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Ring Closing Metathesis as the Key Step in the Synthesis of Furan-substituted *C*-Aryl Glycosides

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Abstract: The synthesis of didehydro-dideoxy C-glycosides with furan substituents using ring closing metathesis as the key step is described. The approach described herein gives access to both epimers. Assignment of the relative configuration of the products was achieved by NOESY spectroscopy. © 1997 Elsevier Science Ltd.

C-aryl glycoside antibiotics produced by various *Streptomyces* species often show interesting biological properties such as activity against Gram positive bacteria and antitumour activity.[1] Common structural features[2,3] of these antibiotics are a relatively large aromatic aglycon part (often referred to as chromophore) *C*-glycosidically linked to a 6-deoxyhexopyranose (e.g. ravidomycin[4], the chrysomycins[5]) or a 3,6-dideoxyhexopyranose (e. g. aquayamycin[6], the vineomycins[7], the pluramycins[8]). Most syntheses of *C*-aryl glycosides involve a nucleophilic attack at the anomeric carbon atom in *O*-glycosides.[2,3] Among the arylation reactions the introduction of a furan ring to a glycoside by Lewis acid promoted processes has caused some interest,[9-12] because furans allow several synthetic modifications,[13] for example Diels-Alder reactions directed to the synthesis of larger aromatic systems.[9]

A different approach towards *C*-glycosides involves ring closure reactions, for example hetero Diels-Alder reactions.[2] However, comparatively few syntheses towards *C*-glycosides utilizing transition metal mediated or -catalyzed ring closure reactions have been published so far.

Among the latter group of reactions, ring closing metathesis has become an important synthetic tool[14] for the construction of both carbo- and heterocyclic rings since the development of new ruthenium-based catalysts[15a,b] **A** by Grubbs *et al.* and molybdenum-based catalysts[15c] by Schrock *et al.*

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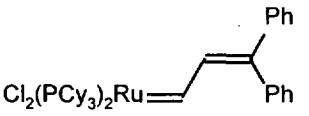
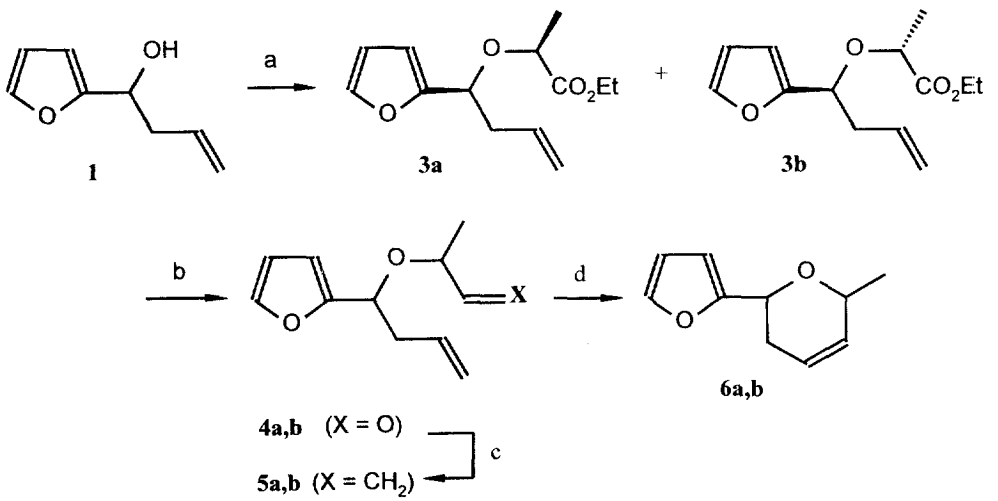


A

Up to now, ring closing metathesis was only used for the construction of very few sixmembered oxacycles, all of them without substituents in the C-6 position.[14]

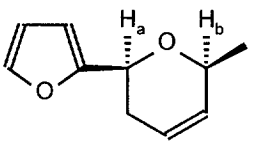
Here we wish to report a synthesis of *C*-glycosyl furan derivatives of 6-deoxy- and 3,6-dideoxy sugars using ring closing metathesis as a key step. Our synthesis starts from cheap starting materials and makes both epimers accessible in comparatively few steps. The flexibility of the approach is illustrated by the fact that both 6-deoxy and 3,6-dideoxy moieties are constructed by very similar methodology. Protecting groups, normally necessary in *C*-glycoside synthesis, are not required for this *de novo* synthesis. The endocyclic double bond formed by the metathesis reaction should allow a wide variety of synthetic transformations for the construction of many different substitution patterns. Our synthesis starts from the alcohols **1**[16a] or **2**[16b], which are easily accessible from furan carbaldehyde in a Grignard reaction. In the first step of the synthesis of the 3,6-dideoxy system alcohol **1** was reacted with sodium hydride and then with ethyl-2-bromopropionate to give a mixture of diastereomeric esters **3a,b**. Separation of diastereoisomers could easily be achieved by column chromatography on silica gel. The diastereoisomer **3a** is less polar and was eluted first.



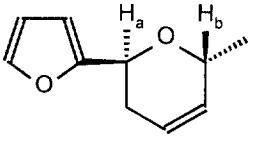
a) NaH, $H_3C(CHBr)COOEt$, THF, 65°C, separate by chromatography; b) DIBAL-H, DCM, -100°C; c) $(PMe(Ph)_3)Br$, BuLi, THF, -78°C; d) 4 mol % **A** for **6a**, 2 mol% **A** for **6b**, DCM.

