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Asymmetric addition of 2-methylfuran and its lithiated derivative to variously *N*,*N*-protected L-alaninals

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Abstract—The asymmetric reaction of 2-methylfuran **2a** and its lithiated derivative **2b** with *N*,*N*-diprotected L-alaninals **1a–c**, carried out under high pressure conditions in the presence of Lewis acid-catalyst, are described. For aldehyde **1a** two diastereoisomeric adducts *anti*-**3a** and *syn*-**3a** were formed, with predominance of the former. In the case of aldehydes **1b** and **1c** only the *anti*-diastereoisomers **3b** or **3c** were formed, but accompanied by two diastereoisomeric oxazolidinones *trans*-**4** and *cis*-**4**. The absolute configuration (via X-ray analysis of *anti*-**5** and chemical correlations) and the extent of asymmetric induction were established. © 2002 Published by Elsevier Science Ltd.

1. Introduction

In the past decade there has been rapidly growing interest in the synthesis of natural products possessing a dense array of stereogenic centres with hydroxy and the amino groups. Among them carbohydrates, including amino sugars, are of great importance.[1–3] During our studies directed towards the synthesis of polyhydroxylated compounds, including carbohydrates the highly stereoselective reaction of 2,3-*O*-isopropylidene-D-glyceraldehyde with 2-methylfuryllithium **2b**, carried out in the presence of zinc bromide, proved to be very useful.[4,5] High pressure reactions of the same aldehyde with 2,5-dimethylfuran also exhibited relatively high *anti*-diastereoselectivity.[6] Similarly, the addition of furyllithium to *N*,*N*-diprotected alaninals led to formation of the *anti*-diastereoisomers.[7] Therefore, we decided to extend our stereochemical studies to various furan derivatives in order to establish the regio- and stereoselectivity of this reaction. Since *N*-monoprotected α-amino aldehydes are unstable towards lithiated furan derivatives, we selected *N*,*N*-diprotected-L-alaninals **1** as model compounds for these studies.

2. Results and discussion

It is known that 2,3-*O*-isopropylidene-D-glyceraldehyde reacts with 2-methylfuran **2a** in the presence of $ClCH_2CO_2H$ to give the desired furylcarbinol.[8] We were intrigued to find out if the same reaction could be conducted with *N*,*N*-diprotected-L-alaninals **1** as substrates (Scheme 1). Aldehydes **1** used in this study were obtained from corresponding alcohols using the TEMPO oxidation method[9] and were synthesised directly prior to use. Though the aldehydes **1** proved to be unreactive towards 2-methylfuran **2a** under normal pressure, we were delighted to find that they did react if a high pressure method was applied.

The reactions of *N*,*N*-diprotected-L-alaninals **1** with **2a** under 20 kbar pressure led to mixtures of products, and regardless of the *N*-protecting group, *anti*-**3** was formed as the major product (Table 1). *N*-Bn-*N*-Ts-L-alaninal **1a** gave a mixture of *anti*- and *syn*-adducts **3a** (86:14) in 43% yield (entry 1), and as expected, the addition of **2a** occurs predominantly from the less hindered side of the Felkin–Anh model, leading to the formation of *anti*-**3a** as the major product. For *N*-Bn-*N*-Cbz- **1b** and *N*-Bn-*N*-Boc-L-alaninal **1c** two compounds were isolated in each case, one of which proved to be the *anti*-adduct **3** (entries 2 and 3). Surprisingly, we did not isolate *syn*-adducts **3** but instead we observed the formation of oxazolidinone **4**. Presumably compounds *trans*-**4** and *cis*-**4** were formed after addition of 2-methylfuran **2a** to α-amino aldehydes **1**.

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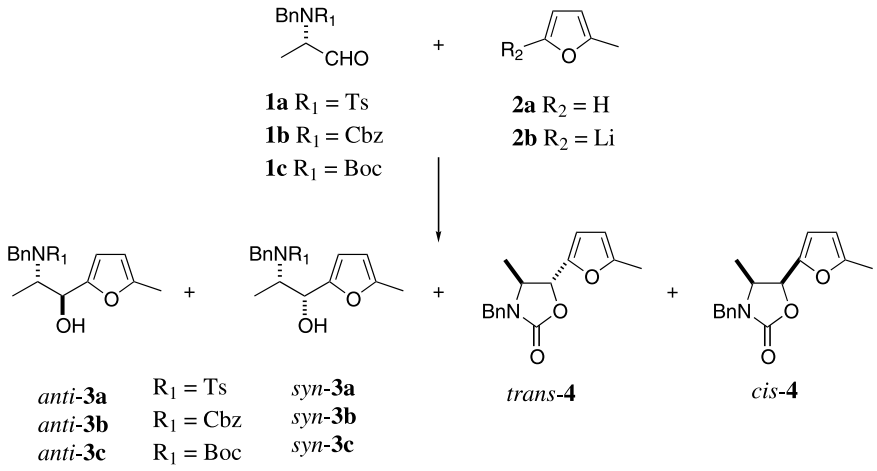


Scheme 1.

