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Synthesis, Structural Characterization and Stereocontrolled Degradation of 2-Azacephams

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Abstract: The enantiomerically pure substituted 2-azacephams **5** were synthesized by intramolecular cyclization of sulfinamides **4**. Their absolute configurations were confirmed by X-ray crystal structure determination of (5*R*,6*R*)-4-benzyl-2-isopropylidene-5-oxo-5-thia-1,4-diazabicyclo[4.2.0]octane-3,8-dione **5a**. Nucleophilic opening of 2-azacephams by methanol occurred rapidly to give sulfinates **8** with excellent regio and stereoselectivity.

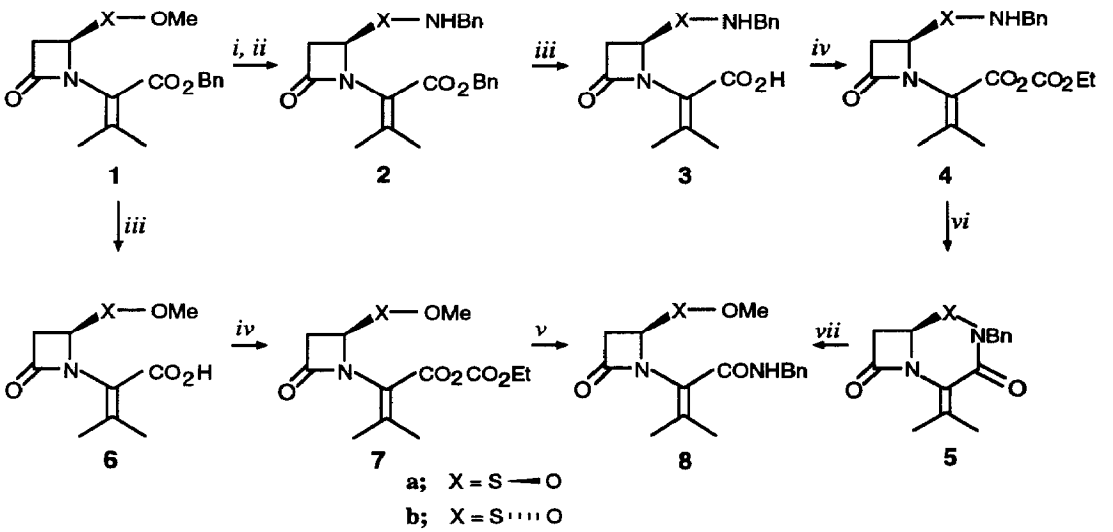
INTRODUCTION

Our continuing interest[1-3] in the synthesis and stereochemistry of 4-oxoazetidine-2-sulfinic and sulfonic acids led us to investigate the sulfinamides as new functionalized monocyclic β-lactams, precursors for 2-azacephams. In the first part of this study[4] we reported the preparation of 4-oxo-azetidine-2-sulfonamides as well as their intramolecular cyclization into the new anhydro 2-azacepham-1,1- dioxide. Now, we wish to present the course of the stereochemical transformation of the sulfinamides **4** into sulfinates **8** which involves the migration of an amino group from sulfur to carbon atom and formation of 2-azacepham-1-oxides **5** as intermediates.

RESULTS AND DISCUSSION

Chemistry

The starting enantiomerically pure 4-oxoazetidine-2-sulfinamides **2a** and **2b**[5] used in the present study were prepared from an epimeric mixture of sulfinates **1a/1b**. Thus, the reaction of sulfinates **1** with an excess of anhydrous hydrogen chloride followed by the treatment of the evaporated residue with benzylamine gave the diastereoisomeric mixture of **2a** and **2b** in a ratio of 3:2. Both diastereoisomers were separated by silica gel column chromatography and each of them was transformed into derivatives **3a** and **3b**.



