Diastereoselective Imino–Aldol Condensation of Chiral 3-(*p*-Tolylsulfinyl)-2-furaldimine and Ester Enolates

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(S_s)-3-(*p*-Tolylsufinyl)-2-furaldimine was synthesized, and condensation of the chiral furaldimine with lithium ester enolates has been examined. The product distribution of the reaction is dependent upon reaction conditions and on the kind of the substituent placed on the esters. Disubstituted ester enolate resulted in the exclusive formation of (4*R*)-β-lactam, while unsubstituted, *tert*-butyl ester enolate preferentially gave (3*R*)-β-amino ester. With the monosubstituted ester enolates, the condensation afforded (4*R*)-β-lactams and/or (3*R*)-β-amino esters as major products. This method has been applied to an efficient route to chiral furyl β-lactams.

Key words asymmetric condensation; chiral furaldimine; sulfoxide; ester enolate; β-lactam; β-amino ester

The biological importance of β-lactams as antibiotics has stimulated the development of efficient procedures for the preparation of this class of compounds. Of the synthetic routes to β-lactams that have been reported, Lewis acid-promoted[1—3] and catalyzed[4—11] condensations of imines with silyl ketene acetals and imino–aldol condensations with ester enolates are powerful methods which involve the efficient construction of stereogenic centers of the β-lactam moiety.[12—14] Chiral versions of these condensations have also been devised by the use of imines with a chiral auxiliary,[1—3,15—29] chiral ester enolate derivatives,[30—36] and chiral Lewis acids.[37—41] In the course of our studies on remote asymmetric induction using chiral sulfoxides, we previously reported the lanthanoid triflate-catalyzed Mukaiyama aldol reaction of sulfinyl aldehyde **1** with silyl ketene acetals.[42] Highly remote stereocontrol of **1** in this reaction led us to examine an enantioselective route to β-lactams by diastereoselective condensation of an aldimine **2** derived from **1** with silyl ketene acetals as well as enolates. We would like to report the details of this condensation using the sulfinyl furaldimine **2**.[43]

Initial experiments were performed with a typical silyl ketene acetal **3a** in the presence of a lanthanoid triflate, which is found to be effective for the aldol condensation of the aldehyde **1**.[42] In fact, the reaction using $Yb(OTf)_3$ proceeded smoothly; diastereoisomeric β-amino esters **4a** and **6a** were produced in a ratio of 1 : 1 (Table 1, entry 1).[44] The use of other lanthanoid triflates did not improve the diastereoselectivity. The relative stereochemistry of the two products **4a** and **6a** was not determined at this stage; however, the configuration at the C(3) position was later determined (*vide infra*). We then turned our attention to using an ester enolate

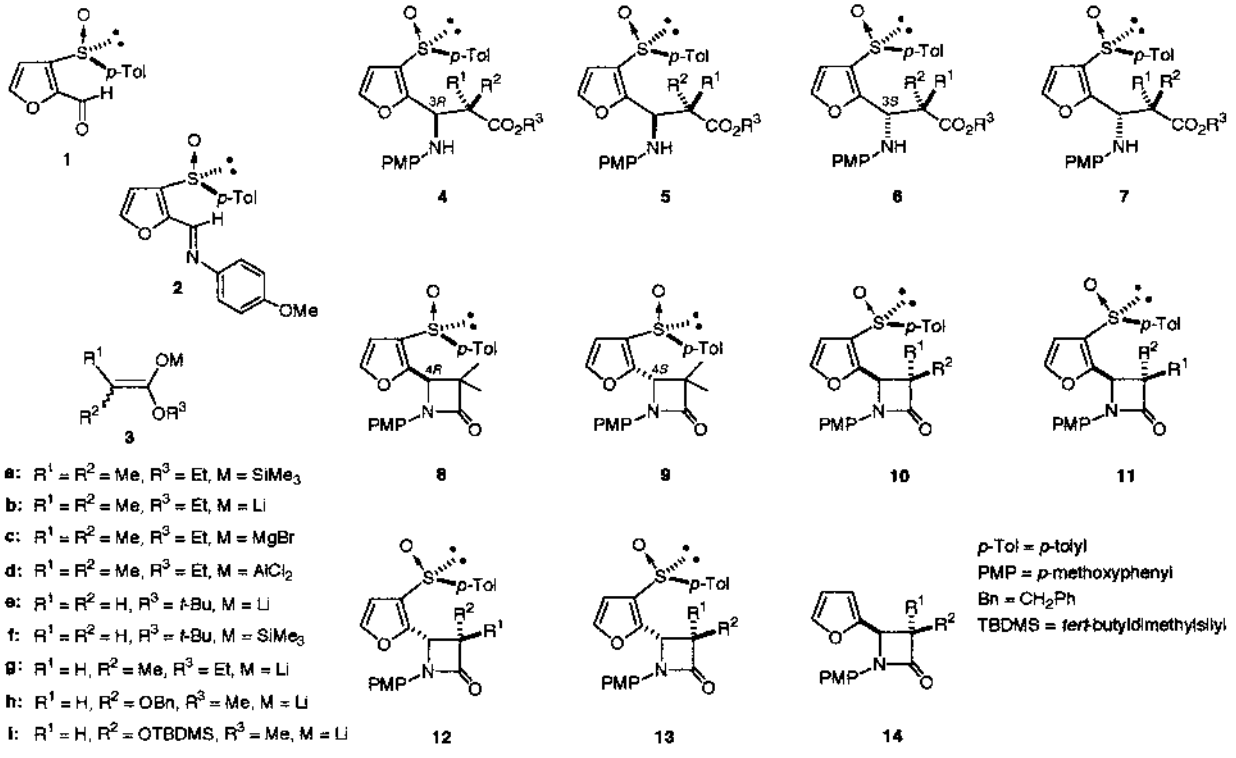

Chart 1

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Table 1. Condensation of **2** with Un- and Disubstituted Ester Enolates **3**[a)]

Entry	3	(eq used)	Solvent	Time/h	Yield/%	Product ratio	De/%
1	**3a**[b)]	(2.0)	THF	15	98	50 : 50 (**4a** : **6a**)	0
2	**3b**	(1.5)	THF	1	67	95.5 : 4.5 (**8** : **9**)[e)]	91
3	**3b**	(1.5)	Et_2O	1	85	98.5 : 1.5 (**8** : **9**)[e)]	97
4	**3b**	(4.0)	THF	1	84	95.5 : 4.5 (**8** : **9**)	91
5	**3b**	(4.0)	Et_2O	1	99	97.5 : 2.5 (**8** : **9**)	95
6	**3c**[c)]	(4.0)	Et_2O	1	70	94 : 6 (**8** : **9**)	88
7	**3d**[d)]	(4.0)	THF	1	93	90 : 10 (**8** : **9**)	80
8	**3e**	(1.5)	THF	1	99	98 : 2 (**4e** : **6e**)	96
9	**3f**[b)]	(2.0)	THF	12	<5	—	—

a) Reaction was carried out at −78 °C for 15 min and then the reaction mixture was allowed to return to room temperature over a period of 45 min, except for entries 1 and 9. *b*) The reaction was conducted at room temperature in the presence of 0.2 eq of $Yb(OTf)_3$ as a promoter. *c*) Prepared by transmetallation of the preformed lithium ester enolate with $MgBr_2 \cdot Et_2O$ at −78 °C. *d*) Prepared by treatment of the lithium ester enolate with $AlCl_3$ at −78 °C. *e*) Small amounts of the *β*-amino esters **4a** and **6a** were also produced in variable yields.

3b, instead of silyl ketene acetals, for the reaction. In contrast to the reaction with **3a**, the *β*-amino esters were not produced in the reaction, whereas *β*-lactams **8** and **9** were obtained exclusively. The metal effect of the addition reaction of **2** is also listed in Table 1, which shows that the lithium enolate **3b** is superior to other metal enolates **3c** and **3d**[31,45,46)] for both diastereoselectivity and yield. Although the reaction was carried out by the use of Et_2O or tetrahydrofuran (THF) as a solvent,[47)] the use of Et_2O for the reaction of **3d**—**3f** gave no better results than THF. Attempts to use other metal enolates[48—52)] derived from **3b** were unsuccessful, and resulted in the recovery of starting material **2**.