Table 1. Addition of 2-methylfuran **2a** to aldehyde **1** in the presence of $ClCH_2CO_2H$ under 20 kbar pressure at 55°C

Entry	Aldehyde	*anti*-**3**:*syn*-**3**:*trans*-**4**:*cis*-**4**	Yield of **3** (%)	Yield of **4** (%)
1	**1a**	86:14:0:0	43	–
2	**1b**	75:0:25:0	34	12
3	**1c**	90:0:9:1	24	3

Disappointed by the results of the high pressure reactions, we turned our attention to a Lewis acid-catalysed addition of 2-methylfuryllithium **2b**. The uncatalysed addition of **2b** to aldehydes **1** proceeded with diastereoselectivities ranging from high (for **1a**, Table 2, entry 1) to very high (for **1b**, Table 3, entry 1 and **1c**, Table 4, entry 1) but with rather moderate yields. *N*-Bn,*N*-Ts-protected **1a** led to exclusive formation of **3** irrespective of the conditions used (Table 2, entries 2–6). In these cases the subsequent oxazolidinone formation reaction did not occur.

The best diastereoselectivity for the reaction of aldehyde **1a** with **2b** was observed when the reaction was carried out in the presence of triethylaluminium. However, a rather low yield (33%) was obtained (entry 6). In the presence of other Lewis acids ($BF_3{\cdot}OEt_2$, $SnCl_4$, $ZnBr_2$ and $AlCl_3$), a mixture of *anti*-**3a** and *syn*-**3a** formed in ratios of around 85:5, again with the *anti*-isomer predominating (Table 2).

The addition of Lewis acids $BF_3{\cdot}OEt_2$, $SnCl_4$, $ZnBr_2$, $AlCl_3$ to the reaction of *N*-Bn,*N*-Cbz-L-alaninal **1b** with furan derivative **2b**, carried out at −78°C, led to only a slight improvement in the yield but a decrease in the diastereoselectivity of the reaction when compared to the uncatalysed reaction. In these cases *trans*-**4** was also formed, in addition to *anti*-**3b** (Table 3). Increasing the temperature of the reaction catalysed by $ZnBr_2$ to −63°C led to higher yield but the formation of *cis*-**4** was observed (Table 3, entry 5).

We were delighted to find that the reaction of *N*-Bn,*N*-Boc-L-alaninal **1c** with furan derivative **2b**, catalysed by $BF_3{\cdot}OEt_2$, afforded *anti*-adduct **3c** exclusively in 95% yield (Table 4, entry 2). The use of $SnCl_4$ caused a sudden drop in the yield but the diastereoselectivity remained at the same very high level (entry 3). A similar result was obtained when the reaction was carried out in the presence of $AlCl_3$ (entry 5). The application of $ZnBr_2$ as a catalyst in this reaction resulted in exclusive formation of oxazolidinones *trans*-**4**:*cis*-**4** in the ratio 85:15 (entry 4). Adduct **3** did not form under these conditions, in contrast to the similar reactions of **1a** and **1b** with **2b**.

The extent of the asymmetric induction was determined on the basis of ^1H NMR spectra. For adducts **3** the integration of separate signals from the methyl group present in the amino acid fragment was used, whereas for oxazolidinone **4** the integration of signals derived from the methyl group present on the oxazolidinone ring was applied, and this measurement was further confirmed by integration of the signals for the methyl group of the furan moiety. Having determined the extent of the asymmetric induction, we studied its direction by establishing the configuration of the newly

Table 2. Addition of **2b** to aldehyde **1a** in the presence of Lewis acids

Entry	Lewis acid	*anti*-**3a**:*syn*-**3a**:*trans*-**4**:*cis*-**4**	Yield of **3** (%)
1	–	83:17:0:0	59
2	$BF_3{\cdot}OEt_2$	85:15:0:0	89
3	$SnCl_4$	83:17:0:0	75
4	$ZnBr_2$	84:16:0:0	61
5	$AlCl_3$	82:18:0:0	95
6	$AlEt_3$	>95:0:0:0	33

Table 3. Addition of 2-methylfuryllithium **2b** to aldehyde **1b** in the presence of Lewis acids

