78 (14).

Anal. Calcd for $C_{19}H_{28}O_{11}S_2$ (496.54): C, 45.97; H, 5.64. Found: C, 45.86; H, 5.78.

5,6–Dideoxy–1,2–*O*–isopropylidene–3–*O*–(4–methoxybenzyl)-α-D-*ribo*-hex-5-enofuranose (4b). A solution of dimesylate **3b** (11.32 g, 22.82 mmol) and dry NaI (17.38 g, 114 mmol) in dry butanone (200 mL) was reacted as described for **4a** to afford the olefin **4b** (5.98 g, 86 %) as an oil; $[\alpha]_D^{20}$ + 53.8 (*c* 1.43, $CHCl_3$); IR (film) 2990 cm^{-1}, 2940, 2840, 1615, 1588, 1516, 1464; ^1H NMR (300 MHz, $CDCl_3$) δ 1.35, 1.61 (s, 6 H, 2 x CH_3), 3.48 (dd, $J_{3,4}$ = 8.9 Hz, $J_{2,3}$ = 4.2 Hz, 1 H, 3-H), 3.80 (s, 3 H, OCH_3), 4.43–4.48 (m, 1 H, 4-H), 4.51–4.54 (m, 1 H, 2-H), 4.55 and 4.67 (AB-signal, $J_{A,B}$ = 11.8 Hz, 2 H, OCH_2Ar), 5.24 (d, $J_{5,6cis}$ = 10.4 Hz, 1 H, CH=CH_2 (H_{cis})), 5.43 (d, $J_{5,6trans}$ = 17.1 Hz, 1 H, CH=CH_2 (H_{trans})), 5.73 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 5.80 (ddd, $J_{5,6trans}$ = 17.1 Hz, $J_{5,6cis}$ = 10.4 Hz, $J_{4,5}$ = 6.6 Hz, 1 H, C*H*=CH_2), 6.88 (d, J_{ortho} = 8.5 Hz, 2 H, Ar-H), 7.28 (d, J_{ortho} = 8.5 Hz, 2 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.37, 26.63 (q, 2 x CH_3), 55.14 (q, OCH_3), 71.74 (t, OCH_2Ar), 77.51, 78.94, 81.38,(d, C-2, C-3, C-4), 103.65 (d, C-1), 112.72 (s, $C(CH_3)_2$, 113.73(d, 2 x C-Ar), 118.42 (t, C-6), 129.45 (d, 2 x C-Ar), 129.49 (s, C-Ar), 134.86 (d, C-5), 159.38 (s, C-Ar); MS (CI / NH_3, pos.) *m/z* (%) 324 (24) [$M^+ + NH_4$], 282 (18), 266 (62), 236 (14), 224 (30), 138 (21), 121 (100).

Anal. Calcd for $C_{17}H_{22}O_5$ (306.36): C, 66.67; H, 7.19. Found: C, 66.55; H, 7.32.

α- and β-3-*O*-Benzyl-5,6-dideoxy-D-*ribo*-hex-5-enofuranose (5a). A solution of acetonide **4a** (10.0 g, 36.2 mmol) in THF (250 mL) and 2 N HCl (200 mL) was refluxed for 4 h (TLC control). The mixture was neutralized by addition of 2 N NaOH, the organic

phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 100 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), filtered and concentrated to yield an anomeric mixture of the oily enofuranose **5a** (8.1 g, 95 %) which was reduced in the subsequent reaction without further purification; $[\alpha]_D^{20}$ +56.4 (*c* 1.54, $CHCl_3$); IR (CH_2Cl_2) 3555 cm^{-1}, 3067, 3036, 2936, 2876, 1607; ^1H NMR (300 MHz, $CDCl_3$, D_2O) selected data: δ 4.45–4.71 (m, 6 H, 2 x OCH_2Ph, 2 x 4-H), 5.15–5.32 (m, 6 H, 2 x 1-H, 4 x 6-H), 5.74 (ddd, $J_{5,6trans}$ = 16.8 Hz, $J_{5,6cis}$ = 10.7 Hz, $J_{4,5}$ = 6.1 Hz, 1 H, C*H*=CH_2 (α-anomer)), 5.90 (ddd, $J_{5,6trans}$ = 17.3 Hz, $J_{5,6cis}$ = 10.1 Hz, $J_{4,5}$ = 7.1 Hz, 1 H, C*H*=CH_2 (β-anomer)),7.26–7.40 (m, 10 H, 2 x Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$), α-anomer: selected data: δ 72.88 (t, OCH_2Ph), 74.07 (d, C-2), 80.89, 80.97 (d, C-3, C-4), 96.42 (d, C-1), 117.14 (t, C-6), 135.44 (d, C-5), 136.82 (s, C-Ar); ^{13}C NMR (75 MHz, $CDCl_3$), β-anomer: selected data: δ 72.72 (t, OCH_2Ph), 75.45 (d, C-2), 82.15, 82.19 (d, C-3, C-4), 101.74 (d, C-1), 117.57 (t, C-6), 137.59 (d, C-5), 137.20 (s, C-Ar); MS (CI / NH_3, pos.) *m/z* (%) 254 (5) [$M^+ + NH_4$], 150 (12), 145 (35), 91 (100) [$PhCH_2^+$].

Anal. Calcd for $C_{13}H_{16}O_4$ (236.27): C, 66.10; H, 6.78. Found: C, 65.94; H, 6.89.

α- and β-5,6-Dideoxy-3-*O*-(4-methoxybenzyl)-D-*ribo*-hex-5-enofuranose (5b). A solution of acetonide **4b** (5.01 g, 16.4 mmol) in THF (125 mL) and 2 N HCl (125 mL) was refluxed for 3 h as described for **5a** to afford the oily enofuranose **5b** (3.96 g, 91 %) as a 1:1 anomeric mixture; $[\alpha]_D^{20}$ +39.3 (*c* 1.62, $CHCl_3$); IR (CH_2Cl_2) 3600 cm^{-1}, 3555, 3009, 2938, 2915, 2840, 1613, 1514; ^1H NMR (300 MHz, $CDCl_3$, D_2O) selected data: δ 3.79 (s, 3 H, OCH_3, β-anom.) 3.85 (s, 3 H, OCH_3, α-anom.), 4.41 and 4.71 (AB-signal, $J_{A,B}$ = 11.3 Hz, 2 H, OCH_2Ar, β-anom.), 5.26 (d, *J* = 10.2 Hz, 1 H, CH=CH_2 (H_{cis}), β-anom.), 5.37 (d, *J* = 17.1 Hz, 1 H, CH=CH_2, (H_{trans}), β-anomer), 5.90 (ddd, *J* = 17.2 Hz, *J* = 10.2 Hz, *J* = 7.1 Hz, 1 H, C*H*=CH_2, β-anom.), 5.72–5.80 (m, 1 H, C*H*=CH_2, α-anom.); ^{13}C NMR (75 MHz, $CDCl_3$) (α-anomer) δ 55.72 (q, OCH_3), 70.45 (d, C-2), 73.22 (t, OCH_2Ar), 81.24, 81.30, (d, C-3, C-4), 97.08 (d, C-1), 114.51 (d, 2 x C-Ar, 117.76 (t, C-6), 129.21 (s, C-Ar), 130.13 (d, 2 x C-Ar), 135.87 (d, C-5), 138.12, 160.16 (s, 2 x C-Ar); ^{13}C NMR (75 MHz, $CDCl_3$) (β-anomer) δ 55.09 (d, OCH_3), 68.84 (t, OCH_2Ar), 75.11 (d, C-2), 75.71 (d, C-3), 84.51 (d, C-4), 105.59 (d, C-1), 113.65 (d, 2 x C-Ar), 117.17 (t, C-6), 129.21 (s, C-Ar), 129.57 (d, 2 x C-Ar), 135.11 (s, C-Ar), 137.19 (d, C-5), 159.11 (s, C-Ar); MS (CI / NH_3, pos.) *m/z* (%) 284 (8) [$M^+ + NH_4$], 256 (100), 224 (8), 164 (38), 146 (97), 121 (44).