Predominant formation of the *β*-lactams reflects that the ring closure reaction proceeds at a greater rate on geminal (*i.e.* dimethyl) substitution.[53,54)] It is also probable that the product distribution (*β*-lactam *vs.* *β*-amino ester) depends on the reaction conditions (amounts of enolate and/or the solvent used) and the type of enolate. In some case where the reaction was carried out with less than 2 eq of the lithium enolate (entries 2 and 3), the reaction gave not only *β*-lactams but also *β*-amino esters. However, the use of more than 2 eq of the enolate resulted in the exclusive formation of *β*-lactams and in good yield.[55)] From the viewpoint of reproducibility for *β*-lactam formation, the use of 4 eq of the lithium enolate gave optimum yields.

Since it is difficult to determine the stereochemistry at the C(4) position of **8** and **9** spectroscopically, the stereochemical assignment of the major azetidinone **8** was confirmed by single crystal X-ray analysis (Fig. 1, see Experimental). At this stage, the configuration of the C(3) position of the *β*-amino ester **4a** was confirmed by the transformation the *β*-lactam **8** into **4a** (see Experimental).

When the reaction was carried out with an unsubstituted lithium ester enolate **3e** under similar conditions, the (3*R*)-*β*-amino ester **4e** was obtained exclusively, accompanied by a small amount of (3*S*)-isomer **6e** (96% diastereoisomeric excess (de)), in quantitative yield. Stereochemical assignments are tentatively determined by analogy with the results obtained with **2** and **3a**. Attempts for the reaction of **3f** were unsuccessful, and resulted in the mass recovery of the starting material. This result reflects that some silyl ketene acetals readily isomerize to the *α*-silyl esters by a lanthanoid triflate prior to the reaction.[56)]

With the accessibility of monosubstituted lithium ester enolates, we next examined the condensation of **2** with **3g**—**i**

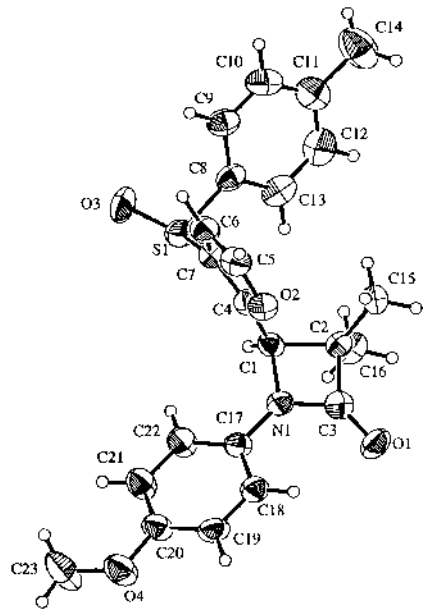

Fig. 1. X-Ray Crystal Structure of Compound **8**

(Table 2). With the enolates **3g**—**i**, THF was used as a solvent, since when the reaction was carried out in Et_2O, *β*-amino esters were also produced in variable yields. Reactions carried out with more than 2 eq of the enolate gave better yields (entry 1 *vs.* entry 2 in Table 2). Condensation with the (*E*)-enolate enriched **3g** gave rise to *syn*-*β*-lactam **10g** and *anti*-*β*-lactam **11g** as the major isomers, respectively. In contrast, with the enolate **3g** {(*Z*)-isomer enriched}, *syn*-*β*-amino ester **4g** and *anti*-*β*-amino ester **5g** were produced as the major products (Table 2, entry 3). Under the conditions by the use of (*Z*)-isomer enriched enolate **3g** generated in the presence of hexamethylphosphoramide (HMPA), the ratio of *syn*- and *anti*-esters was reversed, preferentially affording the *anti*-*β*-amino ester **5g**.[57,58)]

The major *syn*-*β*-lactam **10g** was isolated in isomerically pure form, and the stereochemistry was unequivocally established by single crystal X-ray analysis (Fig. 2, see Experimental). The *anti* relationship of the *β*-lactam **11g** was assumed by the vicinal coupling constant between C(3) and C(4) protons ($J_{syn} > J_{anti}$)[1—36)] in the ^{1}H-NMR spectrum. Finally, the absolute stereochemistry was confirmed by the transformation of **10g** into **11g** by an epimerization experi-

Table 2. Condensation of **2** with Lithium Enolates **3g**—**3i**[a)]

Entry	Enolate	(eq used)	Product ratio		De/% of amino esters		De/% of β-lactams		Total yield/%
			4 : **5** : **6** : **7**	**10** : **11** : **12** : **13**	*syn*	*anti*	*syn*	*anti*	
1	**3g**[d)]	(1.5)	—	25.7 : 23.3 : 1.0 : 3.4	—		93	75	72[b)]
2	**3g**[d)]	(4.0)	—	17.0 : 7.7 : 1.0 : 1.3	—		89	71	89[b)]
3	**3g**[e)]	(4.0)	5.0 : 10.7 : 1.0 : 1.8	—	67	71	—		74[c)]
4	**3h**[d)]	(1.5)	—	9.7 : 21.9 : 1.7 : 1.0	—		70	91	67[b)]
5	**3i**[d)]	(1.5)	109.3 : 18.3 : <0.1 : <0.1	2.8 : 14.4 : 0.2 : 1.0	>98	>98	85	87	89

a) The reaction was conducted at −78 °C (0.5—1.5 h) in THF as solvent, then the mixture was allowed to warm up to the temperature (indicated in Experimental section). *b*) Small amounts of the corresponding β-amino esters **4g**—**7g** were also produced in variable yields. The ratio of the β-amino esters was not determined. *c*) The reaction was carried out in the presence of HMPA. Small amounts of the β-lactams **10g**—**13g** were also produced in variable yields. The product ratio of β-lactams was not determined. *d*) (*E*)-Enolate predominantly formed. *e*) (*Z*)-Enolate predominantly formed.

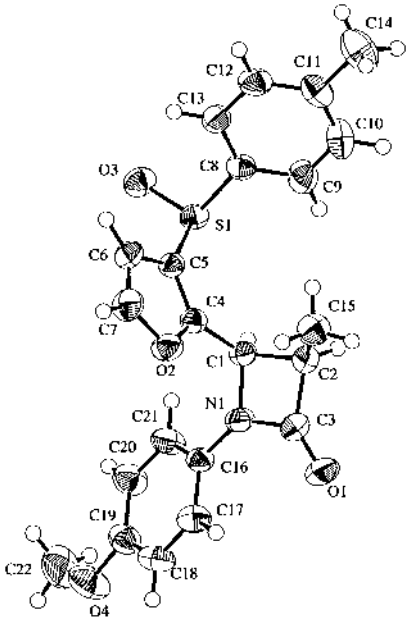

Fig. 2. X-Ray Crystal Structure of Compound (±)-**10g**

ment using the usual method.[4,5)]

We have also examined the reaction of the enolates bearing an alkoxy substituent. It was reported that the lithium enolate of (benzyloxy)acetate esters,[59—63)] such as **3h**, is less reactive toward a certain aldimine.[64)] The reaction of **3h** and **2** proceeded smoothly to give *syn*-β-lactam **10h** and *anti*-β-lactam **11h** as major products, with good (for *anti*-β-lactams) to excellent (for *syn*-β-lactams) diastereoselectivities. In this case, the product ratio of *syn*- and *anti*-β-lactams was reversed. With the silyloxy enolate **3i** {(*E*)-enolate enriched[65)]}, (3*R*)-amino esters **4i** and **5i** were produced as the major *syn*- and *anti*-products, accompanied by small amounts of (3*R*)-β-lactams **10i** and **11i**. The relative stereochemistry at the C(2) and C(3) positions in **4i**—**7i** was assumed by the vicinal coupling constant in the ^{1}H-NMR spectrum.[66)] The relationship of the esters **4i** and **5i** with the β-lactams **10i** and **11i** was confirmed by chemical correlation: the amino esters **4i** and **5i** were cyclized, respectively, into **10i** and **11i** upon treatment with lithium hexamethyldisilazide.[12—14,30—36)]