Entry	Lewis acid	*anti*-**3b**:*syn*-**3b**:*trans*-**4**:*cis*-**4**	Yield of *anti*-**3b** (%)	Yield of **4** (%)
1	–	>95:0:0:0	56	–
2	$BF_3{\cdot}OEt_2$	81:0:19:0	56	13
3	$SnCl_4$	83:0:17:0	56	11
4	$ZnBr_2$	83:0:17:0	51	10
5	$ZnBr_2$[a]	64:0:29:17	51	29
6	$AlCl_3$	82:0:18:0	71	16
7	$AlCl_3$[a]	83:0:17:0	49	27

[a] Reactions were carried out at −63°C

Table 4. Addition of 2-methylfuryllithium **2b** to aldehyde **1c** in the presence of Lewis acids

Entry	Lewis acid	*anti*-**3c**:*syn*-**3c**:*trans*-**4c**:*cis*-**4c**	Yield of *anti*-**3c** (%)	Yield of **4** (%)
1	–	>95:0:0:0	33	–
2	$BF_3{\cdot}OEt_2$	>95:0:0:0	95	–
3	$SnCl_4$	>95:0:0:0	64	–
4	$ZnBr_2$	0:0:85:15	–	61
5	$AlCl_3$	95:0:5:0	60	4

formed stereogenic centre. Furylcarbinol **3a** was transformed into the *O*-protected derivative **5** using triphenylsilyl chloride,[10] which afforded suitable single crystals for X-ray analysis (Fig. 1).

The X-ray crystal structure provided final proof of the structure and stereochemistry of products. Compound **3a** bears the amino and the hydroxy groups unequivocally in an *anti*-orientation, this means that the newly formed stereogenic centre has (*S*)-absolute configuration. The other diastereoisomer of **3a** possesses the opposite (*R*)-configuration. For the remaining two adducts **3b** and **3c** chemical correlations with **3a** were used as shown in Scheme 2. In order to assign the stereochemical course of the addition of 2-methylfuran **2a** to *N*-Bn,*N*-Cbz-L-alaninal **1b**, the Cbz- group in the major product **3b** was replaced with a Tosyl group[11] giving adduct *anti*-**3a**. The ^1H and ^{13}C NMR spectra

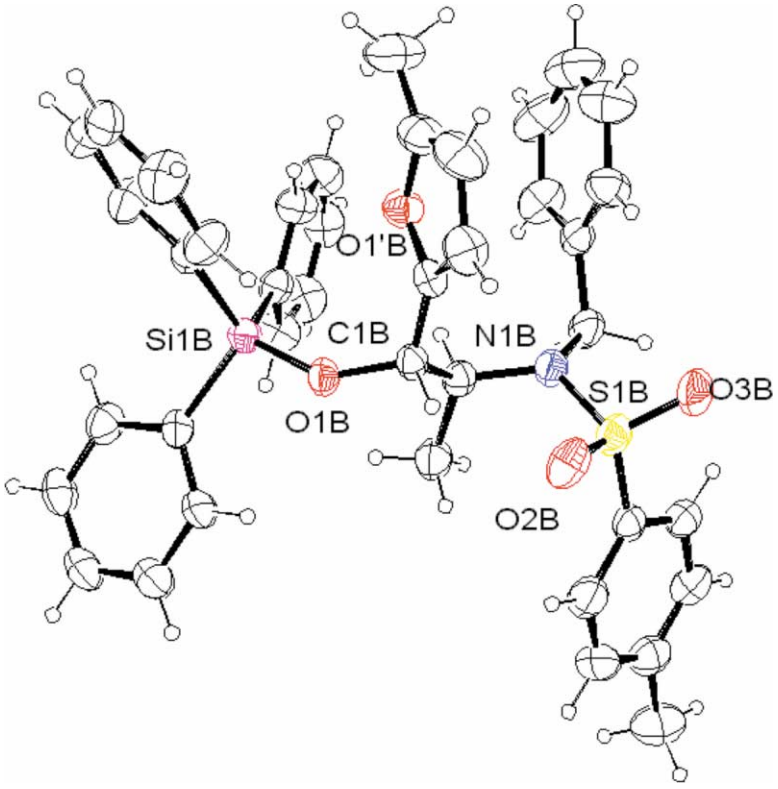
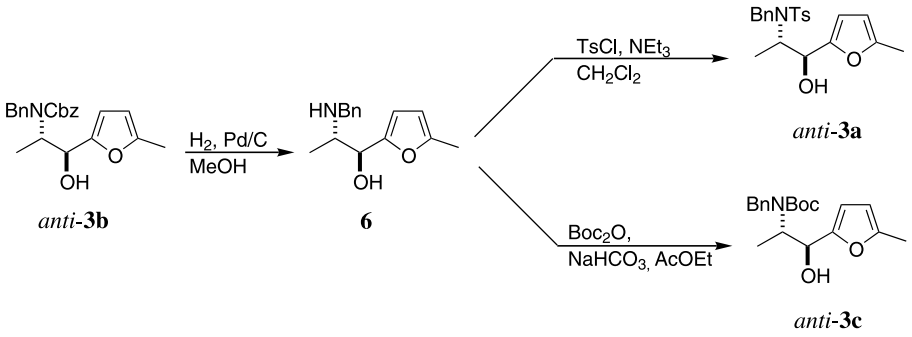


Figure 1. ORTEP diagram of the molecule **5**, showing thermal ellipsoids at 30% probability level and C1(*S*), C2(*S*) configuration of the chirality centres.