Anal. Calcd for $C_{14}H_{18}O_5$ (266.29): C, 63.16; H, 6.77. Found: C, 63.31; H, 6.62.

(2*S*,3*R*,4*R*)-3-*O*-Benzyl-5-hexen-1,2,4-triol (6a). A solution of the furanose **5a** (15.02 g, 63.3 mmol) in dry THF (350 mL) was treated portionwise with lithium alanate (6.30 g, 166.7 mmol). The suspension was refluxed for 3 h (TLC control) and then hydrolyzed carefully by dropwise addition of ice-water. The organic phase was separated, the aqueous phase acidified by addition of 3 N HCl and extracted with ethyl acetate (2 x 150 mL). The combined organic phases were successively washed with aqueous $NaHCO_3$, water and brine. The solution was dried ($MgSO_4$), filtered and concentrated to yield the triol **6a** after column chromatography on silica gel (CH_2Cl_2/3 % methanol) (12.02 g, 85 %) which solidified: mp 68 °C; $[\alpha]_D^{20}$ +17.2 (*c* 0.26, $CHCl_3$); IR (CH_2Cl_2) 3535 cm^{-1}, 3065, 2886, 1605, 1455; ^1H NMR (400 MHz, $CDCl_3$, D_2O) δ 3.45 (t, J = 6.0 Hz, 1 H, 3-H), 3.66 (dd, $J_{1a,1b}$ = 11.6 Hz, $J_{1a,2}$ = 5.8 Hz, 1 H, 1a-H), 3.77 (dd, $J_{1a,1b}$ = 11.6 Hz, $J_{1b,2}$ = 3.4 Hz, 1 H, 1b-H), 3.81–3.86 (m, 1 H, 2-H), 4.34 (t, J = 5.9 Hz, 1 H, 4-H), 4.58 and 4.65 (AB-signal, $J_{A,B}$ = 10.8 Hz, 2 H, OCH_2Ph), 5.21 (dt, $J_{5,6cis}$ = 11.1 Hz, J = 1.2 Hz, 1 H, CH=CH_2 (H_{cis})), 5.34 (dt, $J_{5,6trans}$ = 17.0 Hz, J = 1.3 Hz, 1 H, CH=CH_2 (H_{trans})), 5.99 (ddd, $J_{5,6trans}$ = 17.0 Hz, $J_{5,6cis}$ = 10.8 Hz, $J_{4,5}$ = 6.3 Hz, 1 H, C*H*=CH_2), 7.24–7.34 (m, 5 H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.31 (t, C-1), 72.61, 73.50, 82.00 (d, C-2, C-3, C-4), 73.75 (t, OCH_2Ph), 116,61 (t, C-6), 127.86, 127.92, 128.36 (d, 5 x C-Ar), 137.27 (d, C-5), 137.75 (s, C-Ar); MS (EI) *m/z* (%) 238 (1) [M^+], 220 (5), 181 (12), 108 (67), 91 (100), 85 (10).

Anal. Calcd for $C_{13}H_{18}O_4$ (238.28): C, 65.55; H, 7.56. Found: C, 65.48; H, 7.69.

(2*S*,3*R*,4*R*)-3-*O*-(4-Methoxybenzyl)-5-hexen-1,2,4-triol (6b). A solution of furanose **5b** (3.23 g, 12.1 mmol) in dry THF (80 mL) was reduced with lithium alanate (3.20 g, 84.7 mmol) as described for **5a** to afford the triol **6b** (2.17 g, 67 %) as an oil; $[\alpha]_D^{20}$ +25.4 (*c* 0.74, $CHCl_3$); IR (CH_2Cl_2) 3550 cm^{-1}, 3023, 2950, 2882, 1613, 1509, 1455; ^1H NMR (300 MHz, $CDCl_3$) δ 3.49 (t, J = 6.0 Hz, 1 H, 3-H), 3.54–3.76 (m, 6 H, 3 x OH, 1-H, 2-H), 3.78 (s, 3 H, OCH_3), 4.35 (t, J = 5.5 Hz, 4-H), 4.51 and 4.59 (AB-signal, $J_{A,B}$ = 10.9 Hz, 2 H, OCH_2Ar), 5.22–5.26 (m, 1 H, CH=CH_2 (H_{cis}, J = 10.6 Hz)), 5.33–5.40 (m, 1 H, CH=CH_2 (H_{trans}, J = 16.9 Hz)), 6.00 (ddd, $J_{5,6trans}$ = 16.9 Hz, $J_{5,6cis}$ = 10.6 Hz, $J_{4,5}$ = 6.1 Hz, 1 H, C*H*=CH_2), 6.87 (d, J_{ortho} = 8.5 Hz, 2 H, Ar-H), 7.24 (d, J_{ortho} = 8.5 Hz, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.08 (q, OCH_3), 63.19 (t, CH_2OH), 72.41, 73.40 (d, C-2, C-3), 73.32 (t, OCH_2Ar), 81.36 (d, C-4), 113.73 (d, 2 x C-Ar), 116.49 (t, C-6), 129.47 (d, 2 x C-Ar), 129.66 (s, C-Ar), 137.15 (d, C-5), 159.22 (s, C-Ar); MS (FAB, NBA) *m/z* (%) 267 (2) [M^+ –H], 241 (4), 121 (100) [MPM^+].

Anal. Calcd for $C_{14}H_{20}O_5$ (268.31): C, 62.69; H, 7.46. Found: C, 62.61; H, 7.39.

(2*R*,4*S*,5*R*,6*R*)–5–Benzyloxy–4–hydroxymethyl–2-phenyl-6-vinyl-[1,3]dioxane (7a). A solution of triol **6a** [(11.03 g, (46.2 mmol) in dry $CHCl_3$ (300 mL) was treated with benzaldehyde (19.61 g, 184.8 mmol) and trifluoroacetic acid (1.5 mL)]. The solution was refluxed for 7 h (TLC control) and the water formed during the reaction was trapped by 3 Å molecular sieves placed in a dropping funnel which was used as a reflux column. The solution was then washed with aqueous $NaHCO_3$, (2 x 100 mL), the organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (2 x 50 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), filtered and concentrated to yield the benzylidene acetal **7a** (12.00 g, 80 %) which solidified as white crystals: mp 91.5 °C; $[\alpha]_D^{20}$ +24.38 (*c* 1.3, $CHCl_3$); IR (CH_2Cl_2) 3374 cm^{-1}, 3064, 2945, 2867, 1498, 1453; ^1H NMR (400 MHz, $CDCl_3$) δ 2.13 (m, 1 H, OH), 3.47 (t, *J* = 9.2 Hz, 1 H, 5-H), 3.75–3.80 (m, 2 H, C*H*$_2$OH), 3.91–3.94 (m, 1 H, 4-H), 4.19 (dd, *J* = 9.2 Hz, *J* = 6.5 Hz, 1 H, 6-H), 4.57 and 4.69 (AB-signal, $J_{A,B}$ = 10.8 Hz, 2 H, OCH_2Ph), 5.33 (dt, *J* = 10.6 Hz, *J* = 1.2 Hz, 1 H, CH=C*H*$_2$ (H_{cis})), 5.55 (dt, *J* = 17.2 Hz, *J* = 1.2 Hz, 1 H, CH=C*H*$_2$ (H_{trans})), 5.64 (s, 1 H, 2-H), 6.07 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 6.5 Hz, 1 H, C*H*=CH_2), 7.34–7.41 (m, 8 H, Ar-H), 7.54-7.57 (m, 2 H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 61.98 (t, CH_2OH), 73.49, 80.49, 81.35 (d, C-4, C-5, C-6), 74.71 (t, OCH_2Ph), 100.38 (d C-2), 118.65 (t, CH=*C*H_2), 126.27, 128.09, 128.14, 128.27, 128.52, 129.07 (d, 10 x C-Ar), 135.06 (d, *C*H=CH_2), 137.48, 137.50 (s, 2 x C-Ar); MS (EI) *m/z* (%) 326 (1) [M^+], 269 (3), 179 (20), 164 (40), 91 (100) [$PhCH_2^+$].