Scheme 1

The separated diastereoisomers were reduced with DIBAL-H to the corresponding aldehydes **4a,b** followed by a Wittig olefination to give the allylic-homoallylic ethers **5a,b**. Both diastereoisomers of **5** underwent ring closing metathesis in the presence of catalyst **A** to give **6a,b** in good yield. However, a significant difference in reactivity could be observed. For diastereomer **6b** reaction was drawn to completion with 2 mol% catalyst within 3 hours, whereas **6a** required 4 mol% catalyst and 12 hours. The relative configuration of diastereomers **6a** and **6b** was elucidated by NOESY experiments: **6a** shows a cross peak between the two protons α to the ring oxygen (H_a and H_b), which could not be observed in the case of the diastereomer **6b**, indicating a *cis*-configuration. On the other hand, for **6b** a cross peak between the methyl group and H_a indicates the *trans*-configuration.



6a

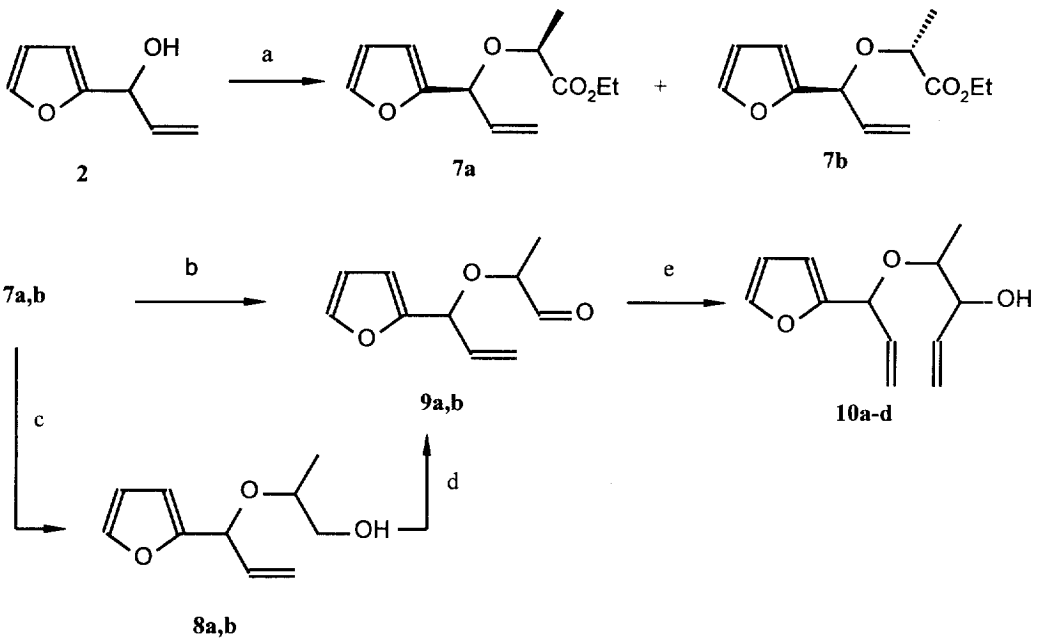


6b

In the following we describe an approach towards the 6-deoxysystem. The synthesis starts from the allylic alcohol **2** which was transformed to the diastereomeric esters **7a,b** by the procedure employed for the preparation of esters **3**. The diastereomeric esters **7** were separated by chromatography and the single diastereomers transformed into the aldehydes **9a** and **9b** either by direct reduction with DIBAL-H or by a two step-procedure involving reduction to the alcohols **8a,b** followed by Swern oxidation. **9a** was treated with vinylmagnesium chloride to give the allylic alcohols **10a,b** as a 2:1 mixture of diastereomers. The same ratio of diastereomers was observed when aldehyde **9b** was transformed into the diastereomeric alcohols **10c,d**.

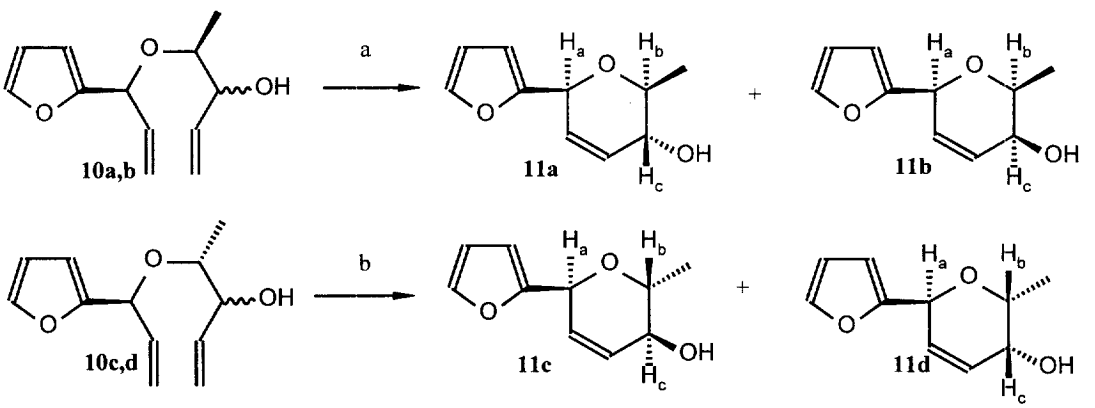
In the presence of 2 mol% ruthenium catalyst **A** ring closing metathesis was achieved for **10a,b** in good yield to give the *C*-glycosyl furans **11a,b**. The ratio of diastereomers was **11a** : **11b** = 2:1, thereby reflecting the ratio in the starting material. By the same procedure **11c,d** were accessible from **10c,d** (scheme 3), however, 5% of Ru catalyst are necessary to draw the reaction to completion.