Although the detailed reaction mechanism is not clear, it is likely that some facts obtained are consistent with the stereochemical outcome which involves a Zimmerman–Traxler transition state model[67,68)] (Fig. 3). It is assumed that S→O is *trans* and coplanar to C=C of the furan ring in the reacting conformer (A), as predicted by the X-ray crystal structure of the products. With the (*E*)-enolates, a chelating model A would be favored over transition state (B). The six-membered chelate B should not be preferentially attained by a severe steric repulsion of the alkoxy group with the bulky *p*-tolyl substituent. The reaction of **3g** and **3i** thereby gave, respectively, the (4*R*)-*syn*-β-lactam **10g** and the (3*R*)-*syn*-ester **4i** as major isomers. It is probable that the *anti*-major products **11g** and **5i** were also produced from the (*Z*)-enolates of **3g** and **3i** through a transition state (C). According to this hypothesis, the reaction of **3h**, which can be considered to form (*E*)-enolate predominantly,[59)] seemed to afford the *syn*-β-lactam **10h** as the major product in preference to the *anti*-β-lactam; however, (4*R*)-*anti*-β-lactam **11h** was produced predominantly. This fact suggests that (*Z*)-enolate **3h** would react faster than (*E*)-enolate **3h** *via* the transition state C.[15)] In this case, the enolate geometry, as well as epimerization during the reaction, appear to play roles in determining the product distribution. On the other hand, when the reaction was carried out with the enolate **3g** generated in the presence of HMPA, the reaction was stereochemically complex, *anti*-products being produced predominantly (Table 2, entry 3). Since it is difficult to interpret the effects of HMPA on the structure of enolates,[69,70)] the reversal in selectivity of (*E*)- and (*Z*)-enolate condensations remains unexplained. It is likely that the (*Z*)-enolate **3g** reacts with **2** to produce *anti*-product **5g** preferentially *via* a certain open transition state.[69,70)] A strongly coordinating solvent, HMPA, should inhibit the effective chelation in the transition state, and, in some case, promote epimerization[30,57,58)]; therefore, the reaction in the presence of this additive resulted in lower levels of diastereoselectivity (≈70% de's).

Having successfully obtained chiral sulfinyl β-lactams, the usefulness of these stereoselective syntheses was exemplified by easy entry to the optically active furyl β-lactam **14a**. This β-lactam has been synthesized by aldimine–boron enolate condensation in the presence of a chiral amino alcohol; however, the optical yield is unsatisfactory.[48)] We prepared optically active **14a** with high enantiomeric excess by desulfinylation of the sulfinyl β-lactam **8a** with Raney nickel in good yield. In a similar manner, the furyl β-lactam **14g** was also obtained from **10g**. Other optically active furyl β-lactams would be obtained by a similar reaction sequence. This procedure would be of value for the preparation of chiral β-lactams containing a 4-furylazetidinone moiety which is a latent carbacephem building block.[71)]

In summary, chirally functionalized, sulfinyl β-lactams

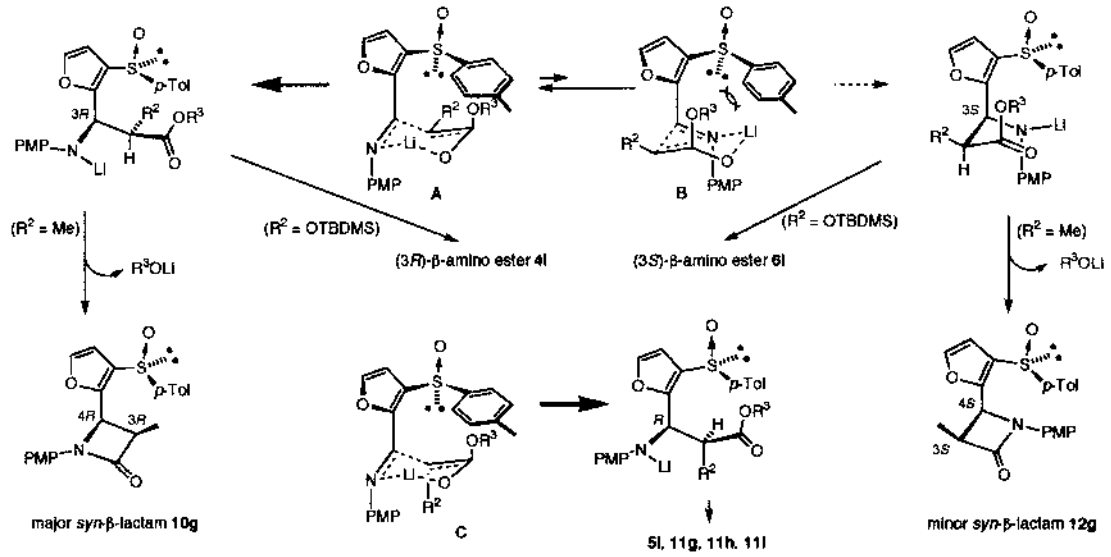

Fig. 3

were synthesized from sulfinyl imine and lithium enolates with high diastereoselectivity and in excellent yield. In sharp contrast to 1,2- or 1,3-asymmetric inductions in imine–ester enolate condensations reported previously, our results revealed that 1,4-stereocontrol (=remote asymmetric induction) has been achieved by the use of the sulfinyl furaldimine **2**.

Experimental

Melting points were determined with a Yanaco micro melting point apparatus and are uncorrected. IR spectra were recorded in $CHCl_3$ solution on a Perkin-Elmer Spectrum One FT-IR spectrometer. ^{1}H-NMR spectra were measured in $CDCl_3$ solution with tetramethylsilane as an internal standard, on a JEOL JNM-GX270 (270 MHz) or EX-400 (400 MHz) spectrometer. The following abbreviations are used: singlet (s), doublet (d), triplet (t), doublet of doublets (dd), doublet of triplets (dt), doublet of quartets (dq), doublet of multiplets (dm), multiplet (m) and broad (br). *J*-Values are given in Hz. Mass spectra were taken with a JEOL JMS-D300 or JMS-SX102A spectrometer. Optical rotations were recorded on a JASCO DIP-360 digital polarimeter. The symbol S_s expresses that the absolute configuration of the sulfinyl center is *S*. Extracts were dried over anhydrous $MgSO_4$ before the evaporation of solvents on a rotary evaporator under reduced pressure. Dry THF and diethyl ether were freshly distilled from sodium benzophenone ketyl prior to use. *m*-CPBA was used after purification by washing with pH 7.5 phosphate buffer, according to a previously reported method.[72] TLC analyses were performed using Merck precoated Silica $60F_{254}$ plates (0.2 mm). Column chromatography was carried out on Merck silica (70—230 mesh) or Merck silica (230—400 mesh). Raney nickel was purchased from Acros Organics and used for reaction after washing with EtOH by decantation several times.

(S_s)-(*N*-*p*-Methoxyphenyl)-3-(*p*-tolylsulfinyl)-2-furaldimine (2) To a vigorously stirred suspension of **1**[42] (1.97 g, 8.4 mmol) and anhydrous $MgSO_4$ (4.2 g) in dry benzene (75 ml) was added *p*-anisidine (2.08 g, 16.8 mmol) in one portion at room temperature. After being stirred overnight, the reaction mixture was filtered off with the aid of a short pad of Celite. The filtrate was concentrated under reduced pressure, and the crude product was purified by flash column chromatography on silica (hexane–AcOEt 2 : 1) to give **2** (2.21 g, 77%), which solidified on standing in a refrigerator. mp 60—61 °C (Et_2O); $[\alpha]_D^{24}$ −443.9° (c=1.0, $CHCl_3$); ^{1}H-NMR (270 MHz) δ: 2.40 (3H, s, Me), 3.85 (3H, s, OMe), 6.65 (1H, d, J=1.8, furan), 6.95 (2H, br d, J=8.9, *p*-methoxyphenyl), 7.30 (2H, d, J=8.2, *p*-tolyl), 7.33 (2H, br d, J=8.9, *p*-methoxyphenyl), 7.53 (1H, d, J=1.8, furan), 7.65 (2H, d, J=8.2, *p*-tolyl), 8.67 (1H, s, CH=N). IR cm^{-1} ($CHCl_3$) 1625 (CH=N), 1040 (S→O). Electron impact (EI)-MS *m*/*z* 339 (M^+), 323, 322, 245, 78, 63. *Anal.* Calcd for $C_{19}H_{17}NO_3S$: C, 67.24; H, 5.05; N, 4.13. Found C, 67.38; H, 5.07; N, 4.04. EI-HR-MS Calcd. 339.0929. Found 339.0922.