Scheme 2.

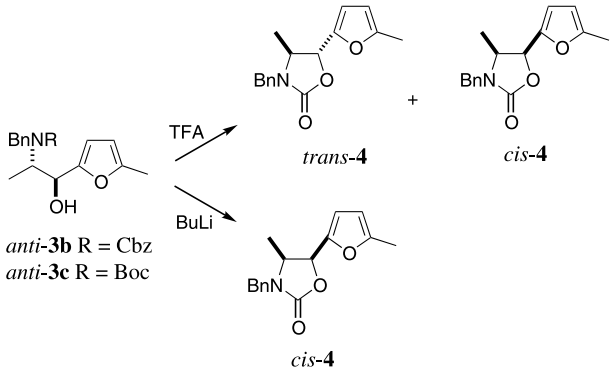
for **3a** obtained from **3b** were identical to those taken for *anti*-**3a** obtained from the reaction of **1a** with **2a**. Therefore the *anti*-configuration was assigned for compound **3b**. Hydrogenation[12] of *anti*-**3b** gave the monoprotected derivative **6**, which was further subjected to the reaction with Boc_2O[13] affording adduct **3c**. The analytical data for compound **3c** were identical with those obtained for the compound **3c** being the result of the addition of **2a** to *N*-Bn,*N*-Boc-L-alaninal **1c**. We concluded that the major product of the reaction of **2a** with **1c** possesses the amino and the hydroxy groups also in the *anti*-orientation.

In order to establish the relative configuration of oxazolidinones formed upon the addition of 2-methylfuran **2a** or its derivative **2b** to *N*-Bn,*N*-Cbz- **1b** or *N*-Bn,*N*-Boc-L-alaninal or **1c** corresponding *anti*-adducts were transformed into oxazolidinones **4** (Scheme 3). Treatment of *anti*-**3b** or *anti*-**3c** with trifluoroacetic acid led to a diastereoisomeric mixture of oxazolidinones **4** with *trans*-predominance in both cases whereas treatment of *anti*-**3b** with BuLi afforded exclusively *cis*-**4**. If we assume that inversion of the configuration at the carbon atom substituted with the hydroxy group is, as reported,[14] highly unlikely to proceed under basic conditions, it must occur under acidic conditions. The results presented suggest that the main oxazolidinone **4**, formed during the addition reaction in the presence of a Lewis acid, has the methyl and the furyl groups in a *trans*-relationship.

Furthermore, the oxazolidinones *trans*-**4** and *cis*-**4** were distinguished on the strength of NOE difference measurements (Fig. 2). The illustrated NOE measurements (11%) on the oxazolidinone ring **4** (**4** being the result of the treatment of **3b** with BuLi), established the *cis*-relationship between the newly formed hydroxyl- and adjacent methyl-bearing stereocentre, thereby securing the stereochemical assignments of compounds **4**. Hence the second diastereoisomer of **4** unequivocally has the methyl and furyl substituents in a *trans*-relationship and the formation of this compound was observed during the reactions described in this paper.

3. Conclusions

The diastereoselective additions of 2-methylfuran **2a** and its lithiated derivative **2b** to *N*,*N*-diprotected-L-alaninals **1** proceed via the Felkin–Anh transition state[15,16] and attack by a furyl reagent occurs from the less hindered side of the model, predominantly affording *anti*-furylcarbinol **3**. Regardless of the *N*-protecting group we were able to obtain the *anti*-adducts **3** with very high diastereoselectivities by choosing appropriate reaction conditions. Although it was not possible to directly reverse the stereochemical course of the addition, the trifluoroacetic acid-catalysed oxazolidinone formation reaction offers a means to access the *syn*-diastereoisomer **3**.



Scheme 3.

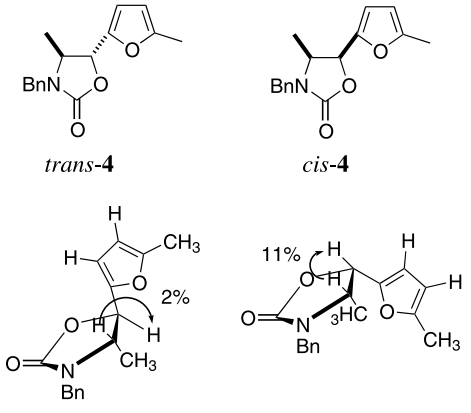


Figure 2.