NOESY-experiments were used to determine the relative configuration and assignment of the diastereomers **11** (scheme 3). Thus, in both diastereomers **11a,b** a cross peak between the protons α to the ring oxygen (H_a and H_b) was observed, indicating a *cis*-configuration of methyl group and furan substituent. The relative configuration at *C*-OH was elucidated by analysis of the coupling constant $^3J(H_b\text{-}H_c)$. For the major isomer $^3J(H_b\text{-}H_c)$ has a value of 8.3 Hz, in the case of the minor isomer a 1.9 Hz coupling was observed. For both diastereomers **11a,b** the dihedral angle (H_b-C-C-H_c) was calculated (167° for **11a** and 53° for **11b**) on an AM 1 level[17] and from these the expected coupling constants using the Karplus equation.



a) NaH, Me(CHBr)COOEt, THF, 65°C, separate by chromatography; b) DIBAL-H, DCM, -100°C; c) $LiAlH_4$, THF, -78°C; d) DMSO, $(COCl)_2$, NEt_3, DCM, -78°C to 0°C; e) $CH_2CHMgCl$ in THF, Et_2O, -78°C.

Scheme 2



a) 2 mol % **A**, DCM; b) 5 mol % **A**, DCM.

Scheme 3

Comparison of the observed coupling constants with the expected values suggests that **11a** is the major isomer. Additionally, in the NOESY experiment a cross peak between the methyl group and H_c is observed only for **11a**, giving further evidence for the *trans* configuration between methyl and hydroxy group. Determination of the relative configuration for the couple **11c,d** was achieved analogously.

An interesting diastereoselectivity was observed if the metathesis reaction of **10c,d** was interrupted at 50% conversion. In this case the ratio of diastereomers in the product (**11c** : **11d** = 6:1) does not reflect the ratio in the starting material (**10c** : **10d** = 2:1). One explanation is, that in the metallacyclobutane transition state for **11c** the number of unfavorable interactions between the substituents and the ligand sphere of the catalyst is lower than in the case of **11d**: In the latter case a repulsive interaction between the hydroxy group at *C*-OH and the catalyst is likely, making the ring closure of **10d** considerably slower compared to its diastereomer **10c**.

An extension of this methodology to the synthesis of other *C*-aryl glycosides and the effect of relative configuration in ring closing metathesis reactions are currently under investigation.

EXPERIMENTAL

All experiments were conducted in dry reaction vessels in an atmosphere of dry argon. Solvents were purified by standard procedures. ^{1}H NMR spectra were recorded at 400 MHz in $CDCl_3$ with $CHCl_3$ as internal standard (δ = 7.24). ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ with $CDCl_3$ (δ = 77.00) as internal standard. The number of coupled protons was analysed by DEPT experiments and is denoted by a number in parenthesis following the chemical shift value. IR spectra were recorded as films on NaCl plates and the peak intensities are defined as strong (s), medium (m), and weak (w). Mass spectra were obtained at 70 eV.

Ethyl-2-(1-furan-2-yl—but-3-enyloxy)propionate (3). NaH (1.8 g 80% dispersion in mineral oil, 60 mmol) is suspended in dry THF (20 mL) under an Ar atmosphere. A solution of alcohol **1** (5.5 g, 40 mmol) in dry THF (20 mL) is added dropwise with stirring at ambient temperature. The mixture is heated to reflux for 30 min and then cooled to 0°C. A solution of ethyl-2-bromopropionate (7.8 mL, 60 mmol) in THF (20 mL) was added slowly and the mixture heated to reflux for 2 h. After cooling to room temperature the mixture was hydrolyzed by addition of water (40 mL), the organic layer was separated and the aqueous layer extracted with ether. The combined organic layers were washed with saturated NH_4Cl solution and dried over $MgSO_4$. After evaporation of the solvent the mixture was distilled (68°C, 0.28 mbar). The diastereomers were separated by chromatography on silica using hexanes/MTBE mixtures of increasing polarity. Yield: Diastereomer **3a** (less polar) 2.80 g; diastereomer **3b** (more polar) 2.2 g (total yield 52%).

Anal.: Found: C, 65.3; H, 7.6, Calc. for $C_{13}H_{18}O_4$ C, 65.5; H, 7.6%; LRMS (EI): m/z 238 (M+, 5), 197(95) 121(80) 97(100). **Diastereomer a**: ^{1}H NMR: δ 7.35 (dd, 1, J = 1.7, 0.7), 6.28 (dd, 1, J = 3.2, 1.8), 6.12 (d, 1, J = 3.2), 5.74 (ddt, 1, J = 17.2, 10.2, 6.9), 5.03 (dm, 1, J = 17.2), 4.97 (dm, 1, J = 10.2), 4.43 (t, 1, J =