Ethyl (3*R*/3*S*)-3-(*N*-*p*-Methoxyphenylamino)-2,2-dimethyl-3-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]propanoate (4a=5a and 6a=7a) (Table 1, Entry 1) To a suspension of $Yb(OTf)_3$ (11 mg, 17.7 mmol) in dry THF (0.5 ml) was added **2** (30 mg, 88.4 mmol) at room temperature under nitrogen. After 15 min, the silyl ketene acetal **3a**[73] (33 mg, 0.17 mol) in dry THF (0.5 ml) was added dropwise *via* syringe. After being stirred for 15 h at room temperature, the reaction mixture was quenched with H_2O (10 ml). The aqueous layer was extracted with EtOAc (20 ml×2), and the combined organic phase was washed with brine, dried, and concentrated. The crude product was purified by column chromatography on silica (hexane–EtOAc 2 : 1) to give an inseparable mixture of **4a** and **6a** (39 mg, 98%) in a ratio of 1 : 1 as a colorless oil: IR cm^{-1} ($CHCl_3$) 1726 (C=O), 1039 (S→O). EI-MS *m*/*z* 455 (M^+), 439, 340, 324. *Anal.* Calcd for $C_{25}H_{29}NO_5S$: C, 65.92; H, 6.42; N, 3.08. Found C, 65.76; H, 6.41; N, 3.07. EI-HR-MS Calcd. 455.1767. Found 455.1761. **4a**: ^{1}H-NMR (270 MHz) δ 1.23 (3H, t, J=7.1, Me), 1.33 (3H, s, Me), 1.40 (3H, s, Me), 2.34 (3H, s, Me), 3.73 (3H, s, OMe), 4.21 (2H, q, J=7.1, CH_2), 4.5 (1H, br, NH), 5.07 (1H, br s, CH), 6.12 (1H, d, J=1.8, furan), 6.58 (2H, dt, J=8.7, 2.2, *p*-methoxyphenyl), 6.74 (2H, dt, J=8.7, 2.2, *p*-methoxyphenyl), 7.09 (2H, d, J=8.1, *p*-tolyl), 7.14 (2H, d, J=8.1, *p*-tolyl), 7.27 (1H, d, J=1.8, furan). **6a**: ^{1}H-NMR (270 MHz) δ: 1.28 (3H, t, J=7.1, Me), 1.40 (6H, s, Me×2), 2.35 (3H, s, Me), 3.72 (3H, s, OMe), 4.22 (2H, q, J=7.1, CH_2), 4.5 (1H, br, NH), 5.07 (1H, br s, CH), 6.12 (1H, d, J=1.8, furan), 6.58 (2H, dt, J=8.7, 2.2, *p*-methoxyphenyl), 6.74 (2H, dt, J=8.7, 2.2, *p*-methoxyphenyl), 7.03 (2H, d, J=8.1, *p*-tolyl), 7.14 (2H, d, J=8.1, *p*-tolyl), 7. 28 (1H, d, J=1.8, furan).

The absolute stereochemistry at the C(3) position of **4a** was determined by the transformation of **8** into **4a** by ring-cleavage followed by esterification of the resulting acid, as follows: A solution of **8** (55.7 mg, 0.14 mmol) in dry EtOH (2 ml) was treated with a NaOEt solution (4.2 ml, 0.42 mmol, 1 mol dm^{-3} in EtOH) at room temperature for 1 h. Although the formation of a small amount of **4a** was detected on TLC, the corresponding acid was predominantly produced. The crude acid (38.3 mg, 0.084 mmol) obtained was thus treated with *N*,*N*′-dicyclohexylcarbodiimide and 4-(*N*,*N*-dimethylamino)pyridine in dry EtOH, affording **4a** (16.4 mg, 39%), whose spectroscopic data were in good agreement with those of **4a** obtained by the reaction of **2** and **3a**.

Typical Procedure for the Preparation of β-Lactams (Table 1, Entry 5) (4*R*)-1-(*p*-Methoxyphenyl)-3,3-dimethyl-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (**8**): To a solution of lithium diisopropylamide [prepared from diisopropylamine (0.08 ml, 0.59 mmol) and *n*-BuLi (0.396 ml, 0.59 mmol, 1.50 mol dm^{-3} in hexane)] in dry Et_2O (2 ml) at −78 °C was added ethyl isobutyrate (0.08 ml, 0.59 mmol) *via* syringe. After being stirred for 0.5 h at −78 °C, a solution of **2** (50.4 mg, 0.15 mmol) in dry Et_2O (3 ml) was slowly added. After being stirred for 1 h at the same temperature, the mixture was slowly warmed up to room temperature (during 45 min). The reaction mixture was then quenched with 3% HCl (5 ml), and the aqueous layer was extracted with EtOAc (7 ml×3). The combined organic phase was washed with brine, dried, and concentrated. The crude product was purified

by column chromatography on silica (hexane–EtOAc 7 : 1→1 : 1) to give a mixture of **8** and **9** (59.7 mg, 99%) as a solid. **8**: mp 150—152 °C (Et_2O); $[\alpha]_D^{23}$ −30.9° (c=1.3, $CHCl_3$); ^{1}H-NMR (270 MHz) δ: 1.12 (3H, s, Me), 1.54 (3H, s, Me), 2.41 (3H, s, Me), 3.76 (3H, s, OMe), 5.22 (1H, s, CH), 6.46 (1H, d, J=1.8, furan), 6.79 (2H, dt, J=8.9, 2.2, *p*-methoxyphenyl), 7.14 (2H, dt, J=8.9, 2.2, *p*-methoxyphenyl), 7.31 (2H, d, J=8.1, *p*-tolyl), 7.36 (1H, d, J=1.8, furan), 7.42 (2H, d, J=8.1, *p*-tolyl). IR cm^{-1} ($CHCl_3$) 1740 (C=O), 1030 (S→O). EI-MS m/z 409 (M^+), 393, 392, 323, 244, 201, 149. *Anal.* Calcd for $C_{23}H_{23}NO_4S$: C, 67.46; H, 5.66; N, 3.42. Found C, 67.39; H, 5.72; N, 3.56. The minor isomer **9** was inseparable from **8** by column chromatography. The product ratio (97.5 : 2.5, 95% de) was estimated by the integration of the geminal methyl signals of **8** (δ 1.12 and 1.54) and **9** (δ 0.99 and 1.43) in the ^{1}H-NMR spectrum.

An analytical sample of **8** for X-ray analysis was obtained by recrystallization from Et_2O. X-Ray measurement was performed on a Rigaku AFC5R diffractometer with Cu–$K\alpha$ radiation. Crystal data for **8**: $C_{23}H_{23}NO_4S$, M=409.5, monoclinic, space group $P2_1/c$ (No 14), a=11.072(4) Å, b=9.032(5) Å, c=21.936(5) Å, β=101.95(3)°, V=2146(1) Å^3, D_{calc}=1.267 g cm^{-3}, Z=4; Number of reflections observed ($I>3\sigma(I)$)=1901, R=0.056, R_w=0.094. Further details of the X-ray structure data are available on request from the Cambridge Crystallographic Data Centre (deposition number CCDC 177885).

(4*S*)-1-(*p*-Methoxyphenyl)-3,3-dimethyl-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (**9**): ^{1}H-NMR (270 MHz) δ: 0.99 (3H, s, Me), 1.43 (3H, s, Me), 2.43 (3H, s, Me), 3.76 (3H, s, OMe), 5.22 (1H, s, CH), 6.40 (1H, d, J=1.8, furan), 6.87 (2H, dm, J=8.8, *p*-methoxyphenyl), 7.21 (2H, dm, J=8.8, *p*-methoxyphenyl), 7.25 (2H, d, J=8.0, *p*-tolyl), 7.34 (1H, d, J=1.8, furan), 7.56 (2H, d, J=8.1, *p*-tolyl).