Anal. Calcd for $C_{20}H_{22}O_4$ (326.39): C, 73.62; H, 6.75. Found: C, 73.64; H, 6.75.

(2*R*,4*R*,5*R*,6*R*)–4–hydroxymethyl–5–(4–methoxybenzyloxy)–2-phenyl-6-vinyl-[1,3]dioxane (7b). A solution of the triol **6b** (982 mg, 3.7 mmol) in dry $CHCl_3$ (30 mL) was converted to the benzylidene acetal as described for **7a** to yield **7b** (1.304 g, 78 %) as a white solid: mp 122 °C (diethyl ether/petroleum ether); $[\alpha]_D^{20}$ +37.1 (*c* 0.32, $CHCl_3$); IR (CH_2Cl_2) 3600 cm^{-1}, 3065, 2876, 1613, 1514; ^1H NMR (300 MHz, $CDCl_3$) δ 2.10 (bs, 1 H, OH), 3.44–3.50 (m, 1 H, 5-H), 3.75–3.80 (m, 2 H, C*H*$_2$OH), 3.82 (s, 3 H, OCH_3), 3.92–3.96 (m, 1 H, 4-H), 4.18–4.23 (m, 1 H, 6-H), 4.53 and 4.64 (A,B-signal, $J_{A,B}$ = 10.5 Hz, 2 H, OCH_2Ph), 5.38 (d, *J* = 10.5 Hz, 1 H, CH=C*H*$_2$ (H_{cis})), 5.57 (d, *J* = 17.1 Hz,1 H, CH=C*H*$_2$ (H_{trans})), 5.65 (s, 1 H, 2-H), 6.09 (ddd, *J* = 17.1 Hz, *J* = 10.5 Hz, *J* = 6.6 Hz, 1 H, C*H*=CH_2), 6.91 (d, J_{ortho} = 8.5 Hz, 2 H, Ar-H), 7.27 (d, J_{ortho} = 8.5 Hz, 2 H, Ar-H), 7.37–7.40 (m, 3 H, Ar-H), 7.52–7.55 (m, 2 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.12 (q, OCH_3), 61.81 (t, CH_2OH), 72.99, 80.34, 81.23 (d, C-4, C-5, C-6),

74.19 (t, OCH_2Ph), 100.20 (d, C-2), 113.74 (d, 2 x C-Ar), 118.46 (t, $CH=CH_2$), 126.12, 128.11, 128.90, 129.72 (d, 7 x C-Ar), 129.48, 137.33, 159.35 (s, 3 x C-Ar), 134.95 (d, $CH=CH_2$); MS (CI / NH_3, pos.) *m/z* (%) 374 (1) [$M^+ + NH_4$], 357 (5) [$M^+ + H$], 179 (18), 137 (42), 121 (100) [MPM^+].

Anal. Calcd for $C_{21}H_{24}O_5$ (356.42): C, 70.79; H, 6.74. Found: C. 70.48; H, 6.72.

(2*R*,4*R*,5*R*,6*R*)-5-Benzyloxy-4-formyl-2-phenyl-6-vinyl-[1,3]dioxane (8a). A solution of freshly prepared pyridinium dichromate (PDC) (418 mg, 1.11 mmol) and acetic acid anhydride (484 mg, 4.74 mmol) in dry CH_2Cl_2 (5 mL) was treated with a solution of the alcohol **7a** (514 mg, 1.58 mmol) in dry CH_2Cl_2 (2 mL). The mixture was refluxed for 2 h, the chromium salts were precipated by addition of ethyl acetate and the filtered solution was passed through a column of silica gel and eluted with ethyl acetate. The colorless filtrate was evaporated at reduced pressure and traces of acetic acid and pyridine were removed by repeated (3 x) azeotropic distillation with toluene to afford an oil of **8a** (476 mg 93 %).

(2*R*,4*S*,5*R*,6*R*)-4-formyl-5-(4-methoxybenzyloxy)-2-phenyl-6-vinyl-[1,3]dioxane (8b). Alcohol **7b** (634 mg, 1.78 mmol) was oxidized with PDC (467 mg, 1.24 mmol) as described for **8a** to afford the aldehyde **8b** (573 mg, 91 %) as an oil.

(1*R*)- and (1*S*,2*R*,4*R*,5*R*,6*R*)-5-Benzyloxy-4-[1-hydroxyethyl]-2-phenyl-6-vinyl-[1,3]dioxane (9a). A solution of methylmagnesium iodide [prepared from magnesium turnings (92 mg, 3.78 mmol) and methyl iodide (534 mg, 3.76 mmol) in dry diethyl ether (20 mL)] was treated with a solution of the aldehyde **8a** (300 mg, 0.923 mmol) in diethyl ether (20 mL). The solution was stirred for 12 h at 20 °C and was then hydrolyzed by addition of a saturated aqueous solution of NH_4Cl (10 mL). The organic phase was separated and the aqueous phase extracted with diethyl ether (2 x 20 mL). The combined organic phases were washed with water, dried ($MgSO_4$), filtered and concentrated to yield the alcohol **9a** (294 mg, 94 %, 1 : 1 mixture of diastereoisomers) which was oxidized to the ketone without further purification.

(1*S*)- and (1*R*,2*R*,4*S*,5*R*,6*R*)-4-[1-hydroxyethyl]-5-(4-methoxybenzyloxy)-2-phenyl-6-vinyl-[1,3]dioxane (9b). Aldehyde **8b** (111 mg, 0.31 mmol) was reacted with methylmagnesium iodide [from Mg (135 mg, 5.55 mmol) and methyl iodide (112 mg, 5.51 mmol)] as described for **9a** to afford **9b** as an oily 1 : 1 mixture of diastereoisomers (491 mg, 72 %).

(2*R*,4*R*,5*R*,6*R*)-4-Acetyl-5-benzyloxy-2-phenyl-6-vinyl-[1,3]dioxane (10a). The secondary alcohol **9a** (326 mg, 0.96 mmol) was oxidized with PDC/Ac_2O (248 mg, 0.66

mmol)/(294 mg, 2.88 mmol) as described for **8a** to afford the oily ketone **10a** (308 mg, 95 %); $[\alpha]_D^{20}$ +46.8 (*c* 1.1, $CHCl_3$); IR (CH_2Cl_2) 3065 cm^{-1}, 2872, 1730 (C=O), 1455, 1395; ^1H NMR (300 MHz, $CDCl_3$) δ 2.29 (s, 3 H, CH_3), 3.56 (t, *J* = 9.2 Hz, 1 H, 5-H), 4.22 (d, *J* = 9.2 Hz, 1 H, 4-H), 4.22–4.28 (m, 1 H, 6-H), 4.61 and 4.67 (AB-signal, $J_{A,B}$ = 10.4 Hz, 2 H, OCH_2Ph), 5.40 (dt, *J* = 10.6 Hz, *J* = 1.3 Hz, 1 H, CHC=CH_2 (H_{cis})), 5.59 (dt, *J* = 17.2 Hz, *J* = 1.3 Hz, 1 H, CH=CH_2 (H_{trans})), 5.68 (s, 1 H, 8-H), 6.09 (ddd, *J* = 17.2 Hz, *J* = 10.6 Hz, *J* = 6.4 Hz, 1 H, C*H*=CH_2), 7.30–7.57 (m, 10 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.15 (q, CH_3), 73.56 (d, C-6), 74.25 (t, OCH_2Ph), 81.28, 83.66 (d, C-4, C-5), 100.30 (d, C-2), 119.09 (t, CH=*C*H_2), 126.18, 128.23, 128.45, 128.55, 129.17 (d, 10 x C-Ar), 134.50 (d, *C*H=CH_2), 136.98, 137.27 (s, 2 x C-Ar), 204.42, (s, C-7); MS (CI / NH_3, pos.) *m/z* (%) 356 (24) [M^+ + NH_4], 256 (22), 250 (43), 233 (100), 177 (8), 121 (10), 91 (8).