4. Experimental

4.1. General remarks

All chemicals were used as received unless otherwise noted. Reagent grade solvents ($CHCl_3$, CH_2Cl_2, hexanes, AcOEt) were distilled prior to use. All reported NMR spectra were recorded with a Bruker spectrometer at 500 (^{1}H NMR) and 125 (^{13}C NMR) MHz or Varian Gemini spectrometer at 200 (^{1}H NMR) and 50 (^{13}C NMR) MHz. Chemical shifts are reported as d values relative to TMS peak defined at d = 0.00 (^{1}H NMR) or d = 0.0 (^{13}C NMR). IR spectra were obtained on a Perkin–Elmer 1640 FTIR. Mass spectra were obtained on an AMD-604 Intectra instrument using the EI or LSIMS technique. Chromatography was performed on silica (Kieselgel 60, 200–400 mesh). Optical rotations were recorded using a JASCO DIP-360 polarimeter with a thermally jacketed 10 cm cell. Melting points were determined using Kofler hot-stage apparatus and are uncorrected.

High pressure reactions were carried out in a piston–cylinder type apparatus with working volume of about 90 mL. Construction details have been reported previously.[17] Pressure was measured with a manganine coil calibrate to 0.1 kbar. Temperatures were measured with a thermocouple calibrated to 1°C.

4.2. High pressure reactions of 2-methylfuran, 2a with *N*,*N*-diprotected L-alaninals, 1

A Teflon ampoule containing a solution of **1** (0.2 mmol), 2-methylfuran **2a** (0.76 mmol) and chloroacetic acid (0.04 mmol) in dry CH_2Cl_2 (2 mL) was placed in a high-pressure vessel filled with pentane. The pressure was slowly (10 min) evaded to 20 kbar at 55°C. After 24 h the reaction mixture was cooled and decompressed. Further it was diluted with CH_2Cl_2 (4 mL) and water (5 mL) then extracted with Et_2O (2×10 mL). The combined organic extracts were washed with satd $NaHCO_{2aq}$ (10 mL), water (10 mL) and brine (10 mL), dried over $MgSO_2$. Flash chromatography (hexanes/AcOEt, gradually from 9:1 to 7:3) afforded a mixture of *anti*- and *syn*-diastereoisomers type **3** and/or oxazolidinones **4**.

4.3. Addition of 2-methylfurylllithium, 2b to L-alaninals, 1

4.3.1. Preparation of 2-methylfuryllithium, 2b. To a cold solution of 2-methylfuran (0.6 mmol) in dry THF (10 mL) was slowly added a solution of *n*-BuLi in hexane (1.6 M, 0.6 mmol) and the resulting mixture was stirred at rt for 4 h.

4.3.2. Addition of 2-methylfuryllithium, 2b to *N*,*N*-diprotected L-alaninals, 1 with no catalyst added: general procedure. A precooled solution of 2-methylfuryllithium **2b** (0.6 mmol) in dry THF (10 mL) was added dropwise to a cold solution (−78°C) of an α-amino aldehyde **1** (0.2 mmol) in dry THF (15 mL). After stirring for 0.5 h, satd NH_4Cl_{aq} (10 mL) was added and the reaction mixture was allowed to reach rt. Then, it was diluted with water (25 mL) and extracted with Et_2O (2×10 mL). The combined organic extracts were washed with brine (10 mL), HCl (1 M, 10 mL), satd $NaHCO_{2aq}$ (10 mL), and again with brine (10 mL), dried over $MgSO_2$. Flash chromatography (hexanes/AcOEt, gradually from 9:1 to 7:3) afforded a mixture of *anti*- and *syn*-diastereoisomers type **3** and/or oxazolidinones **4**.

4.3.3. Addition of 2-methylfuryllithium, 2b to *N*,*N*-diprotected L-alaninals 1 in the presence of Lewis acid: general procedure. To a cold solution (−78°C) of an α-amino aldehyde **1** (0.2 mmol) in dry THF (15 mL) was slowly added a Lewis acid [$BF_3{\cdot}OEt_2$, $AlCl_3$ or $ZnBr_2$ (0.2 mmol) or $SnCl_4$ (0.1 mmol)] and, after stirring for 1 h at rt, the solution was cooled to −78 or −63°C. The precooled solution of 2-methylfuryllithium **2b** (3 mmol) in dry THF (10 mL) was added dropwise. After stirring for 1 h, satd NH_4Cl_{aq} (10 mL) was added and the reaction mixture was allowed to reach rt. Standard work-up followed by flash chromatography (hexanes/AcOEt, gradually from 9:1 to 7: 3) afforded a mixture of *anti*- and *syn*-diastereoisomers type **3** and/or oxazolidinones **4**.