7.0), 4.20-4.10 (m, 2), 3.89 (q, 1, J = 6.9), 2.69 (dt, 1, J = 14.2, 7.0), 2.57 (dt, 1, J = 14.2, 7.0), 1.27 (d, 3, J = 6.9), 1.25 (t, 3, J = 7.1). ^{13}C NMR ($CDCl_3$) δ 173.20(0), 153.29(0), 142.46(1), 133.84(1), 117.02(2), 109.87(1), 108.56(1), 73.32(1), 71.69(1), 60.64(2), 38.63(2), 18.75(3), 14.13(3). IR (NaCl, neat) 3078(m), 2984(s), 2930(s), 1747(s), 1643(m), 1270(s), 1013(s), 922(s), 743(m) cm^{-1}. **Diastereomer b**: ^{1}H NMR ($CDCl_3$) δ 7.37 (dd, 1, J = 1.7, 0.7), 6.28 (dd, 1, J = 3.3, 1.8), 6.25 (d, 1, J = 3.3), 5.73 (ddt, 1, J = 17.1, 10.3, 7.0), 5.08 (dm, 1, J = 17.1), 5.01 (dm, 1, J = 10.3), 4.38 (t, 1, J = 7.0), 4.18 (q, 1, J = 7.0), 4.05-3.90 (m, 2), 2.72 (dtt, 1, J = 14.1, 7.0, 1.9), 2.62 (dtt, 1, J = 14.2, 7.0, 1.9), 1.37 (d, 3, J = 7.0), 1.16 (t, 3, J = 7.0). ^{13}C NMR ($CDCl_3$) δ 172.96(0), 152.23(0), 142.32(1), 133.77(1), 117.35(2), 109.76(1), 108.48(1), 74.96(1), 74.02(1), 60.63(2), 38.02(2), 18.63(3), 13.94(3). IR (NaCl, neat) 3078(m), 2983(s), 2936(s), 1749(s), 1732(s), 1643(w), 1120(s), 1014(s), 921(s), 742(m) cm^{-1}.

2-(1-Furan-2-yl-but-3-enyloxy)propionic aldehyde (4a, b). To a solution of the ester **3a** or **3b** (4.4 g, 18.5 mmol) in DCM (50 mL) was added dropwise at -100°C a solution of DIBAL-H (3.96 mL, 22.2 mmol) in DCM (25 mL). The mixture was stirred at a temperature between -90°C and -100°C for 1 h and then quenched with methanol (10 mL). Stirring was continued at -70°C for 30 min and the mixture then warmed to ambient temperature. It was quickly washed with 1N HCl (50 mL), the organic layer was separated and immediately washed with satd. $NaHCO_3$ sol (2 x 40 mL). The organic extract was dried over $MgSO_4$, filtered and evaporated. The residue was purified by distillation (52°C, 0.56 mbar) to give 2.8 g (78%) of **4a** or **4b**.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.0; H, 7.3. Found: C, 67.6; H, 7.5%. LRMS (EI) m/z 153(50), 121(100). **Diastereomer a**: ^{1}H NMR ($CDCl_3$) δ 9.60 (d, 1, J = 1.8), 7.39 (dd, 1, J = 1.8, 0.8), 6.32 (dd, 1, J = 3.3, 1.8), 6.25 (d, 1, J = 3.3), 5.78 (ddt, 1, J = 17.1, 10.0, 7.0), 5.10 (dm, 1, J = 17.1), 5.04 (dm, 1, J = 10.0), 4.49 (t, 1, J = 7.0), 3.83 (qd, 1, J = 7.0, 1.8), 2.73 (dtt, 1, J = 14.2, 7.0, 1.2), 2.63 (dt, 1, J = 14.2, 7.0, 1.2), 1.17 (d, 3, J = 7.0). ^{13}C NMR ($CDCl_3$) δ 203.35(1), 153.10(0), 142.54(1), 133.58(1), 117.62(2), 110.03(1), 108.53(1), 77.57(1), 74.17(1), 38.57(2), 15.64(3). IR (NaCl, neat) 3079(m), 2981(s), 1735(s), 1643(m), 1151(s), 1091(s), 1012(s), 922(s), 743(m) cm^{-1}. **Diastereomer b**: ^{1}H NMR ($CDCl_3$) δ 9.26 (d, 1, J = 2.0), 7.39 (dd, 1, J = 1.8, 0.8), 6.31 (dd, 1, J = 3.3, 1.8), 6.29 (d, 1, J = 3.3), 5.75 (ddt, 1, J = 17.1, 10.3, 6.8), 5.10 (dm, 1, J = 17.1), 5.04 (dm, 1, J = 10.3), 4.44 (t, 1, J = 7.1), 3.78 (qd, 1, J = 7.0, 2.0), 2.74 (dtt, 1, J = 14.3, 7.0, 1.3), 2.64 (dtt, 1, J = 14.3, 6.8, 1.3), 1.24 (d, 3, J = 7.0). ^{13}C NMR ($CDCl_3$) δ 203.53(1), 152.98(0), 142.68(1), 133.60(1), 117.53(2), 110.18(1), 109.21(1), 78.79(1), 74.36(1), 38.35(2), 15.78(3). IR (NaCl, neat) 3078(m), 2983(s), 1749(s), 1732(s), 1643(w), 1091(s), 1012(s), 921(s), 742(m) cm^{-1}.