For determination of the diastereoisomeric relationship between **8** and **9**, an analytical sample was independently prepared by the following sequence. Treatment of essentially pure **8** with Zn–$TiCl_4$[74] afforded the corresponding sulfide (77% yield), which was oxidized with *m*-CPBA to produce a mixture of **8** and *ent*-**9** (=the enantiomer of **9**) in a rough ratio of 1 : 1 (78% yield). Since the assignment of all ^{1}H-NMR signals of a 1 : 1 mixture of **8** and *ent*-**9** were applicable to those of the product mixture of **8** and **9**, the diastereoisomeric relationship of the product was confirmed.

Relative stereochemistries of other products were also confirmed in a similar manner. In some cases, however, deoxygenation of the sulfinyl group with Zn–$TiCl_4$ did not proceed without hydrolysis of the ester group; therefore, deoxygenation was carried out by SmI_2–HMPA.[75]

***tert*-Butyl (3*R*)-3-(*N*-*p*-Methoxyphenylamino)-3-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]propanoate (4e)** To a solution of lithium diisopropylamide [prepared from diisopropylamine (0.029 ml, 0.22 mmol) and *n*-BuLi (0.15 ml, 1.47 mol dm^{-3} in hexane)] in dry THF (4 ml) at −78 °C was added *tert*-butyl acetate (0.029 ml, 0.22 mmol) *via* syringe. After 0.5 h at −78 °C, a solution of **2** (50 mg, 0.147 mmol) in dry THF (1 ml) was slowly added. After being stirred for 1 h at −78 °C, the reaction mixture was quenched with saturated NH_4Cl solution (5 ml), and the aqueous layer was extracted with EtOAc (10 ml×3). The combined organic phase was washed with brine, dried, and concentrated. The crude product was purified by column chromatography on silica (hexane–EtOAc 3 : 1) to give a mixture of **4e** and **6e** (66 mg, 99%) as a colorless oil. Isomerically pure **4e** was obtained by preparative HPLC (hexane–AcOEt 7 : 1). The product ratio was determined by the integration of pertinent signals of **4e** and **6e** (5.13 and 5.21 ppm for methine protons) in the ^{1}H-NMR spectrum and by HPLC (Develosil, 254 nm, hexane–EtOAc 3 : 1, 1.0 ml/min, **4e**: 95.9 min; **6e**: 88.4 min). **4e**: A colorless oil; $[\alpha]_D^{22}$ −69.4° (c=0.3, $CHCl_3$) ^{1}H-NMR (270 MHz) δ: 1.43 (9H, s, *t*-Bu), 2.36 (3H, s, Me), 2.88 (2H, d, J=6.8, CH_2), 3.74 (3H, s, OMe), 4.4 (1H, br, NH), 5.13 (1H, t, J=6.8, CH), 6.20 (1H, d, J=2.0, furan), 6.60 (2H, dm, J=8.9, *p*-methoxyphenyl), 6.75 (2H, dm, J=8.9, *p*-methoxyphenyl), 7.19 (2H, d, J=8.2, *p*-tolyl), 7.28 (1H, d, J=2.0, furan), 7.30 (2H, d, J=8.2, *p*-tolyl). IR cm^{-1} ($CHCl_3$) 1725 (C=O), 1035 (S→O). EI-MS m/z 455 (M^+), 439, 340, 324, 261. EI-HR-MS Calcd for $C_{25}H_{29}NO_5S$: 455.1766. Found 455.1758.

tert-Butyl (3*S*)-3-(*N*-*p*-Methoxyphenylamino)-3-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]propanoate (**6e**): ^{1}H-NMR (270 MHz) δ: 1.46 (9H, s, *t*-Bu), 2.35 (3H, s, Me), 2.87 (2H, d, J=6.3, CH_2), 3.73 (3H, s, OMe), 4.3 (1H, br, NH), 5.21 (1H, t, J=6.3, CH), 6.17 (1H, d, J=2.0, furan), 6.70 (2H, dm, J=9.0, *p*-methoxyphenyl), 6.76 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.07 (2H, d, J=8.3, *p*-tolyl), 7.15 (2H, d, J=8.3, *p*-tolyl), 7.29 (1H, d, J=2.0, furan).

(3*R*,,4*R*)-1-(*p*-Methoxyphenyl)-3-methyl-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (10g) (Table 2, Entry 1) This reaction was carried out under the experimental conditions described for the preparation of **8**. The product was obtained as a mixture of **10g**—**13g** in 72% yield. The product ratio was determined by integration of the H-4 signals of the crude mixture in the ^{1}H-NMR spectrum. Isomerically pure **10g** was obtained by preparative TLC (hexane–EtOAc 2 : 1, 5 developments), followed by recrystallization from Et_2O. **10g**: mp 113—114 °C (Et_2O); $[\alpha]_D^{19}$ +20.8° (c=0.8, $CHCl_3$); ^{1}H-NMR (270 MHz) δ: 1.16 (3H, d, J=7.6, Me), 2.43 (3H, s, Me), 3.76 (3H, s, OMe), 3.77 (1H, dq, J=7.6, 5.6, H-3), 5.55 (1H, d, J=5.6, H-4), 6.41 (1H, d, J=2.0, furan), 6.79 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.17 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.30 (2H, d, J=8.3, *p*-tolyl), 7.37 (1H, d, J=2.0, furan), 7.41 (2H, d, J=8.3, *p*-tolyl). IR cm^{-1} ($CHCl_3$) 1749 (C=O), 1036 (S→O). EI-MS m/z 395 (M^+), 378, 322, 230, 229. *Anal.* Calcd for $C_{22}H_{21}NO_4S$: C, 66.82; H, 5.35; N, 3.54. Found C, 66.77; H, 5.54; N, 3.47. EI-HR-MS Calcd: 395.1191. Found 395.1199.

Although an analytical crystalline sample of (+)-**10g** for X-ray analysis was not obtained, a suitable sample for X-ray analysis of (±)-**10g** [mp 179—180 °C (from MeOH)] was obtained by the reaction from (±)-**2** and **3g**. X-Ray measurement was performed on a Rigaku RAXIS-RAPID diffractometer with Mo–$K\alpha$ radiation. Crystal data for (±)-**10g**: $C_{22}H_{21}NO_4S$, M=395.5, triclinic, space group $P\bar{1}$ (No 2), a=11.244(2) Å, b=11.755(3) Å, c=8.168(2) Å, α=99.05(1)°, β=109.73(1)°, γ=91.52(2)°, V=999.9(4) Å^3, D_{calc}=1.313 g cm^{-3}, Z=2; Number of reflections observed ($I>2\sigma(I)$)=3584, R=0.045, R_w=0.067. Further details of the X-ray structure data are available on request from the Cambridge Crystallographic Data Centre (deposition number CCDC 177886).

(3*S*,4*R*)-1-(*p*-Methoxyphenyl)-3-methyl-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (**11g**): A colorless oil; ^{1}H-NMR (270 MHz) δ: 1.51 (3H, d, J=7.3, Me), 2.41 (3H, s, Me), 3.60 (1H, dq, J=7.3, 2.4, H-3), 3.76 (3H, s, OMe), 5.04 (1H, d, J=2.4, H-4), 6.33 (1H, d, J=2.0, furan), 6.79 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.24 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.29 (2H, d, J=8.3, *p*-tolyl), 7.35 (1H, d, J=2.0, furan), 7.42 (2H, d, J=8.3, *p*-tolyl). IR cm^{-1} ($CHCl_3$) (a mixture of **11g**—**13g**) 1748 (C=O). EI-MS (a mixture of **11g**—**13g**) m/z 395 (M^+), 378, 322, 230, 229. EI-HR-MS (a mixture of **11g**—**13g**) Calcd for $C_{22}H_{21}NO_4S$: 395.1191. Found 395.1194.