4.3.4. (1*S*,2*S*)-*N*-Benzyl-*N*-[2-(5-methylfuran)-2-yl-2-hydroxy-1-methylethyl]-4-methylbenzenesulfonamide, *anti*-3a. Yield 37%; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.12 (d, J = 6.8 Hz, 3H), 1.97 (brs, 1H), 2.23 (d, J = 1.0 Hz, 3H), 2.44 (s, 3H), 4.21 (dq, J = 3.4 Hz, J = 6.8 Hz, 1H), 4.27 (AB/2, J = 15.9 Hz, 1H), 4.57 (AB/2, J = 15.9 Hz, 1H), 4.70 (d, J = 4.4 Hz, 1H), 5.87 (dq, J = 3.1 Hz, J = 1.0 Hz, 1H), 6.03 (d, J = 3.1 Hz, 1H), 7.21–7.26 (m, 7H), 7.6 (m, 2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 12.9, 13.2, 21.0, 49.7, 58.7, 71.9, 106.7, 108.8, 127–129 (Ar), 138.4, 138.5, 143.8, 152.0, 152.6; IR (film): 1496, 2943, 3435 cm^{-1}; LSIMS (+) NBA 821 $(2M+Na)^+$, 422 $(M+Na)^+$. Anal. calcd for $C_{22}H_{25}NO_4S$: C, 66.14; H, 6.31; N, 3.51. Found: C, 66.12; H, 6.28; N, 3.49%. $[\alpha]_D^{20}$ = +19.6 (*c* 0.9, CH_2Cl_2).

4.3.5. (1*S*,2*R*)-*N*-Benzyl-*N*-[2-(5-methylfuran)-2-yl-2-hydroxy-1-methylethyl]-4-methylbenzenesulfonamide, *syn*-3a. Yield 6%; ^{1}H NMR (500 MHz, toluene-d_8, 90°C): δ 0.85 (d, J = 6.6 Hz, 3H), 1.98 (s, 3H), 2.40 (s, 3H), 2.4–2.5 (brs, 1H), 4.33 (m, 1H), 4.22 (AB/2, J = 15.9 Hz, 1H), 4.47 (AB/2, J = 15.6 Hz, 1H), 4.7 (m, 1H), 5.63 (dq, J = 3.0 Hz, J = 1.0 Hz, 1H), 5.97 (d, J = 3.0 Hz, 1H), 7.2–7.4 (m, 7H), 7.61–7.66 (m, 2H); ^{13}C NMR (125 MHz, toluene-d_8): δ 13.2, 15.9, 21.1, 49.0, 59.4, 70.1, 106.7, 108.8, 127–129 (Ar), 138.3, 138.6, 143.3, 150.9, 153.1; IR (film): 1499, 2943, 3440 cm^{-1}; LSIMS (+) NBA $C_{22}H_{25}NO_4S$ 821 $(2M+Na)^+$, 422 $(M+Na)^+$.

4.3.6. (1*S*,2*S*)-*N*-Benzyl,*N*-[2-(5-methylfuran)-2-yl-2-hydroxy-1-methylethyl]carbamic acid benzyl ester *anti*-3b. Yield 35%; ^{1}H NMR (500 MHz, toluene-d_8, 90°C): δ 1.25 (d, J = 7.0 Hz, 3H), 1.78 (brs, 1H), 1.95 (d, J = 0.9 Hz, 3H), 3.95 (dq, J = 5.5 Hz, J = 7.0 Hz, 1H), 4.21 (AB/2, J = 15.8 Hz, 1H), 4.33 (AB/2, J = 15.8 Hz, 1H), 4.89 (brs, 1H), 5.02 (m, 2H), 5.69 (dq, J = 2.0 Hz, J = 0.9 Hz, 1H), 6.1–6.6 (m, 1H), 7.0–7.1 (m, 10H); ^{13}C

NMR (125 MHz, toluene-d_8, 90°C): δ 13.3, 15.4, 28.6, 51.7, 51.9, 59.0, 59.5, 71.5, 71.9, 106.6, 107.9, 125–129 (Ar), 137.0, 151.1, 154.4, 157.0; IR (film): 1696, 2941, 3429 cm^{-1}; LSIMS (+) NBA 402 (M+Na)$^+$; HR EI $C_{23}H_{25}NO_4$ (M)$^+$ calcd 379.1784, found 379.1779; $[\alpha]_D^{20}=-25.0$ (c 1.1, CH_2Cl_2).