2-[1-(1-Methyl-allyloxy)-but-3-enyl]furan (5a,b). Methyltriphenylphosphonium bromide (6.7 g, 18.8 mmol) was suspended in THF (80 mL) and a solution of LiBu in hexane (19.0 mL, 18.8 mmol) added dropwise at -80°C. Stirring was continued at ambient temperature for 15 min and the mixture again cooled to -80°C. Aldehyde **4a** or **4b** (2.4 g, 12.5 mmol) was added dissolved in THF (20 mL). Stirring was continued at -80°C for 1 h and at ambient temperature for 2 h. Water (80 mL) was added and the mixture was extracted with MTBE. The organic extracts were dried over $MgSO_4$, filtered, evaporated and the residue purified by Kugelrohr distillation (75°C, 0.3 mbar) to give 1.9 g (72%) of ether **5a** or **5b**.

LRMS (EI) m/z 193(M^+ + 1, 2), 121(100), 97(10), 55(20). **Diastereomer a**: ^{1}H NMR ($CDCl_3$) δ 7.39 (dd, 1, J = 1.8, 0.8), 6.33 (dd, 1, J = 3.3, 1.8), 6.22 (d, 1, J = 3.3), 5.74 (ddt, 1, J = 17.1, 10.0, 7.0), 5.69 (ddd, 1, J = 16.8, 10.5, 6.8), 5.17 (dm, 1, J = 10.8), 5.14 (dm, 1, J = 16.8), 5.06 (dm, 1, J = 17.1), 5.00 (dm, 1, J = 10.3), 4.42 (t, 1, J = 7.0), 3.82 („pent.“, 1, J = 7.0), 2.70-2.50 (m, 2), 1.18 (d, 3, J = 6.5). ^{13}C NMR ($CDCl_3$) δ

154.64(0), 141.90(1), 140.04(1), 134.28(1), 116.90(2), 116.39(2), 109.78(1), 106.02(1), 74.28(1), 71.36(1), 39.14(2), 21.68(3). IR (NaCl, neat) 3079(m), 2979(s), 2931(s), 1643(m), 1152(s), 1078(s), 1011(s), 994(s), 924(s), 739(m) cm^{-1}. **Diastereomer b**: ^1H NMR ($CDCl_3$) δ 7.36 (dd, 1, J = 1.8, 0.8), 6.30 (dd, 1, J = 3.3, 1.8), 6.23 (d, 1, J = 3.3), 5.77 (ddt, 1, J = 17.1, 10.0, 7.0), 5.74 (ddd, 1, J = 17.3, 10.3, 6.5), 5.11 (dm, 1, J = 17.1), 5.09 (dm, 1, J = 17.3), 5.03 (dm, 1, J = 10.0), 5.01 (dm, 1, J = 10.3), 4.45 (t, 1, J = 6.8), 3.98 („pent.“, 1, J = 7.0), 2.65 (dt, 1, J = 14.2, 7.0), 2.59 (dt, 1, J = 14.2, 7.0), 1.25 (d, 3, J = 6.4). ^{13}C NMR ($CDCl_3$) δ 154.94(0), 141.72(1), 140.37(1), 134.17(1), 117.10(2), 114.68(2), 109.84(1), 107.16(1), 74.89(1), 72.30(1), 38.57(2), 20.47(3). IR (NaCl, neat) 3079(m), 2977(s), 2930(s), 2872(s), 1642(m), 1152(s), 1077(s), 1011(s), 992(s), 920(s), 736(m) cm^{-1}.

2-Furan-2-yl-6-methyl-3,6-dihydro-2*H*-pyran (6a, b). Ru-catalyst **A** (40 mg, 0.04 mmol, 2 mol% in the case of diastereomer **b**, 80 mg, 0.08 mmol, 4 mol% in the case of diastereomer **a**) was dissolved in DCM (15 mL). Diene **5a** or **5b** (385 mg, 2.0 mmol) was added via syringe and the mixture was stirred at ambient temperature for 2 hours in the case of diastereomer **b** and for 12 hours in the case of diastereomer **a**. After completion of the reaction (control by TLC) the reaction mixture was exposed to air and purified by chromatography on silica using hexanes/MTBE (5:1) as eluent to give 290 mg (88%) of **6a** or **6b**.

LRMS (EI) m/z 164(M^+, 23), 97(83), 68(100), 67(76), 53(20). HRMS (EI) Calcd. for $C_{10}H_{12}O_2$ 164.0837, found: 164.0839. **Diastereomer a**: ^1H NMR ($CDCl_3$) δ 7.32 (dd, 1, J = 1.8, 0.8), 6.25 (dd, 1, J = 3.3, 1.8), 6.22 (d, 1, J = 3.3), 5.77 (ddt, 1, J = 10.3, 5.5, 2.0), 5.59 (ddt, 1, J = 10.3, 2.8, 1.3), 4.59 (dd, 1, J = 11.0, 3.3), 4.35 (m, 1), 2.51 (ddm, 1, J = 17.3, 11.0), 2.08 (dd“t“d, 1, J = 17.3, 5.5, 3.3, 1.3), 1.20 (d, 3, J = 6.8). ^{13}C NMR ($CDCl_3$) δ 154.42(0), 142.30(1), 131.36(1), 123.56(1), 110.01(1), 106.78(1), 71.58(1), 69.37(1), 28.61(2), 21.18(3). IR (NaCl, neat) 3033(m), 2975(s), 2837(m), 1653(m), 1373(s), 1261(s), 1185(s), 1105(s), 1065(s), 883(s), 736(s) cm^{-1}. **Diastereomer b**: ^1H NMR ($CDCl_3$) δ 7.40 (dd, 1, J = 1.8, 0.8), 6.34 (dd, 1, J = 3.3, 1.8), 6.29 (d, 1, J = 3.3), 5.87 (dddd, 1, J = 10.3, 4.5, 3.3, 2.3), 5.71 (dq, 1, J = 10.3, 2.3), 4.88 (dd, 1, J = 7.0, 4.8), 4.29 (m, 1), 2.47 (ddm, 1, J = 17.3, 7.0), 2.35 (ddt, 1, J = 17.3, 4.8, 1.8), 1.31 (d, 3, J = 6.8). ^{13}C NMR ($CDCl_3$) δ 154.51(0), 142.12(1), 130.95(1), 122.67(1), 109.94(1), 106.97(1), 68.10(1), 64.15(1), 27.84(2), 20.06(3). IR (NaCl, neat) 3033(m), 2974(s), 2928(m), 1190(s), 1101(s), 1079(s), 1015(s), 737(s) cm^{-1}.