Anal. Calcd for $C_{21}H_{22}O_4$ (338.40): C, 74.56; H, 6.51. Found: C, 74.07; H, 6.48.

(2*R*,4*R*,5*R*,6*R*)-4-Acetyl-5-(4-methoxybenzyloxy)-2-phenyl-6-vinyl-[1,3]dioxane (10b). The mixture of epimeric alcohols **9b** (364 mg, 0.98 mmol) was oxidized with PDC (256 mg, 0.68 mmol) and acetic acid anhydride (300 mg, 2.95 mmol) as described for **8a** to yield the ketone **10b** (302 mg, 86 %) which solidified as a white solid: mp 104 °C; $[\alpha]_D^{20}$ +39.1 (*c* 0.38, $CHCl_3$); IR (CH_2Cl_2) 3056 cm^{-1}, 2954, 2863, 1745 (C=O), 1641, 1453; ^1H NMR (300 MHz, $CDCl_3$) δ 2.28 (s, 3 H, 2'-H), 3.56 (t, *J* = 9.2 Hz, 1 H, 5-H), 3.81 (s, 3 H, OCH_3), 4.20 (d, *J* = 9.2 Hz, 4-H), 4.18–4.25 (m, 1 H, 6-H), 4.53 and 4.59 (A,B-signal, $J_{A,B}$ = 10.1 Hz, 2 H, OCH_2Ar), 5.38–5.42 (m, 1 H, CH=CH_2 (H_{cis}, *J* = 10.5 Hz)), 5.54–5.61 (m, 1 H, CH=CH_2 (H_{trans}, *J* = 17.2 Hz)), 5.66 (s, 1 H, 2-H), 6.08 (ddd, *J*= 17.2 Hz, *J* = 10.5 Hz, *J* = 6.5 Hz, 1 H, C*H*=CH_2), 6.89 (d, J_{ortho} = 8.7 Hz, 2 H, Ar-H), 7.25 (d, J_{ortho} = 8.7 Hz, 2 H, Ar-H), 7.38 – 7.55 (m, 5 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.97 (q, C-2'), 55.11 (q, OCH_3), 73.15, 73.74, 81.16 (d, C-4, C-5, C-6), 83.60 (t, OCH_2Ar), 100.13 (d, C-2), 113.67 (d, 2 x C-Ar), 118.83 (t, CH=*C*H_2), 126.06, 128.11, 128.98, 130.03 (d, 7 x C-Ar), 134.47 (d, *C*H=CH_2), 136.88 (s, 2 x C-Ar), 159.35 (s, C-Ar), 204.29 (s, C-1'); MS (CI /NH_3, pos.) *m/z* (%) 386 (13) [M^+ + NH_4], 266 (100), 233 (21), 121 (16), 85 (8).

Anal. Calcd for $C_{22}H_{24}O_5$ (368.43): C, 71.74; H, 6.52. Found: C, 71.65; H, 6.63.

(2*R*,4*R*,5*R*,6*R*)-4-Acetyl-5-hydroxy-2-phenyl-6-vinyl-[1,3]dioxane (10c). A suspension of the MPM ether **10b** (180 mg, 0.5 mmol), dichlorodicyano benzoquinone (DDQ) (159 mg, 0.7 mmol), CH_2Cl_2 (8.0 mL) and water (0.4 mL) was stirred vigorously

at 20 °C for 24 h (TLC control). The mixture was filtered over celite and the red filtrate was washed with aqueous $NaHCO_3$. The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), filtered and concentrated to yield after purification by column chromatography on silica gel (CH_2Cl_2) the alcohol **10c** (109 mg, 90 %) as white needles: mp 90 °C (CH_2Cl_2/petroleum ether); $[\alpha]_D^{20}$ +47.2 (*c* 0.12, $CHCl_3$); IR (CH_2Cl_2) 3065 cm^{-1}, 2847, 1789, 1604, 1391; ^1H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3 H, 2'-H), 3.42 (d, *J* = 1.8 Hz, 1 H, OH), 3.63 (dt, *J* = 9.1 Hz, *J* = 1.8 Hz, 1 H, 5-H), 4.04 (d, *J* = 9.1 Hz, 4-H), 4.11–4.15 (m, 1 H, 6-H), 5.33–5.36 (m, 1 H, CH=C*H*$_2$ (H_{cis}, *J* = 10.7 Hz)), 5.49–5.54 (m, 1 H, CH=C*H*$_2$ (H_{trans}, *J* = 17.2 Hz)), 5.70 (s, 1 H, 2-H), 6.05 (ddd, *J* = 17.2 Hz, *J* = 10.7 Hz, *J* = 5.5 Hz, 1 H, C*H*=CH_2), 7.38–7.55 (m, 5 H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.70 (q, C-2'), 67.49 (d, C-5), 80.62 (d, C-6), 83.22 (d,C-4), 100.53 (d, C-2), 118.22 (t, CH=*C*H_2), 126.14, 128.27, 129.16 (d, 5 x C-Ar), 133.96 (d, *C*H=CH_2), 137.01 (s, C-Ar), 210.70 (s, C-1'); MS (CI / NH_3, pos.) *m/z* (%) 266 (28) [$M^+ + NH_4$], 160 (16), 143 (100) [M^+ – PhCO].

Anal. Calcd for $C_{14}H_{16}O_4$ (248.28): C, 67.74; H, 6.45. Found: C, 67.59; H, 6.32.

(2*R*,4*R*,5*R*,6*R*)-4-Acetyl-2-phenyl-5-trimethylsilanyloxy-6-vinyl-[1,3]dioxane (10d). A solution of the alcohol **10c** (98 mg, 0.4 mmol) in dry THF (1.5 mL) was treated successively with pyridine (55 mg, 0.7 mmol) and trimethylsilyl chloride (106 mg, 0.99 mmol) and the suspension was stirred for 24 h at 20 °C. The mixture was then diluted with diethyl ether (5 mL) and hydrolyzed by addition of 1 N HCl (1 mL). The organic phase was separated and the aqueous phase extracted with diethyl ether (2 x 3 mL). The combined organic phases dried ($MgSO_4$), filtered, concentrated at reduced pressure and purified by filtration through a short column of silica gel to yield the silyl ether **10c** (106 mg, 84 %) as an oil. $[\alpha]_D^{20}$ + 56.2 (*c* 0.17, $CHCl_3$); IR (film) 2963 cm^{-1}, 2843, 1726, 1496; ^1H NMR (300 MHz, $CDCl_3$) δ 0.10 (s, 9 H, $Si(CH_3)_3$), 2.32 (s, 3 H, 2'-H), 3.67 (t, *J* = 8.9 Hz, 1 H, 5-H), 4.07–4.12 (m, 2 H, 4-H, 6-H), 5.35 (d, *J* = 10.6 Hz, 1 H, CH=C*H*$_2$ (H_{cis})), 5.49 (d, *J* = 17.1 Hz, 1 H, CH=C*H*$_2$ (H_{trans})), 5.67 (s, 1 H, 2-H), 5.95 (ddd, *J* = 17.1 Hz, *J* = 10.6 Hz, *J* = 6.6 Hz, 1 H, C*H*=CH_2), 7.37–7.41 (m, 3 H, Ar-H), 7.51–7.55 (m, 2 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.46 (q, $Si(CH_3)_3$), 26.96 (q, C-2'), 67.78 (d, C-5), 82.43, 85.34 (d, C-4, C-6), 100.10 (d, C-2), 119.03 (t, CH=*C*H_2), 126.05, 128.08, 128.94 (d, 5 x C-Ar), 134.23 (d, *C*H=CH_2), 136.94 (s, C-Ar), 204.10 (s, C-1'); MS (CI / NH_3, neg.) *m/z* (%) 319 (3) [M^+ – H], 283 (2), 190 (14), 121 (12), 85 (100).

Anal. Calcd for $C_{17}H_{24}O_4Si$ (320.46): C, 63.75; H, 7.50. Found: C, 63.94; H, 7.64.