4.3.7. (1*S*,2*S*)-*N*-Benzyl,*N*-[2-(5-methylfuran)-2-yl-2-hydroxy-1-methylethyl]carbamic acid *tert*-butyl ester, *anti*-3c. Yield 24%; ^{1}H NMR (500 MHz, toluene-d_8, 90°C): δ 1.09 (d, $J=7.1$ Hz, 3H), 1.34 (s, 9H), 1.87 (s, 1H), 2.02 (brs, 3H), 4.13 (AB/2, $J=15.7$ Hz, 1H), 4.47 (AB/2, $J=15.7$ Hz, 1H), 4.65 (dq, $J=5.9$ Hz, $J=7.1$ Hz, 1H), 4.91 (brs, 1H), 5.72 (dq, $J=2.3$ Hz, $J=1.1$ Hz, 1H), 6.11 (d, $J=2.3$ Hz, 1H), 6.9–7.1 (m, 5H); ^{13}C NMR (125 MHz, toluene-d_8, 90°C): δ 13.3, 15.4, 28.6, 51.7, 51.9, 59.0, 59.4, 71.5, 71.9, 106.6, 107.9, 125–129 (Ar), 137.7, 151.1, 151.3, 154.0; IR (film): 1564, 1753, 2923 cm^{-1}; EI m/z 335 (M)$^+$, 271, 124, 178, 134; HR EI $C_{20}H_{27}NO_4$ (M)$^+$ calcd 345.1940, found 345.1936. Anal. calcd for $C_{20}H_{27}NO_4$: C, 69.54; H, 7.88; N, 4.06. Found C, 69.51; H, 7.92; N, 4.04%. $[\alpha]_D^{20}=+25.3$ (c 0.9, CH_2Cl_2).

4.4. Chemical correlations

4.4.1. Oxazolidinone formation under acidic conditions. To a solution of *anti*-**3b** or *anti*-**3c** (0.3 mmol) in CH_2Cl_2 (10 mL) was slowly added CF_3CO_2H (1.5 mmol). After 1 h stirring at rt, the reaction mixture was diluted with water (5 mL) and extracted with Et_2O (2×10 mL). The combined organic phases were washed with brine (10 mL), dried over $MgSO_4$. Flash chromatography (hexanes/AcOEt, gradually from 9:1 to 7:3) afforded a mixture of oxazolidinones **4**.

4.4.2. Oxazolidinone formation using BuLi. To a precooled (−20°C) solution of **3b** (0.05 mmol) in dry THF (10 mL) was slowly added a solution of BuLi in hexane (1.6 M, 0.06 mmol). The reaction mixture was allowed to reach rt and was stirred at that temperature for 1 h. The mixture was diluted with water (25 mL) and extracted with Et_2O (2×10 mL). The combined organic phases were washed with brine (10 mL), HCl (1 M, 10 mL), satd $NaHCO_{3aq}$ (10 mL) and again with brine (10 mL) and dried over $MgSO_4$. Flash chromatography (hexanes/AcOEt, gradually from 9:1 to 7:3) afforded a mixture of oxazolidinones *cis*-**4** in the yield of 96%.

4.4.3. (4*S*,5*R*)-3-Benzyl-4-methyl-5-(5-methylfuran-2-yl)oxazolidinon-2-one, *trans*-4. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.21 (d, $J=7.3$ Hz, 3H), 2.23 (d, $J=0.8$ Hz, 3H), 4.17 (AB/2, $J=15.3$ Hz, 1H), 4.82 (AB/2, $J=15.3$ Hz, 1H), 4.85 (d, $J=7.3$ Hz, 2H), 5.91 (dq, $J=3.2$ Hz, $J=0.8$ Hz, 1H), 6.22 (d, $J=3.2$ Hz, 1H), 7.32 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.5, 17.6, 46.0, 54.4, 76.5, 106.5, 111.3, 127–128 (Ar), 135.9, 147.2, 153.9, 157.3; IR (film): 1565, 1755, 2923 cm^{-1}; EI m/z 271 (M)$^+$, 136, 122, 111, 91; HR EI $C_{16}H_{17}NO_3$ (M)$^+$ calcd 271.1208, found 271.1209; $[\alpha]_D^{20}=-144.5$ (c 1.3, CH_2Cl_2).