(3*S*,4*S*)-1-(*p*-Methoxyphenyl)-3-methyl-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (**12g**): ^{1}H-NMR (270 MHz) δ: 1.00 (3H, d, J=7.6, Me), 2.41 (3H, s, Me), 3.69 (1H, dq, J=7.6, 5.6, H-3), 3.76 (3H, s, OMe), 5.62 (1H, d, J=5.6, H-4), 6.40 (1H, d, J=2.0, furan), 6.80 (2H, dm, J=9.2, *p*-methoxyphenyl), 7.20 (2H, dm, J=9.2, *p*-methoxyphenyl), 7.35 (2H, d, J=8.3, *p*-tolyl), 7.37 (1H, d, J=2.0, furan), 7.57 (2H, d, J=8.3, *p*-tolyl).

(3*R*,4*S*)-1-(*p*-Methoxyphenyl)-3-methyl-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (**13g**): ^{1}H-NMR (270 MHz) δ: 1.42 (3H, d, J=7.3, Me), 2.43 (3H, s, Me), 3.47 (1H, dq, J=7.3, 2.5, H-3), 3.76 (3H, s, OMe), 5.13 (1H, d, J=2.5, H-4), 6.34 (1H, d, J=2.0, furan), 6.81 (2H, dm, J=9.5, *p*-methoxyphenyl), 7.24 (2H, dm, J=9.5, *p*-methoxyphenyl), 7.31 (2H, d, J=8.3, *p*-tolyl), 7.35 (1H, d, J=2.0, furan), 7.53 (2H, d, J=8.3, *p*-tolyl).

Ethyl (2*R*,3*R*)-3-(*N*-*p*-Methoxyphenylamino)-2-methyl-3-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]propanoate (5g) (Table 2, Entry 3) To a solution of lithium diisopropylamide [prepared from diisopropylamine (0.24 ml, 1.8 mmol) and *n*-BuLi (1.24 ml, 1.8 mmol, 1.50 mol dm^{-3} in hexane)] in dry THF (5 ml) at −78 °C was added HMPA (0.65 ml, 3.7 mmol). After being stirred for 0.5 h at that temperature, ethyl propionate (0.21 ml, 1.8 mmol) was added *via* syringe. After being stirred for 1.5 h at −78 °C, a solution of **2** (158 mg, 0.47 mmol) in dry THF (6 ml) was slowly added. After being stirred for 4 h at the same temperature, the reaction mixture was quenched with saturated NH_4Cl solution (10 ml), and the aqueous layer was extracted with EtOAc (15 ml×3). The combined organic phase was washed with brine, dried, and concentrated. The crude product was purified by flash chromatography on silica (hexane–EtOAc 4 : 1→5 : 2) to give a mixture of **4g**—**7g** (196 mg, 95%) as a colorless oil. The ester **5g** was separated from other products by preparative TLC (hexane–EtOAc 3 : 1, 5 developments). The product ratio was determined by integration of the H-3 methine signals of the crude product in the ^{1}H-NMR spectrum.

For determination of the diastereoisomeric relationship between **5g** and **7g**, an analytical sample was independently prepared by the following sequence. Deoxygenation of an essentially pure **5g** with SmI_2–HMPA afforded the *anti*-ester sulfide ($J_{2,3}$=9.6 Hz in the ^{1}H-NMR spectrum) (quantitative yield), which was oxidized with *m*-CPBA to produce a mixture of **5g** and *ent*-**7g** (83% yield). On the other hand, in the case of **4g**, which was inseparable from *anti*-ester **5g**, the *syn*-ester **4g** contaminated by a small amount of **5g** was treated with SmI_2–HMPA to give a mixture of *syn*- and *anti*-sulfides, each of which was separable by chromatography. After separation from the *anti*-sulfide, the isomerically pure *syn*-sulfide ($J_{2,3}$=6.8 Hz in the ^{1}H-NMR spectrum) was oxidized with *m*-CPBA to produce an analytical sample of the *syn*-esters **4g** and *ent*-**6g**. Since all the ^{1}H-NMR signals of the four possible products derived from this reaction sequence were spectroscopically ap-

plicable to those of the crude product mixture, the diastereoisomeric relationship of the products was confirmed. **5g**: a colorless oil; $[\alpha]_D^{24}$ −37.3° (c=0.1, $CHCl_3$). ^{1}H-NMR (400 MHz) δ: 1.18 (3H, d, J=7.0, Me), 1.25 (3H, t, J=7.1, Me), 2.36 (3H, s, Me), 3.12 (1H, dq, J=8.2, 7.0, H-2), 3.73 (3H, s, OMe), 4.20 (2H, q, J=7.1, CH_2), 4.5 (1H, br, NH), 4.95 (1H, d, J=8.2, H-3), 6.16 (1H, d, J=2.0, furan), 6.60 (2H, dm, J=8.8, *p*-methoxyphenyl), 6.74 (2H, dm, J=8.8, *p*-methoxyphenyl), 7.18 (2H, d, J=8.5, *p*-tolyl), 7.21 (2H, d, J=8.5, *p*-tolyl), 7.29 (1H, d, J=2.0, furan). EI-MS m/z 441 (M^+), 424, 340, 324, 122. IR cm^{-1} ($CHCl_3$) 1730 (C=O), 1040 (S→O). EI-HR-MS Calcd for $C_{24}H_{27}NO_5S$: 441.1610. Found 441.1601.

Ethyl (2*S*,3*R*)-3-(*N*-*p*-Methoxyphenylamino)-2-methyl-3-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]propanoate (**4g**): ^{1}H-NMR (400 MHz) δ: 1.19 (3H, t, J=7.1, Me), 1.36 (3H, d, J=7.1, Me), 2.36 (3H, s, Me), 3.13 (1H, m, H-2), 3.73 (3H, s, OMe), 4.12 (2H, q, J=7.1, CH_2), 4.3 (1H, br, NH), 5.11 (1H, d, J=5.9, H-3), 6.15 (1H, d, J=2.2, furan), 6.6—7.4 (9H, m, ArH). IR cm^{-1} ($CHCl_3$) (a mixture of **4g** and **6g**) 1729 (C=O), 1039 (S→O). EI-MS (a mixture of **4g** and **6g**) m/z 441 (M^+), 424, 340, 324, 122. EI-HR-MS (a mixture of **4g** and **6g**) Calcd for $C_{24}H_{27}NO_5S$: 441.1610. Found 441.1601.

Ethyl (2*R*,3*S*)-3-(*N*-*p*-Methoxyphenylamino)-2-methyl-3-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]propanoate (**6g**): ^{1}H-NMR (400 MHz) δ: 1.23 (3H, t, J=7.1, Me), 1.40 (3H, d, J=7.2, Me), 2.35 (3H, s, Me), 3.13 (1H, m, H-2), 3.73 (3H, s, OMe), 4.22 (2H, dq, J=7.1, 4.2, CH_2), 4.3 (1H, br, NH), 5.03 (1H, d, J=7.2, H-3), 6.16 (1H, d, J=2.2, furan), 6.6—7.4 (9H, m, ArH).

Ethyl (2*S*,3*S*)-3-(*N*-*p*-Methoxyphenylamino)-2-methyl-3-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]propanoate (**7g**): ^{1}H-NMR (400 MHz) δ: 1.19 (3H, d, J=6.8, Me), 1.28 (3H, t, J=7.1, Me), 2.35 (3H, s, Me), 3.10 (1H, m, H-2), 3.73 (3H, s, OMe), 4.22 (2H, m, CH2), 4.4 (1H, br, NH), 4.98 (1H, d, J=9.8, H-3), 6.13 (1H, d, J=2.0, furan), 6.72 (4H, m, *p*-methoxyphenyl), 7.00 (2H, d, J=7.8, *p*-tolyl), 7.14 (2H, d, J=7.8, *p*-tolyl), 7.30 (1H, d, J=2.0, furan).