Ethyl-2-(1-furan-2-yl-allyloxy)propionate (7a, b). Prepared from alcohol **2** (8.0 g, 64 mmol), NaH (750 mg 80% dispersion in mineral oil, 96 mmol) and ethyl-2-bromopropionate (12.5 mL, 96 mmol) following the procedure for esters **3**. Yield: 3.4 g of diastereomer **a**, 3.3 g of diastereomer **b**. Combined yield 46%.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.3; H, 7.2. Found: C, 63.9; H, 7.3%. LRMS (EI) m/z 224 (M^+, 15), 123(100) 102(85). **Diastereomer a**: ^1H NMR ($CDCl_3$) δ 7.39 (dd, 1, J = 1.8, 0.8), 6.32 (dd, 1, J = 3.2, 1.8), 6.28 (d, 1, J = 3.3), 6.07 (ddd, 1, J = 17.3, 10.3, 6.3), 5.35 (dt, 1, J = 17.3, 1.5), 5.24 (dm, 1, J = 10.3), 4.98 (d, 1, J = 6.3), 4.25-4.00 (m, 2), 3.99 (q, 1, J = 6.8), 1.36 (d, 3, J = 6.8), 1.26 (t, 3, J = 7.1). ^{13}C NMR ($CDCl_3$) δ 173.07(0), 152.59(0), 142.71(1), 135.05(1), 117.55(2), 110.08(1), 108.59(1), 74.95(1), 72.02(1), 60.72(2), 18.67(3), 14.09(3). IR (NaCl, neat) 3085(w), 2985(s), 2939(s), 1747(s), 1645(m), 1201(s), 1140(s), 1012(s), 742(m) cm^{-1}. **Diastereomer b**: ^1H NMR ($CDCl_3$) δ 7.36 (dd, 1, J = 1.8, 0.8), 6.29 (dd, 1, J = 3.3, 1.8), 6.26 (d, 1, J = 3.3), 5.99 (ddd, 1, J = 17.3, 10.3, 7.4), 5.34 (dm, 1, J = 17.3), 5.31 (dm, 1, J = 10.3), 4.90 (t, 1, J = 7.3), 4.20-4.08 (m, 3), 1.39 (d, 3, J = 6.8), 1.23 (t, 3, J = 7.3). ^{13}C NMR ($CDCl_3$) δ 172.83(0), 152.68(0), 142.63(1), 134.11(1), 118.64(2), 109.97(1), 107.98(1), 75.27(1), 71.85(1), 60.62(2), 18.50(3), 14.00(3). IR (NaCl, neat) 3083(m), 2985(s), 2936(s), 2938(s), 1747(s), 1732(s), 1644(w), 1139(s), 1059(s), 1013(s), 741(m) cm^{-1}.

2-(1-Furan-2-yl-allyloxy)propan-1-ol (8a, b). $LiAlH_4$ (148 mg, 3.90 mmol) was added to a solution of the ester **7** (1.75 g, 7.80 mmol) in THF (50 mL) at -80°C. The mixture is warmed to ambient temperature and stirred for 5 hours. Water (4 mL) was carefully added and the precipitate filtered off, washed with small portions of THF. The combined organic extracts were dried over $MgSO_4$, filtered and the solvent evaporated. The residue was purified by Kugelrohr distillation (125°C, 0.4 mbar) to give 1.00 g (71%) of the alcohol **8a** or **8b**.

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.9; H, 7.7. Found: C, 65.7; H, 7.9%. LRMS (EI) m/z 182 (M^+, 15), 107(100) 79(36). **Diastereomer a**: ^{1}H NMR ($CDCl_3$) δ 7.37 (dd, 1, J = 1.8, 0.8), 6.31 (dd, 1, J = 3.3, 1.8), 6.24 (d, 1, J = 3.3), 6.01 (ddd, 1, J = 17.3, 10.3, 7.0), 5.35 (dm, 1, J = 17.3), 5.28 (dm, 1, J = 10.3), 4.92 (d, 1, J = 7.0), 3.73 (m, 1), 3.54 (ddd, 1, J = 11.6, 8.0, 3.5), 3.47 (ddd, 1, J = 11.6, 7.0, 4.8), 2.21 (dd, 1, J = 7.8, 4.8), 1.06 (d, 3, J = 6.3). ^{13}C NMR ($CDCl_3$) δ 153.72(0), 142.43(1), 135.38(1), 118.02(2), 110.17(1), 107.49(1), 74.27(1), 73.90(1), 66.32(2), 16.10(3). IR (NaCl, neat) 3441(s, br), 2971(s), 2931(s), 2876(s), 1644(m), 1077(s), 1011(s), 930(s), 740(s) cm^{-1}. **Diastereomer b**: ^{1}H NMR ($CDCl_3$) δ 7.34 (dd, 1, J = 1.8, 0.8), 6.27 (dd, 1, J = 3.3, 1.8), 6.21 (d, 1, J = 3.3), 6.00 (ddd, 1, J = 17.3, 10.5, 6.3), 5.35 (dt, 1, J = 17.1, 1.5), 5.20 (dt, 1, J = 10.5, 1.5), 4.91 (d, 1, J = 6.3), 3.60 (dqd, 1, J = 7.0, 6.3, 3.5), 3.48 (m, 1), 3.40 (dd, 1, J = 11.0, 7.0), 2.22 (s, br, 1), 1.08 (d, 3, J = 6.3). ^{13}C NMR ($CDCl_3$) δ 153.41(0), 142.65(1), 135.67(1), 117.19(2), 110.16(1), 107.96(1), 74.36(1), 74.31(1), 66.32(2), 16.42(3). IR (NaCl, neat) 3549(s, br), 2972(s), 2877(s), 1644(w), 1150(m), 1011(m), 991(m) cm^{-1}.