(2*R*,4*R*,5*R*,6*R*)-4-Acetyl-2-phenyl-5-*tert*-butyldimethylsilanyloxy-6-vinyl-[1,3]dioxane (10e). A solution of alcohol **10c** (64 mg, 0.26 mmol), imidazole (112 mg, 1.64 mmol) and *tert*-butyldimethylsilyl chloride (170 mg, 1.13 mmol) in dry DMF (1 mL) was stirred for 4 days at 70 °C (TLC control). The reaction mixture was hydrolyzed by addition of water (1 mL) and extracted twice with diethyl ether (2 x 10 mL). The combined organic phases were dried ($MgSO_4$), filtered, concentrated and purified by filtration through a short column of silica gel to yield the oily silyl ether **10e** (69 mg, 75 %); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.01 (s, 3 H, $SiCH_3$), 0.09 (s, 3 H, $SiCH_3$), 0.91 (s, 9 H, $C(CH_3)_3$), 2.34 (s, 3 H, CH_3), 3.74 (m, 1 H, 5-H), 4.12 (m, 2 H, 4-H, 6-H), 5.37 (d, J = 10.4 Hz, 1 H, CH=CH_2 (H_{cis})), 5.52 (d, J = 17.2 Hz, 1 H, CH=CH_2 (H_{trans})), 5.69 (s, 1 H, 2-H), 6.02 (ddd, J = 17.2 Hz, J = 10.4 Hz, J = 6.6 Hz, 1 H, C*H*=CH_2), 7.40–7.55 (m, 5 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.37 (q, $SiCH_3$), –3.66 (q, $SiCH_3$), 17.83 (s, $C(CH_3)_3$), 25.63 (q, 3 x CH_3), 26.99 (q, $COCH_3$), 67.52 (d, C-5), 82.57, 85.89 (d, C-4, C-6), 100.03 (d, C-2), 119.19 (t, CH=CH_2), 126.07, 128.06, 128.92 (d, Ar-C), 134.51 (d, *C*H=CH_2), 137.00 (s, Ar-C), 203 69 (s, CO).

Reaction of metallated 2,5-dimethylbenzene with the methyl ketone 10a.

Method 1: A solution of 2-bromo-1,4-dimethoxybenzene (650 mg, 3.0 mmol) in dry THF (10 mL) was treated at –80 °C with a solution of *n*-BuLi (2 mL, 1.5 M in *n*-hexane, 1 equiv). The solution was stirred for 15 min at –50 °C and was then treated with a solution of ketone **10a** (501 mg, 1.5 mmol) in dry THF (5 mL). Stirring was continued for 30 min at the temperatures indicated in Table 1. The reaction was then quenched with aqueous solution of NH_4Cl (15 mL), the phases were separated and the aqueous phase extracted with diethyl ether (2 x 15 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated at reduced pressure. The residue was separated by column chromatography on silica gel (petroleumether/15 % ethyl acetate) to yield the isomers **12a** and **13a** as indicated in Table 1. The reaction was also performed in diethyl ether (entry 4), by addition of tetramethylenediamine (TMEDA) (348 mg, 3.0 mmol, entry 5) or hexamethylphosphoric acid triamide (HMPT) (538 mg, 3.0 mmol, entry 6) or in 2,5-dimethoxytetrahydrofuran at –25 °C (entry 7).

Method 2: A solution of 2-bromo-1,4-dimethoxybenzene (650 mg, 3.0 mmol) in dry THF (15 mL) was lithiated at –60 °C with *n*-BuLi (2 mL, 1.5 M in *n*-hexane, 1 equiv).

The solution was added dropwise at –90 °C to a suspension of $CeCl_3$ (1.481 g, 6.0 mmol) in dry THF (20 mL) and the mixture was stirred for 1 h at –78 °C. A solution of ketone **10a** (499 mg, 1.5 mmol) in dry THF (5 mL) was then added and the mixture was stirred for 2 h at –78 °C to yield the ratio of **12a/13a** indicated in Table 1 (entry 8).

Method 3: A suspension of lithium (112 mg, 16 mmol), magnesium chloride (785 mg, 8 mmol) and naphthalene (218 mg, 17 mmol) in dry THF (10 mL) was stirred vigorously for 36 h at 20 °C. The black suspension of highly active magnesium was then treated with a solution of 2-bromo-1,4-dimethoxybenzene (650 mg, 3.0 mmol) in dry THF (5 mL) and the mixture was refluxed for 2 h. The Grignard reagent was then treated with a solution of ketone **10a** at the temperatures indicated in Table 1 (entries 9 and 10). The reaction was also performed in diethyl ether (entry 11).

Method 4: Chlorotriisopropoxy titanium was prepared by mixing a solution of Ti(*O-i*-Pr)$_4$ (21.31 g, 0.075 mol) in dry *n*-hexane (25 mL) at 0 °C with $TiCl_4$ (4.75 g, 0.025 mol). The solvent was removed and the residue was distilled at reduced pressure (0.1 mbar) to yield a colorless liquid (23.6 g, 90 %), bp: 53 °C. A solution of 2-bromo-1,4-dimethoxybenzene (416 mg, 1.9 mmol) in dry THF (5 mL) was lithiated at –90 °C with *n*-BuLi (1.2 mL, 1.6 M in *n*-hexane, 1.9 mmol, 1 equiv). After 10 min ClTi(*O-i*-Pr)$_3$ (0.95 mL, 2 M in *n*-hexane, 1 equiv) was added and the yellow suspension was allowed to warm to 0 °C and react with ketone **10a** (498 mg, 1.5 mmol) in dry THF (5 mL) (entry 12, Table 1).

Data for (2*R*,4*R*,5*R*,6*R*)-5-Benzyloxy-4-[(1*R*)-1-hydroxy-1-(2,5-dimethoxyphenyl)-ethyl]-2-phenyl-6-vinyl-[1,3]dioxane (12a). $[\alpha]_D^{20}$ +9.1 (*c* 1.61, $CHCl_3$); IR (CH_2Cl_2) 3553 cm^{-1}, 3063, 2938, 2838, 1495, 1466, 1455; ^1H NMR (300 MHz, $CDCl_3$) δ 1.79 (s, 3 H, 2'-H), 3.74 (t, *J* = 9.1 Hz, 1 H, 5-H), 3.78 (s, 6 H, 2 x OCH_3), 3.85 (s, 1 H, OH), 4.30 (dd, *J* = 9.0 Hz, *J* = 7.0 Hz, 1 H, 6-H), 4.53 (d, *J* = 9.1 Hz, 1 H, 4-H), 4.67 and 4.76 (AB-signal, $J_{A,B}$ = 10.4 Hz, 2 H, OCH_2Ph), 5.39–5.43 (m, 1 H, CH=CH_2 (H_{cis}, *J* = 10.4 Hz)), 5.57 (s, 1 H, 2-H), 5.56–5.64 (m, 1 H, CH=CH_2 (H_{trans}, *J* = 17.3 Hz)), 6.16 (ddd, *J* = 17.3 Hz, *J* = 10.4 Hz, *J* = 7.0 Hz, 1 H, C*H*=CH_2)), 6.77 (dd, J_{ortho} = 8.8 Hz, J_{meta} = 3.0 Hz, 1 H, 4"-H), 6.83 (d, J_{ortho} = 8.8 Hz, 1 H, 3"-H), 7.14 (d, J_{meta} = 3.0 Hz, 1 H, 6"-H), 7.27–7.39 (m, 10 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.60 (q, C-2'), 55.53, 55.89 (q, 2 x OCH_3), 72.83 (t, OCH_2Ph), 74.35 (d, C-5), 76.65 (s, C-1'), 81.80 (d, C-6), 83.14 (d, C-4), 99.11 (d, C-2), 111.89 (d, C-4"), 112.18 (d, C-3"), 113.22 (d, C-6"), 119.03 (t, CH=*C*H_2), 125.67, 127.49, 127.52, 127.80, 128.21, 128.30 (d, 10 x C-Ar),

135.49 (d, *C*H=CH_2), 135.78 (s, C-1"), 137.57, 137.60 (s, 2 x C-Ar), 150.61, 153.46 (s, C-2", C-5"); MS (CI / NH_3, pos.) *m/z* (%) 494 (8) [$M^+ + NH_4$], 477 (62) [$M^+ + H$], 373 (100), 250 (10), 227 (90), 181 (10), 138 (8), 121 (28).