4.4.4. (4*S*,5*S*)-3-Benzyl-4-methyl-5-(5-methylfuran-2-yl)oxazolidinon-2-one, *cis*-4. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.95 (d, $J=7.3$ Hz, 3H), 2.25 (d, $J=0.8$ Hz, 3H), 4.17 (AB/2, $J=15.3$ Hz, 1H), 4.83 (AB/2, $J=15.3$ Hz, 1H), 5.36 (d, $J=8.4$ Hz, 2H), 5.91 (dq, $J=3.2$ Hz, $J=1.0$ Hz, 1H), 6.25 (d, $J=3.2$ Hz, 1H), 7.4–7.3 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.0, 14.0, 44.9, 53.8, 73.0, 106.2, 110.9, 127–128 (Ar), 136.0, 146.8, 153.2, 157.7; IR (film): 1564, 1753, 2923 cm^{-1}; EI m/z 271 (M)$^+$, 136, 122, 111, 91; HR EI $C_{16}H_{17}NO_3$ (M)$^+$ calcd 271.1208, found 271.1205; $[\alpha]_D^{20}=+40.5$ (c 0.5, CH_2Cl_2).

4.5. (1*S*,2*S*)-*N*-Benzyl-*N*-[2-(5-methylfuran-2-yl)-2-triphenylsilanyloxy-1-methylethyl]-4-methylbenzenesulfonamide, 5

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.37 (d, $J=6.9$ Hz, 3H), 1.90 (s, 3H), 2.00 (s, 3H), 3.92 (AB/2, $J=15.7$ Hz, 1H), 4.43 (AB/2, $J=15.7$ Hz, 1H), 4.63 (dq, $J=8.4$ Hz, $J=6.9$ Hz, 1H), 4.91 (d, $J=8.4$ Hz, 1H), 5.53 (dq, $J=3.1$ Hz, $J=1.0$ Hz, 1H), 5.75 (d, $J=3.1$ Hz, 1H), 6.9–7.2 (m, 20H), 7.55 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.2, 16.2, 20.1, 49.4, 58.7, 72.3, 106.5, 110.7, 140–127 (Ar), 151.2, 152.1; IR (KBr): 1114, 1150, 1338, 3068 cm^{-1}; LSIMS (+) NBA 680 (M+Na)$^+$; mp = 135–136°C $[\alpha]_D^{20}=-39.3$ (c 1.1, CH_2Cl_2).

4.5.1. X-Ray crystallography of compound 5. X-Ray diffraction measurement of the suitable crystal compound **5** was carried out with a Nonius MACH3 diffractometer using graphite monochromated Cu Kα radiation (see Table 5). Intensities were collected at room temperature using ω–2θ scan technique. Intensity of the three control reflections measured every 200 reflections showed no loss of intensity. The data were corrected for Lorentz and polarisation factors. The structure was solved by direct methods[18] [xray 1] and refined by a full-matrix least-squares procedure with the use of the SHELXL program[19] [xray 2]. The non-hydrogen atoms were refined anisotropically, whereas H-atoms were placed at their calculated positions and

Table 5. Crystallographic data and refinement details for **5**

Empirical formula	$C_{40}H_{39}NO_4SSi$
Formula weight	657.87
Wavelength (Å)	1.54178
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	
a (Å)	10.819(2)
b (Å)	12.065(2)
c (Å)	54.622(5)
Volume (Å^3)	7130(2)
Z	8
Absorption coefficient (mm^{-1})	1.453
Reflections collected	7896
Independent reflections	7130 [R(int) = 0.0278]
Data/restrains/parameters	7130/0/848
Final R indices [$I>2\sigma(I)$]	$R_1=0.0448$, $wR_2=0.1173$
Absolute structure parameter	0.01(2)

their thermal parameters were set at the level 20% higher that for the parent atoms. Crystallographic data for **5** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbered CCDC 191344. Copies of the data can be obtained free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1233-336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.6. (2*S*)-(*N*-Benzylamino)-(1*S*)-(5-methylfuran-2-yl)propan-1-ol, 6

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.03 (d, $J=6.4$ Hz, 3H), 2.25 (d, $J=0.9$ Hz, 3H), 2.52 (brs, 1H), 3.05 (m, 1H), 3.75 (AB/2, $J=13.2$ Hz, 1H), 3.93 (AB/2, $J=13.2$ Hz, 1H), 4.58 (d, $J=1.6$ Hz, 1H), 4.69 (brs, 1H), 5.89 (dq, $J=3.0$ Hz, $J=0.9$ Hz, 1H), 6.31 (d, $J=3.0$ Hz, 1H), 7.2–7.5 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 13.9, 17.8, 45.9, 54.4, 106.6, 111.3, 127–129 (Ar), 135.8, 147.1, 153.7, 157.3; IR (film): 1496, 2943, 3435 cm^{-1}; LSIMS (+) NBA 268 $(M+Na)^+$ 246 $(M+H)^+$, 271, 124, 178, 134; HR LSIMS $C_{15}H_{19}NO_2$ $(M+H)^+$ calcd 246.1494, found 246.1494.

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