2-(1-Furan-2-yl-allyloxy)propionaldehyde (9a, b). 9a, b are either prepared from the esters **7a, b** by reduction with DIBAL-H following the procedure given for aldehydes **4a, b** or by Swern oxidation of alcohols **8a, b**: To a solution of oxalyl chloride (0.48 mL, 5.48 mmol) in DCM (10 mL) was added a solution of DMSO (0.58 mL, 8.22 mmol) in DCM (10 mL) at -80°C. After 5 min. at -80°C a solution of the alcohol **8a** or **8b** (500 mg, 2.74 mmol) in DCM (10 mL) was added and stirring at this temperature was continued for 15 min. Triethylamine (2.7 mL, 19.18 mmol) was added dropwise at -80°C and the mixture warmed to 0°C. Stirring at this temperature was continued for 3 hours. The reaction mixture was hydrolyzed by addition of satd. NH_4Cl solution, the aqueous layer extracted with DCM and the combined organic extracts dried over $MgSO_4$. After evaporation of the solvent the residue was purified by Kugelrohr distillation (120°C, 0.2 mbar) to give aldehyde **9a** or **9b** (400 mg, 81%).

LRMS (EI) m/z 179(M^+ - 1, 2), 107(100). **Diastereomer a**: ^{1}H NMR ($CDCl_3$) δ 9.61 (d, 1, J = 1.8), 7.39 (dd, 1, J = 1.8, 0.8), 6.33 (dd, 1, J = 3.3, 1.8), 6.28 (d, 1, J = 3.3), 6.05 (ddd, 1, J = 17.1, 10.3, 6.8), 5.37 (dm, 1, J = 17.1), 5.31 (dm, 1, J = 10.3), 4.97 (d, 1, J = 6.8), 3.92 (qd, 1, J = 7.0, 1.8), 1.25 (d, 3, J = 7.0). ^{13}C NMR ($CDCl_3$) δ 203.31(1), 152.47(0), 142.87(1), 134.61(1), 118.71(2), 110.28(1), 108.58(1), 77.76(1), 75.27(1), 15.50(3). IR (NaCl, neat) 2982(m), 2934(m), 1732(s), 1645(m), 1152(m), 1088(m), 1062(m), 1012(s), 736(s) cm^{-1}. **Diastereomer b**: ^{1}H NMR ($CDCl_3$) δ 9.45(d, 1, J = 2.0), 7.38 (dd, 1, J = 1.8, 0.8), 6.32 (dd, 1, J = 3.3, 1.8), 6.29 (d, 1, J = 3.3), 6.04 (ddd, 1, J = 17.3, 10.3, 6.5), 5.38 (dm, 1, J = 17.3), 5.31 (dm, 1, J = 10.3), 4.92 (d, 1, J = 6.5), 3.89 (qd, 1, J = 7.0, 2.0), 1.27 (d, 3, J = 7.0). ^{13}C NMR ($CDCl_3$) δ 203.54(1), 152.38(0), 142.93(1), 134.33(1), 118.24(2), 110.35(1), 109.02(1), 78.09(1), 75.29(1), 15.65(3). IR (NaCl, neat) 2982(m), 2934(m), 1732(s), 1013(s), 741(m) cm^{-1}.

4*S-(1*S**-Furan-2-yl-allyloxy)pent-1-en-3-ol (*S**, *S**-10a, b).** A solution of vinylmagnesium chloride in THF (1.7M, 1.50 mL, 2.50 mmol) was added to a solution of the aldehyde **9a** (400 mg, 2.2 mmol) in ether (20 mL) at -80°C with a syringe. The mixture was kept at -80°C for 2 h and then hydrolyzed by addition of satd. NH_4Cl solution (20 mL). The mixture was extracted with MTBE, dried over $MgSO_4$, filtered and the solvent evaporated. The residue was purified by Kugelrohr distillation (120°C, 0.3 mbar) to give 360 mg (78%) of **10a, b** as an inseparable mixture of diastereomers (ratio 2:1). The spectroscopical data are given for the major isomer **10a**.