(3*R*,4*R*)-3-Benzyloxy-1-(*p*-methoxyphenyl)-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (10h) To a solution of lithium diisopropylamide [prepared from diisopropylamine (0.04 ml, 0.3 mmol) and *n*-BuLi (0.19 ml, 0.3 mmol, 1.58 mol dm^{-3} in hexane)] in dry THF (3 ml) at −78 °C was added ethyl (benzyloxy)acetate[60—62] (58 mg, 0.3 mmol) *via* syringe. After being stirred for 0.5 h at −78 °C, a solution of **2** (68 mg, 0.2 mmol) in dry THF (3 ml) was slowly added. After being stirred for 1 h at the same temperature, the mixture was slowly warmed up to room temperature (during 45 min). The reaction mixture was then quenched with saturated NH_4Cl (5 ml), and the aqueous layer was extracted with EtOAc (7 ml×3). The combined organic phase was washed with brine, dried, and concentrated. The crude product was purified by column chromatography on silica (hexane–EtOAc 5 : 2) to give a mixture of **10h**—**13h** (65 mg, 67%) as a colorless oil. The product mixture was further purified by preparative TLC (hexane–EtOAc 3 : 1, 6 developments) to afford *anti*-isomers (**11h** and **13h**, 46%) and *syn*-isomers (**10h** and **12h**, 8%). The product ratio was determined by integration of methine signals (H-3 and H-4) of the crude mixture in the ^{1}H-NMR spectrum. **10h**: ^{1}H-NMR (270 MHz) δ: 2.37 (3H, s, Me), 3.77 (3H, s, OMe), 4.58 (1H, d, J=11.7, PhCHH), 4.69 (1H, d, J=11.7, PhCHH), 5.11 (1H, d, J=4.9, H-3 or H-4), 5.62 (1H, d, J=4.9, H-4 or H-3), 6.41 (1H, d, J=2.0, furan), 6.77 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.15—7.45 (12H, m, ArH). IR cm^{-1} ($CHCl_3$) (a mixture of **10h** and **12h**) 1759 (C=O), 1043 (S→O). EI-MS (a mixture of **10h** and **12h**) m/z 487 (M^+), 470, 380, 324, 323, 322, 231, 91. EI-HR-MS (a mixture of **10h** and **12h**) Calcd for $C_{28}H_{25}NO_5S$: 487.1453. Found 487.1459.

(3*S*,4*R*)-3-Benzyloxy-1-(*p*-methoxyphenyl)-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (**11h**): ^{1}H-NMR (270 MHz) δ: 2.39 (3H, s, Me), 3.75 (3H, s, OMe), 4.75 (1H, d, J=11.5, PhCHH), 4.89 (1H, d, J=11.5, PhCHH), 5.04 (1H, d, J=1.8, H-3 or H-4), 5.34 (1H, d, J=1.8, H-4 or H-3), 6.32 (1H, d, J=2.0, furan), 6.80 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.20—7.50 (12H, m, ArH). IR cm^{-1} ($CHCl_3$) 1760 (C=O), 1046 (S→O) (a mixture of **11h** and **13h**). EI-MS (a mixture of **11h** and **13h**) m/z 487 (M^+), 470, 380, 324, 323, 322, 231, 91. EI-HR-MS (a mixture of **11h** and **13h**) Calcd for $C_{28}H_{25}NO_5S$: 487.1453. Found 487.1452.

(3*S*,4*S*)-3-Benzyloxy-1-(*p*-methoxyphenyl)-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (**12h**): ^{1}H-NMR (270 MHz) δ: 2.35 (3H, s, Me), 3.76 (3H, s, OMe), 4.35 (1H, d, J=11.5, PhCHH), 4.50 (1H, d, J=11.5, PhCHH), 5.07 (1H, d, J=4.4, H-3 or H-4), 5.71 (1H, d, J=4.4, H-4 or H-3), 6.38 (1H, d, J=2.0, furan), 6.84 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.15—7.40 (9H, m, ArH), 7.42 (1H, d, J=2.0, furan), 7. 52 (2H, d, J=8.3, *p*-tolyl).

(3*R*,4*S*)-3-Benzyloxy-1-(*p*-methoxyphenyl)-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (**13h**): ^{1}H-NMR (270 MHz) δ: 2.38 (3H, s, Me), 3.76 (3H, s, OMe), 4.71 (1H, d, J=11.5, PhCHH), 4.75 (1H, d, J=11.5, PhCHH), 4.93 (1H, d, J=1.7, H-3 or H-4), 5.45 (1H, d, J=1.7, H-4 or H-3), 6.39 (1H, d, J=2.0, furan), 6.79 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.20—7.50 (12H, m, ArH).

Methyl (2*S*,3*R*)-2-(*tert*-Butyldimethylsilyloxy)-3-(*N*-*p*-methoxyphenylamino)-3-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]propanoate (4i) To a solution of lithium diisopropylamide [prepared from diisopropylamine (0.29 ml, 2.2 mmol) and *n*-BuLi (1.5 ml, 2.2 mmol, 1.47 mol dm^{-3} in hexane)] in dry THF (10 ml) at −78 °C was added methyl (*tert*-butyldimethylsilyloxy)acetate[76] (451 mg, 2.2 mmol) in dry THF (5 ml) *via* syringe. After being stirred for 0.5 h at −78 °C, a solution of **2** (500 mg, 1.47 mmol) in dry THF (5 ml) was slowly added. After being stirred for 0.5 h at the same temperature, the reaction mixture was warmed up to −30 °C (during 0.5 h). The reaction mixture was then quenched with saturated NH_4Cl solution (15 ml), and the aqueous layer was extracted with EtOAc (20 ml×3). The combined organic phase was washed with brine, dried, and concentrated. The crude product was purified by column chromatography on silica (hexane–EtOAc 3 : 1) to give a mixture of the products. The ester **4i** (534 mg, 67%) and the *anti*-β-lactam **11i** (68 mg, 8%) were purely isolated; however, other isomers, **5i** and **10i** (13% and 0.6% yields, respectively), were inseparable from each other by chromatographic separation. The products **6i**, **7i**, **12i** and **13i** were not obtained in substantial yield. The product ratio of **10i**, **11i**, **12i** and **13i** was thus calculated on the basis of the integration of pertinent signals due to the furan ring (δ: 6.41, 6.35, 6.45 and 6.37, respectively) in the ^{1}H-NMR spectrum. **4i**: mp 82—84 °C (hexane–Et_2O). $[\alpha]_D^{22}$ −117.1° (c=1.0, $CHCl_3$). ^{1}H-NMR (270 MHz) δ: −0.13 (3H, s, SiMe), −0.03 (3H, s, SiMe), 0.87 (9H, s, Si*t*-Bu), 2.38 (3H, s, Me), 3.69 (3H, s, OMe), 3.71 (3H, s, OMe), 4.5—4.8 (1H, br, NH), 4.69 (1H, d, J=2.0, H-2), 5.17 (1H, dd, J=10.5, 2.0, H-3), 6.41 (1H, d, J=2.0, furan), 6.43 (2H, br d, J=9.0, *p*-methoxyphenyl), 6.67 (2H, br d, J=9.0, *p*-methoxyphenyl), 7.17 (2H, d, J=8.3, *p*-tolyl), 7.22 (2H, d, J=8.3, *p*-tolyl), 7.31 (1H, d, J=2.0, furan). IR cm^{-1} ($CHCl_3$) 1755 (C=O), 1030 (S→O). EI-MS m/z 543 (M^+), 527, 340, 324, 149, 69, 57. *Anal.* Calcd for $C_{28}H_{37}NO_6SiS$: C, 61.85; H, 6.86; N, 2.58. Found C, 61.95; H, 6.91; N, 2.57. EI-HR-MS Calcd: 543.2111. Found 543.2118.

Methyl (2*R*,3*R*)-2-(*tert*-Butyldimethylsilyloxy)-3-(*N*-*p*-methoxyphenylamino)-3-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]propanoate (**5i**): ^{1}H-NMR (400 MHz) δ: 0.00 (3H, s, SiMe), 0.09 (3H, s, SiMe), 0.88 (9H, s, Si*t*-Bu), 2.35 (3H, s, Me), 3.73 (3H, s, OMe), 3.74 (3H, s, OMe), 4.4 (1H, br, NH), 4.70 (1H, d, J=5.9, H-2), 5.15 (1H, br, H-3), 6.15 (1H, d, J=2.0, furan), 6.63 (2H, br d, J=9.0, *p*-methoxyphenyl), 6.76 (2H, br d, J=9.0, *p*-methoxyphenyl), 7.17 (2H, d, J=8.3, *p*-tolyl), 7.28 (1H, d, J=2.0, furan), 7.29 (2H, d, J=8.3, *p*-tolyl).