Data for (2*R*,4*R*,5*R*,6*R*)-5-Benzyloxy-4-[(1*S*)-1-hydroxy-1-(2,5-dimethoxyphenyl)-ethyl]-2-phenyl-6-vinyl-[1,3]dioxane (13a). mp 122 °C (diethyl ether); $[\alpha]_D^{20}$ +27.8 (*c* 1.59, $CHCl_3$); IR (CH_2Cl_2) 3553 cm^{-1}, 3034, 2940, 2909, 2869, 2838, 1607, 1588, 1493; ^1H NMR (300 MHz, $CDCl_3$) δ 1.72 (s, 3 H, 2'-H), 3.17 (s, 1 H, OH), 3.51 (t, *J* = 9.1 Hz, 5-H), 3.68 and 4.24 (AB-signal, $J_{A,B}$ = 10.4 Hz, 2 H, OCH_2Ph), 3.74, 3.77 (s, 6 H, 2 x OCH_3), 4.18–4.23 (m, 1 H, 6-H), 4.65 (d, *J* = 9.1 Hz, 4-H), 5.30 (dt, *J* = 10.4 Hz, *J* = 0.8 Hz, 1 H, CH=CH_2 (H_{cis})), 5.51 (dt, *J* = 17.2 Hz, *J* = 1.2 Hz, 1 H, CH=CH_2 (H_{trans})), 5.74 (s, 1 H, 2-H), 6.04 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 6.6 Hz, 1 H, C*H*=CH_2), 6.64 (d, *J* = 1.7 Hz, 2 H, Ar-H), 6.87–6.90 (m, 2 H, Ar-H), 7.20–7.21 (m, 3 H, Ar-H), 7.38–7.41 (m, 4 H, Ar-H), 7.53–7.57 (m, 2 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.72 (q, C-2'), 55.55, 55.67 (q, 2 x OCH_3), 72.41 (t, OCH_2Ph), 73.33 (d, C-5), 74.25 (s, C-1'), 81.64 (d, C-6), 81.93 (d, C-4), 99.18 (d, C-2), 111.77, 111.88 (d, C-4", C-3"), 112.97 (d, C-6"), 118.57 (t, CH=*C*H_2), 125.92, 126.93, 127.20, 127.58, 128.00, 128.60 (d, 10 x C-Ar), 133.63 (s, C-1"), 135.22 (d, *C*H=CH_2), 137.78, 137.98 (s, 2 x C-Ar), 150.62, 153.20 (s, C-2", C-5"); MS (EI) *m/z* (%) 476 (2.5) [M^+], 181 (100) [$M^+ - C_{10}H_{13}O_3$], 91 (39) [$PhCH_2^+$].

Anal. Calcd for $C_{29}H_{32}O_6$ (476.57): C, 73.11; H, 6.72. Found for **12a**: C, 73.05; H, 6.76. Found for **13a**: C, 72.96; H, 6.75.

Crystal Structure Determination of 13a:[25] $C_{29}H_{32}O_6$, M_r = 476.6, monoclinic, space group P 2_1, a = 9.335(5), b = 16.095(8), c = 9.572(4) Å, β = 115.35(2)°, V = 1299(1) $Å^3$, Z = 2, D_r = 1.218 g/cm^3, F(000) = 508, T = 296(1) K. Siemens R3m diffractometer, graphite monochromator, λ(MoKα) = 0.71073 Å, μ = 0.08 mm^{-1}, colorless crystal, size 0.35 x 0.51 x 0.56 mm, ω–2Θ scan, 5064 intensities collected 4 < 2θ < 50°, −11 < h < 11, −19 < k < 19, −11 < l < 11, 3 standards every 400 reflections showed only random deviations, Lp correction, 4593 unique intensities (R_{int} = 0.018), 3800 with F > 4σ(F). Structure solved by direct methods,[26] full-matrix least-squares refinement based on F^2 and 320 parameters,[27] all but H atoms refined anisotropically, H atoms refined with riding model on idealized positions, refinement converged at R1(F) = 0.036, wR2(F^2, all data) = 0.089, S = 1.048, max(Δ/σ) < 0.001, min/max height in final ΔF map −0.15/0.18 e/$Å^3$. Figure 1 shows the molecular structure.

Reaction of metallated 2,5-dimethylbenzene with the methyl ketone 10c. (2*R*,4*R*,5*R*,6*R*)-6-Ethenyl-5-hydroxy-4-[(1*S*)-hydroxy-1-(2,5-dimethoxyphenyl)-ethyl]-2-phenyl-[1,3]dioxane (13c). A solution of 2-bromo-1,4-dimethoxybenzene (325 mg, 1.50 mmol) in dry THF (5 mL) was lithiated as described above with *n*-BuLi (1 mL, 1.5 M in *n*-hexane, 1 equiv). The suspension was then treated with a solution of ketone **10c** (87 mg, 0.35 mmol) in dry THF (2 mL) and the mixture was stirred at −20 °C for 30 min. Workup was performed as described above for **12a** to yield the oily alcohol **13c** (109 mg, 81 %); $[\alpha]_D^{20}$ +35.1 (*c* 0.11, $CHCl_3$); IR (film) 3454 cm^{-1}, 3071, 2937, 2837, 1495, 1454; ^1H NMR (300 MHz, $CDCl_3$) δ 1.77 (s, 3 H, 2'-H), 3.65 (s, 1 H, OH), 3.77 (s, 3 H, OCH_3), 3.81 (t, J = 9.1 Hz, 1 H, 4-H), 3.92 (s, 3 H, OCH_3), 4.15 (d, J = 9.0 Hz, 1 H, 5-H), 4.14–4.17 (m, 1 H, 4-H), 5.12 (s, 1 H), 5.35 (d, J = 10.6 Hz (J_{cis}), 1 H, CH=CH_2 (H_{cis})), 5.53 (d, J = 17.3 Hz (J_{trans}), 1 H, CH=CH_2 (H_{trans})), 5.62 (s, 1 H, H-2), 6.12 (ddd, J = 16.9 Hz, J = 10.6 Hz, J = 5.7 Hz, 1 H, C*H*=CH_2), 6.82 (dd, J_{ortho} = 8.9 Hz, J_{meta} = 2.9 Hz, 1 H, 4'-H), 6.89 (d, J_{ortho} = 8.9 Hz, 1 H, 3'-H), 7.08 (d, J_{meta} = 2.9 Hz, 1 H, 6'-H), 7.32–7.43 (m, 5 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.54 (q, CH_3), 55.54, 55.86 (q, 2 x OCH_3), 67.42 (d, C-5), 77.13 (s), 80.79, 81.83 (d, C-4, C-6), 99.47 (d, C-2), 112.03, 112.94, 114.46, (d, 3 x C-Ar), 117.50 (t, CH=*C*H_2), 125.76, 127.86 128.45 (d, 5 x C-Ar), 132.67, 137.61, 150.32, 153.58 (s, 4 x C-Ar), 134.73 (d, *C*HCH_2); MS (CI / NH_3, pos.) *m/z* (%) 387 (2) [M^+ + H], 386 (6) [M^+], 369 (5), 281 (40), 263 (28), 181 (80), 143 (100).

Anal. Calcd for $C_{22}H_{26}O_6$ (386.44): C, 68.39; H, 6.74. Found: C, 68.28; H, 6.79.