LRMS (EI) m/z 207(M^+ - 1, 2), 107(100), 79(60). ^1H NMR ($CDCl_3$) δ 7.38 (m, 1), 6.31 (m, 1), 6.24 (m, 1), 6.00 (ddd, 1, J = 17.3, 10.3, 6.8), 5.81 (ddd, 1, J = 17.3, 10.8, 6.3), 5.38-5.13 (m, 4), 4.95 (d, 1, J = 6.8), 4.18 (m, 1), 3.65 (qd, 1, J = 6.3, 2.5), 2.32 (d, 1, J = 4.0), 1.03 (d, 3, J = 6.3). ^{13}C NMR ($CDCl_3$) δ 153.65(0), 142.39(1), 136.45(1), 135.45(1), 117.75(2), 116.45(2), 110.18(1), 107.54(1), 75.82(1), 74.77(1), 74.40(1), 14.32(3). IR (NaCl, neat) 3554(s, br.), 3472(s, br.), 2982(s), 1644(m), 1151(m), 1075(m), 1011(s), 991(s), 927(s), 739(s) cm^{-1}.

4*S-(1*R**-Furan-2-yl-allyloxy)pent-1-en-3-ol (10c, d).** Prepared from aldehyde **9b** following the procedure for **9a** in 80% yield.

^1H NMR ($CDCl_3$) δ 7.38 (m, 1), 6.31 (dd, 1, J = 3.0, 1.8), 6.24 (d, 1, J = 3.0), 6.02 (ddd, 1, J = 17.1, 10.3, 6.5), 5.80 (ddd, 1, J = 17.3, 10.5, 6.0), 5.34 (dm, 1, J = 17.1), 5.26 (dm, 1, J = 17.1), 5.25 (dm, 1, J = 10.3), 5.16 (dm, 1, J = 10.5), 4.95 (d, 1, J = 6.0), 4.12 (m, 1), 3.61 (qd, 1, J = 6.3, 3.3), 2.45 (d, 1, J = 5.0), 1.10 (d, 3, J = 6.5). ^{13}C NMR ($CDCl_3$) δ 153.34(0), 142.72(1), 136.27(1), 135.42(1), 117.19(2), 116.39(2), 110.11(1), 107.93(1), 75.82(1), 74.52(1), 74.06(1), 14.53(3). IR (NaCl, neat) 3553(s, br.), 3448(s, br.), 2980(m), 1644(w), 1151(m), 1075(s), 1011(s), 991(s), 927(s) cm^{-1}.

6*S-Furan-2-yl-2*S**-methyl-3,6-dihydro-2*H*-pyran-3-ol (11a, b).** To a solution of the Ru catalyst (15 mg, 0.014 mmol, 2 mol%) was added **10a, b** (140 mg, 0.67 mmol). The mixture was stirred for 10 h at ambient temperature and then exposed to air. Removal of the catalyst was achieved by chromatography over a short column of silica. Hexane/MTBE (4:1) was used as eluent to give 105 mg (87%) of dihydropyran **11a, b**. The spectroscopical data given below are for the major isomer.

LRMS (EI) m/z 180(M^+, 9), 136(100), 107(69), 68(40). HRMS (EI) Calcd. for $C_{10}H_{12}O_3$ 180.0786, found: 180.0787. ^1H NMR ($CDCl_3$) δ 7.37 (dd, 1, J = 1.9, 0.8), 6.31 (dd, 1, J = 3.3, 1.9), 6.27 (d, 1, J = 3.3), 5.91 (d, 1, J = 10.3), 5.88 (d, 1, J = 10.3), 5.19 (s, 1), 3.96 (m, 1), 3.51 (dq, 1, J = 8.3, 6.3), 2.10 (s, br., 1), 1.36 (d, 3, J = 6.3). ^{13}C NMR ($CDCl_3$) δ 152.89(0), 142.73(1), 130.78(1), 127.75(1), 110.24(1), 107.82(1), 75.91(1), 70.23(1), 68.98(1), 18.26(3). IR (NaCl, neat) 3396(s, br.), 2975(m), 2882(m), 1498(m), 1090(s), 1067(s), 1041(s), 1012(s), 796(s), 741(s) cm^{-1}.

6*S-Furan-2-yl-2*R**-methyl-3,6-dihydro-2*H*-pyran-3-ol (11c, d).** Prepared from **10c, d** (163 mg, 0.78 mmol) and Ru-catalyst A (36 mg, 0.04 mmol, 5 mol%) following the procedure given for 11a, b. Yield 115 mg (82%).

GC-LRMS (EI) m/z 179(M^+ -1, 10), 162(20), 135(80), 107(100). ^1H NMR ($CDCl_3$) δ 7.40 (dd, 1, J = 1.8, 0.8), 6.31 (dd, 1, J = 3.3, 1.8), 6.25 (d, 1, J = 3.3), 5.98 (dt, 1, J = 10.3, 1.8), 5.92 (ddd, 1, J = 10.3, 2.8, 1.5),

5.20 (d, 1, J = 2.3), 3.86 (d, br., 1, J = 6.8), 3.52 (dq, 1, J = 7.3, 6.3), 1.87 (s, br., 1), 1.26 (d, 3, J = 6.3). ^{13}C NMR ($CDCl_3$) δ 152.35(0), 142.91(1), 130.61(1), 127.86(1), 110.01(1), 109.15(1), 70.13(1), 68.86(1), 67.64(1), 17.79(3). IR (NaCl, neat) 3390(s, br.), 2974(m), 2880(m), 1090(s), 1065(s), 1043(s), 1012(s), 796(s), 741(s) cm^{-1}.

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