(3*R*,4*R*)-3-(*tert*-Butyldimethylsilyloxy)-1-(*N*-*p*-methoxyphenyl)-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (**10i**): ^{1}H-NMR (400 MHz) δ: 0.00 (3H, s, SiMe), 0.16 (3H, s, SiMe), 0.76 (9H, s, Si*t*-Bu), 2.40 (3H, s, Me), 3.77 (3H, s, OMe), 5.19 (1H, d, J=4.8, H-3 or H-4), 5.66 (1H, d, J=4.8, H-4 or H-3), 6.41 (1H, d, J=2.0, furan), 6.83 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.24 (4H, d×2, J=9.0, 8.4, *p*-methoxyphenyl+*p*-tolyl), 7.39 (1H, d, J=2.0, furan), 7.56 (2H, d, J=8.4, *p*-tolyl).

(3*S*,4*R*)-3-(*tert*-Butyldimethylsilyloxy)-1-(*p*-methoxyphenyl)-4-[(S_s)-3-(*p*-tolylsulfinyl)-2-furyl]-2-azetidinone (**11i**): A colorless oil; $[\alpha]_D^{20}$ −62.7° (c=1.3, $CHCl_3$). ^{1}H-NMR (270 MHz) δ: 0.02 (3H, s, SiMe), 0.11 (3H, s, SiMe), 0.90 (9H, s, Si*t*-Bu), 2.37 (3H, s, Me), 3.75 (3H, s, OMe), 5.12 (1H, d, J=1.6, H-3 or H-4), 5.24 (1H, d, J=1.6, H-4 or H-3), 6.35 (1H, d, J=2.0, furan), 6.64 (2H, dm, J=9.0, *p*-methoxyphenyl), 6.78 (2H, dm, J=9.0, *p*-methoxyphenyl), 7.19 (2H, d, J=8.1, *p*-tolyl), 7.30 (2H, d, J=8.1, *p*-tolyl), 7.37 (1H, d, J=2.0, furan). IR cm^{-1} ($CHCl_3$) 1750 (C=O), 1030 (S→O). EI-MS m/z 511 (M^+), 454, 323, 305, 201, 166. EI-HR-MS Calcd for $C_{27}H_{33}NO_5SiS$: 511.1849. Found 511.1860.

Isomerization Experiment of *syn*-Lactam 10g to *anti*-Lactam 11g A solution of 1,1,1,3,3,3-hexamethyldisilazane (0.034 ml, 0.16 mmol) in dry THF (1.5 ml) was treated with *n*-BuLi (0.11 ml, 0.16 mmol, 1.50 mol dm^{-3} in hexane) at 0 °C under nitrogen. After being stirred for 15 min, the solution was cooled down to −78 °C, and a solution of **10g** (16.5 mg, 0.042 mmol) in dry THF (0.7 ml) was slowly added. After being stirred for 20 min, the reaction mixture was poured into saturated NH_4Cl solution (10 ml). The aqueous layer was extracted with $CHCl_3$ (7 ml×3), and the combined organic phase was washed with brine, dried, and concentrated. The crude product was purified by column chromatography on silica (hexane–EtOAc 5 : 2). Early fractions contained a mixture of **10g** and **11g** (4.2 mg, 25%) in a rough ratio of 1 : 1. Later fractions contained **11g** (6.8 mg, 41%), whose spectral data were in good agreement with those of **11g** obtained by the reaction of **2** and **3g**.

Cyclization Experiment of β-Amino Ester to β-Lactam To a solution of lithium hexamethyldisilazide [prepared from 1,1,1,3,3,3-hexamethyldisilazane (0.0086 ml, 0.04 mmol) and *n*-BuLi (0.032 ml, 0.04 mmol, 1.47 mol dm^{-3} in hexane)] in dry THF (1 ml) at −10 °C under nitrogen was

added a solution of **4i** (20 mg, 0.037 mmol) in dry THF (0.5 ml). After being stirred at the same temperature for 1.5 h, the reaction mixture was quenched with saturated NH_4Cl solution (5 ml). The aqueous layer was extracted with EtOAc (7 ml×3), and the combined organic phase was washed with brine, dried, and concentrated. The crude product was purified by preparative TLC (hexane–EtOAc 3 : 1) to afford **10i** (13 mg, 69%).

In a similar manner, the treatment of **5i** (8.8 mg), contaminated by a small amount of **10i**, with lithium hexamethyldisilazide gave **11i** (2.3 mg, 28%), from which **5i** (3.0 mg, 34%) was recovered unchanged. Isomerization of the *syn*-*β*-lactam **10i** to **11i** was also observed during the reaction.

(4*R*)-4-(2-Furyl)-1-(*p*-methoxyphenyl)-3,3-dimethyl-2-azetidinone (14a) A mixture of **8** (32 mg, 0.078 mmol, 98% de) and Raney nickel (*ca.* 0.3 ml) in EtOH (5 ml) was placed in a glass lecture-bottle. The reaction vessel was then purged with hydrogen until the pressure was 4 atm. The reaction mixture was stirred vigorously at room temperature for 6 h. The reaction mixture was then filtered with the aid of a short pad of Celite. The solid filter was washed with $CHCl_3$, and the combined filtrate was concentrated. The residue was purified by column chromatography on silica using hexane–AcOEt (4 : 1) as an eluent to give **14a** (17 mg, 80%) as a solid. **14a**: mp 86—89 °C (hexane). $[\alpha]_D^{23}$ +145° (*c*=0.30, $CHCl_3$) for 98% ee. ^{1}H-NMR (400 MHz) δ: 1.08 (3H, s, Me), 1.49 (3H, s, Me), 3.76 (3H, s, OMe), 4.74 (1H, s, H-4), 6.23 (1H, br d, *J*=3.3, furan), 6.36 (1H, dd, *J*=3.3, 1.8, furan), 6.81 (2H, dm, *J*=9.1, *p*-methoxyphenyl), 7.26 (2H, dm, *J*=9.1, *p*-methoxyphenyl), 7.41 (1H, dd, *J*=1.8, 0.9, furan). lit.[48] (−)-**14a**: mp 130 °C (dec.); $[\alpha]_D^{23}$ −44.5° (*c*=0.8, $CHCl_3$) for 51% ee (4*S* configuration). Chiral HPLC: Chiralpak AS, 254 nm, hexane–2-propanol 9 : 1; 1.0 ml/min; (*S*): 6.9 min, (*R*): 8.6 min. A racemic sample[77] for chiral HPLC was prepared by the reaction of (±)-**8** (mp 160—161 °C) obtained starting from (±)-**2**.

(3*R*,4*R*)-4-(2-Furyl)-1-(*p*-methoxyphenyl)-3-methyl-2-azetidinone (**14g**) 65% yield from **10g** (91% de), mp 76—77 °C (hexane); $[\alpha]_D^{20}$ +199.5° (*c*=0.1, $CHCl_3$) for 90% ee. lit.[31] $[\alpha]_D^{25}$ +134.8° (*c*=0.6, $CHCl_3$) for >97% ee. ^{1}H-NMR (270 MHz) δ: 1.11 (3H, d, *J*=7.5, Me), 3.65 (1H, dq, *J*=7.5, 5.7, H-3), 3.76 (3H, s, OMe), 5.14 (1H, d, *J*=5.7, H-4), 6.30 (1H, br d, *J*=3.3, furan), 6.37 (1H, dd, *J*=3.3, 1.8, furan), 6.81 (2H, dm, *J*=9.1, *p*-methoxyphenyl), 7.26 (2H, dm, *J*=9.1, *p*-methoxyphenyl), 7.42 (1H, dd, *J*=1.8, 0.7, furan). Chiral HPLC: Chiralpak AS, 254 nm, hexane–2-propanol 9 : 1; 1.0 ml/min; (3*S*,4*S*): 13.9 min; (3*R*,4*R*): 18.0 min.

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