Reaction of the Silyl Ether 10d with 2-Lithio-1,4-dimethoxybenzene (11w). A solution of 2-bromo-1,4-dimethoxybenzene (67 mg, 0.31 mmol) in dry THF (2 mL) was lithiated in the usual manner by reaction at −50 °C with *n*-BuLi (0.2 mL, 1.5 M in *n*-hexane, 1 equiv) and reacted with silyl ether (82 mg, 0.26 mmol) in dry THF (1 mL) for 30 min at −10 °C. Workup was performed as described for **12a** and the crude product mixture in THF (2 mL) was then treated with a 1 M solution of tetrabutylammonium fluoride in THF (0.4 mL, 0.4 mmol). After stirring for 1 h at 20 °C the solvent was removed at reduced pressure and the residue separated by preparative TLC to afford the (*R*)-alcohol **12c** (55 mg, 68 %) from the less polar and (*S*)-alcohol **13c** (19mg, 23 %) from the polar fraction (entry 14, Table 1).

Reaction of the Silyl Ether 10e with 2-Lithio-1,4-dimethoxybenzene (11w). A solution of **11w** [prepared from 2-bromo-1,4-dimethoxybenzene (0.08 ml, 0.54 mmol)

and *n*-BuLi (0.34 ml, 1.5 M in *n*-hexane, 0.54 mmol)] was reacted with the ketone **10e** as described above for the reaction of **10d** with **11w**. The isomeric mixture was then treated with tetrabutylammonium fluoride (63 mg, 0.2 mmol) in THF (0.2 ml) to afford a mixture of **12c** and **13c** (52 mg, 2 steps 49 %) in a ratio of 1 : 1.3 by GC (entry 15, Table 1).

1'-(*R*)- and 1'-(*S*)-(2*R*,4*R*,5*R*,6*R*)-5-Benzyloxy-4-[(*R*)-hydroxy-2,5-dimethoxyphenylmethyl]-2-phenyl-6-vinyl-[1,3]dioxane (14a). A suspension of Li (224 mg, 33 mmol), $MgCl_2$ (1.570 g, 17 mmol) and naphthalene (436 mg, 34 mmol) in dry THF (15 mL) was stirred for 48 h at rt. The mixture was then treated successively with a solution of 2-bromo-1,4-dimethoxybenzene (2.602 g, 12 mmol) in dry THF (15 mL) (30 min reflux) and the aldehyde **8a** (1.012 g, 3 mmol) in dry THF (10 mL) (2 h reflux). Workup was performed as described for **9a** to yield the isomeric mixture of **14a** (1.262 g, 88 %) as an oil. The ketone **8a** can also be treated with **11w** (91 % yield of **14a**).

1'-(*R*)- and 1'-(*S*)-(2*R*,4*R*,5*R*,6*R*)-4-[(*S*)-hydroxy-(2,5-dimethoxyphenyl)-methyl]-5-(4-methoxybenzyloxy)-2-phenyl-6-vinyl-[1,3]dioxane (14b). The aldehyde **8b** was reacted with **11w** as described for **9b** to yield **14b** (1.281 g, 86 %) which was oxidized to the ketone **15b** without purification.

(2*R*,4*R*,5*R*,6*R*)-(5-Benzyloxy-2-phenyl-[1,3]dioxan-4-yl)-(2,5-dimethoxyphenyl-6-vinyl)methanone (15a). The oxidation with PDC (177 mg, 0.47 mmol) and acetic anhydride (201 mg, 1.97 mmol) of **14a** (315 mg, 0.68 mmol) was performed as described for **10a** to yield **15a** (269 mg, 86 %) as an oil. Swern oxidation[28] of **14a** furnished **15a** in 87 % yield; $[\alpha]_D^{20}$ +36.7 (*c* 1.23, $CHCl_3$); IR (CH_2Cl_2) 2985 cm^{-1}, 2863, 1756 (C=O), 1650, 1546, 1440; ^1H NMR (300 MHz, $CDCl_3$) δ 3.79, 3.86 (s, 6 H, 2 x OCH_3), 3.81–3.87 (m, 1 H, 6-H), 4.34 (dd, J = 9.2 Hz, J = 6.4 Hz, 1 H, 5-H), 4.65 and 4.79 (AB-signal, $J_{A,B}$ = 10.2 Hz, 2 H, OCH_2Ph), 5.25 (d, J = 9.2 Hz, 1 H, 4-H), 5.41 (dt, J = 10.5 Hz, J = 1 Hz, 1 H, CH=CH_2 (H_{cis})), 5.61 (dt, J = 17.2 Hz, J = 1.1 Hz, 1 H, CH=CH_2 (H_{trans})), 5.74 (s, 1 H, 2-H), 6.15 (ddd, J = 17.2 Hz, J = 10.5 Hz, J = 6.4 Hz, 1 H, C*H*=CH_2), 6.92 (d, J_{ortho} = 9.0 Hz, 1 H, 3'-H), 7.07 (dd, J_{ortho} = 9.0 Hz, J_{meta} = 3.2 Hz, 1 H, 4'-H), 7.23–7.35 (m, 4 H, Ar-H), 7.46–7.49 (m, 2 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 55.73, 56.29 (q, 2 x OCH_3), 74.31 (d, C-5), 74.38 (t, OCH_2Ph), 81.41, 82.16 (d, C-4, C-6), 100.82 (d, C-2), 113.35, 114.45, 121.03 (d, C-3', C-4', C-6'), 118.70 (t, C-1), 126.85 (s, C-1'), 126.13, 127.73, 128.09, 128.12, 128.23, 128.84 (d, 10 x C-Ar), 134.96 (d, C-2), 137.31, 137.79,(s, 2 x C-Ar), 153.49, 153.61 (s, C-2', C-5'), 195.99 (s,

C=O); MS (EI) *m/z* (%) 460 (1) [M^+], 336 (5),266 (12), 253 (23), 213 (58), 181 (36), 143 (100), 121 (18), 91 (23).

Anal. Calcd for $C_{28}H_{28}O_6$ (460.53): C, 73.04; H, 6.09. Found: C, 72.87; H, 6.14.

(2*R*,4*R*,5*R*,6*R*)-[5-(4-methoxybenzyloxy)-2-phenyl-6-vinyl-[1,3]dioxan-4-yl]-(2,5-dimethoxyphenyl)methanone (15b). The epimeric mixture of the alcohols **14b** (247 mg, 0.50 mmol) was oxidized by PDC (132 mg, 0.35 mmol) and acetic anhydride (154 mg, 1.51 mmol) in dry CH_2Cl_2 (2 mL) as described for **15a** to afford the aryl ketone **15b** (214 mg, 87 %) as an oil; $[\alpha]_D^{20}$ + 41.7 (*c* 0.33, $CHCl_3$); IR ($CHCl_3$) 3005 cm^{-1}, 2937, 2880, 1684, 1610, 1496; ^1H NMR (200 MHz, $CDCl_3$) δ 3.81, 3.82, 3.88 (s, 9 H, 3 x OCH_3), 3.88–3.93 (m, 1 H, 6-H), 4.33 (dd, *J* = 9.1 Hz, *J* = 6.9 Hz, 1 H, 5-H), 4.59 and 4.72 (A,B-signal, $J_{A,B}$ = 9.9 Hz, 2 H, OCH_2Ar), 5.23 (d, *J* = 9.1 Hz, 1 H, 4-H), 5.42 (d, *J* = 10.6 Hz, 1 H, CH=CH_2 (H_{cis})), 5.68 (d, *J* = 17.0 Hz, 1 H, CH=CH_2 (H_{trans})), 5.75 (s, 1 H, 2-H), 6.16 (ddd, *J* = 17.0 Hz, *J* = 10.6 Hz, *J* = 6.4 Hz, 1 H, C*H*=CH_2), 6.85 (d, J_{ortho} = 8.4 Hz, 2 H, Ar-H), 6.95 (d, J_{ortho} = 8.6 Hz, 1 H, 4'-H), 7.13 (dd, J_{ortho} = 8.4 Hz, J_{meta} = 2.9 Hz, 1 H, 3'-H), 7.19 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.29–7.60 (m, 5 H, Ar-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 55.69, 56.24, 56.81 (q, 3 x OCH_3), 74.51 (t, OCH_2Ar), 74.58 (d, C-6), 81.94, 82.71 (d, C-4, C-5), 101.30 (d, C-2), 113.88, 114.14 (d, 3 x C-Ar), 117.19 (t, CH=CH_2), 126.33, 128.60, 129.31, 130.29, 132.76 (d, 9 x C-Ar), 127.46, 130.29 (s, 2 x C-Ar), 135.54 (d, C*H*=CH_2), 137.86, 153.96, 154.10, 159.75 (s, 4 x C-Ar), 196.53 (s, C=O); MS (CI / NH_3, pos.) *m/z* (%) 504 (2) [$M^+ + NH_4$], 455 (2), 370 (4), 271 (32), 248 (21), 208 (100), 192 (42), 127 (14), 121 (10), 85 (24), 79 (12).

Anal. Calcd for $C_{29}H_{30}O_7$ (490.55): C, 71.02; H, 6.12. Found: C, 70.93; H, 6.28.

(2*R*,4*R*,5*R*,6*R*)-(5-hydroxy-2-phenyl-6-vinyl-[1,3]dioxan-4-yl)-(2,5-dimethoxyphenyl)methanone (15c). The MPM ether **15b** (400 mg, 0.82 mmol) was oxidized with DDQ (225 mg, 0.99 mmol) as described for **10c** to yield the oily alcohol **15c** (282 mg, 93 %); $[\alpha]_D^{20}$ +53.2 (*c* 0.21, $CHCl_3$); IR ($CHCl_3$) 3562 cm^{-1}, 2951, 2839, 1670, 1496, 1415; ^1H NMR (300 MHz, $CDCl_3$) δ 3.23 (d, *J* = 2.7 Hz, 1 H, OH), 3.79, 3.86 (s, 6 H, 2 x OCH_3), 3.91 (dt, *J* = 9.0 Hz, *J* = 2.7 Hz, 1 H, 5-H), 4.25 (dd, *J* = 9.2 Hz, *J* = 5.6 Hz, 1 H, 6-H), 4.88 (d, *J* = 9.0 Hz, 1 H, 4-H), 5.37 (d, *J* = 10.6 Hz, 1 H, CH=CH_2 (H_{cis})), 5.56 (dd, *J* = 17.1 Hz, *J* = 1.3 Hz, 1 H, CH=CH_2 (H_{trans})), 5.76 (s, 1 H, 2-H), 6.14 (ddd, *J* = 17.1 Hz, *J* = 10.6 Hz, *J* = 5.6 Hz, 1 H, C*H*=CH_2), 6.92 (d, J_{ortho} = 9.0 Hz, 1 H, 3'-H), 7.07 (dd, J_{ortho} = 9.0 Hz, J_{meta} = 3.2 Hz, 1 H, 4'-H), 7.17 (d, J_{meta} = 3.2 Hz, 6'-H), 7.29–7.32 (m, 3 H, Ar-H), 7.38–7.41 (m, 2 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 56.21, 56.76 (q, 2

x OCH_3), 68.29 (d, C-5), 80.95, (d, C-6), 83.90 (d, C-4), 101.39 (d, C-2), 113.36 (d, C-3'), 114.77 (d, C-6'), 118.47 (t, CH=*C*H_2), 121.30 (d, C-4'), 126.39, 128.56, 129.24 (d, 5 x C-Ar), 126.90 (s, C-1'), 134.91 (d, *C*H=CH_2), 137.81, (s, C-Ar), 153.73, 153.97, (s, C-2', C-5'),191.253 (s, C=O); MS (CI / NH_3, pos.) *m/z* (%) 388 (14) [$M^+ + NH_4$], 371 (8), 353 (16), 273 (32), 265 (100), 256 (8), 233 (12), 209 (10), 165 (10), 121 (22).

Anal. Calcd for $C_{21}H_{22}O_6$ (370.40): C, 68.11; H, 5.95. Found: C, 67.95; H, 5.89.

Reaction of Arylketone 15a with $MeCeCl_2$ and MeI. A suspension of $CeCl_3$ (666 mg, 2.70 mmol) in dry THF (10 mL) was treated at –78 °C with a solution of MeLi (1.6 mL, 2.60 mmol, 1.6 M in diethyl ether). After stirring for 1 h the arylketone **15a** (571 mg, 1.24 mmol) in dry THF (5 mL) was added and the mixture was stirred for 2 h. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (15 mL), the organic phase was separated and the aqueous phases extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), filtered and concentrated. The residue was purified by filtration through a short column of silica gel (petroleum ether / 15 % ethyl acetate) to yield the (*S*)-alcohol **13a** (560 mg, 95 %) (see Table 2, entry 1). The arylketone **15a** (703 mg, 1.5 mmol) was reacted in a similar way in dry diethyl ether (5 mL) with MeMgI prepared from Mg (195 mg, 8.0 mmol) and MeI (228 mg, 1.6 mmol) for 3 h at –20 °C to yield **13a** (671 mg, 92 %) (see Table 2, entry 2).

Reaction of Arylketone 15c with MeMgI. A 3 M solution of MeMgI in diethyl ether (0.25 mL, 0.68 mmol) was added dropwise at –15 °C to a solution of the arylketone **15c** (63 mg, 0.17 mmol) in dry diethyl ether (2 mL) and stirred for 1 h. Workup proceeded as described above to yield after separation by column chromatography on silica gel (CH_2Cl_2) the alcohols **12c** (36 mg, 54 %) and **13c** (21 mg, 32 %) (see Table 2, entry 3).

Data for (2*R*,4*R*,5*R*,6*R*)-5-hydroxy-4-[(1*R*)-hydroxy-1-(2,5-dimethoxyphenyl)ethyl]-2-phenyl-6-vinyl-[1,3]dioxane (12c). $[\alpha]_D^{20}$ +26.2 (*c* 0.10, $CHCl_3$); IR (film) 3451cm^{-1}, 2939, 2835, 1496, 1450; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.65 (s, 3 H, 2'-H), 3.52 (bs, 1 H, OH), 3.61, 3.79 (s, 6 H, 2 x OCH_3), 3.66–3.72 (m, 1 H, 6-H), 3.94 (d, *J* = 9.1 Hz, 1 H, 4-H), 4.03 (t, *J* = 9.0 Hz, 1 H, 5-H), 5.22 (d, *J* = 10.5 Hz, 1 H, CH=C*H*$_2$ (H_{cis})), 5.34 (bs, 1 H, OH), 5.40 (d, *J* = 17.4 Hz, 1 H, CH=C*H*$_2$ (H_{trans}), 5.59 (s, 1 H, 2-H), 5.93 (ddd, *J* = 17.4 Hz, *J* = 10.5 Hz, *J* = 6.4 Hz, 1 H, C*H*=CH_2), 6.70 (dd, J_{ortho} = 8.8 Hz, J_{meta} = 2.7 Hz, 1 H, 4"-H), 6.80 (d, J_{ortho} = 8.8 Hz, 1 H, 3"-H), 7.27–7.32 (m, 4 H, Ar-H), 7.37–7.41 (m, 2 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 27.27 (q, C-2'), 55.42, 56.21 (q, 2 x OCH_3), 67.00 (d, C-5), 78.04 (s, C-1'), 81.62, 84.79 (d, C-4, C-6), 100.25 (d, C-2),

112.80 (d, C-6"), 113.10, 113.67 (d, C-3", C-4"), 117.92 (t, CH=CH_2), 125.93, 127.94, 128.59 (d, 5 x C-Ar), 132.23 (s, C-1"), 134.66 (d, CH=CH_2), 137.61 (s, C-Ar), 150.86, 153.53 (s, C-2", C-5"); MS (CI / NH_3, pos.) *m/z* (%) 387 (14) [M^+ + H], 386 (2) [M^+], 281 (42), 263 (38), 181 (72), 143 (100).

Anal. Calcd for $C_{22}H_{26}O_6$ (386.44): C, 68.39; H, 6.74. C, 68.31; H, 6.82.

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