Scheme 1 *Reagents and conditions: i*, HCl (g)/CH_2Cl_2, r.t., 15 min.; *ii*, $BnNH_2/CH_2Cl_2$, r.t., 30 min; *iii*, $AlCl_3$/anisole/CH_2Cl_2, -10 °C to 0 °C, 1 hr; *iv*, EtOCOCl/Et_3N/CH_2Cl_2, r.t. 1 hr; *v*, $BnNH_2/CH_2Cl_2$ r.t., 30 min; *vi*, Et_3N/CH_2Cl_2, r.t., 1 hr; *vii*, MeOH, r. t. 2 hrs.

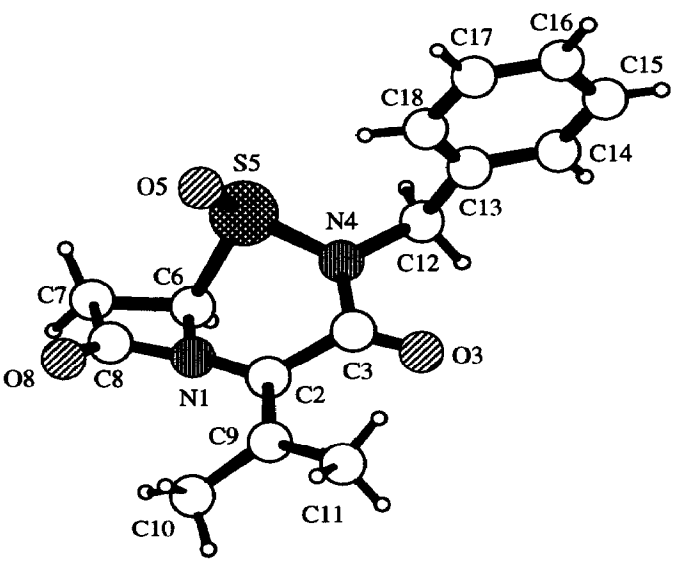


Figure 1 X-Ray molecular structure of (5*R*,6*R*)-4-benzyl-2-isopropylidene-5-oxo-5-thia-1,4-diazabicyclo[4.2.0]octane-3,8-dione **5a**, showing crystallographic numbering sheme

Table 1 Selected ^{1}H NMR chemical shifts and coupling constants (in parenthesis) for compounds **2**, **3**, **4**, **7** and **8**[a]

Compound	3β-H	3α-H	2-H	Me_I	Me_{II}
2a	**2.94** dd (3.2; 15.4)	3.16 dd (4.7: 15.4)	4.77 dd (3.2; 4.7)	**2.08** s	2.21 s
2b	**3.36** dd (2.6; 15.3)	3.14 dd (5.0; 15.3)	4.77 dd (2.6; 5.0)	**1.94** s	2.24 s
3a	**3.00** dd (2.4; 15.6)	3.39 dd (5.5; 15.6)	5.42 dd (2.4; 5.5)	**2.01** s	2.16 s
3b	**3.20**-3.34 overlapped 3β-H and 3α-H		5.06 br	**1.89** s	2.20 s
4a	**3.08** dd (2.5; 15.6)	3.26 dd (5.5; 15.6)	4.87 dd (2.5; 5.5)	**2.16** s	2.28 s
4b	**3.34** dd (2.2; 15.4)	3.84 dd (5.2; 15.4)	4.67 dd (2.2; 5.2)	**2.00** s	2.27 s
7a	**3.15** dd (3.2; 15.5)	3.20 dd (5.3; 15.5)	4.96 dd (3.2; 5.3)	**2.16** s	2.28 s
7b	**3.54** dd (2.6; 15.8)	3.24 dd (5.3; 15.8)	4.80 dd (2.6; 5.3)	**2.08** s	2.31 s
8a	**3.12** dd (3.2; 15.0)	3.15 dd (4.7; 15.0)	4.67 dd (3.2; 4.7)	**1.87** s	2.05 s
8b	**3.47** dd (2.3; 15.7)	3.14 dd (5.2: 15.7)	4.67 dd (2.3; 5.2)	**1.84** s	2.03 s

[a]For more details and further ^{1}H NMR signals see Experimental section in this paper and in ref. 3.

All attempts to cleave the benzyl ester group by hydrogenolysis with palladium on charcoal were unsuccessful. However, removal of the ester protecting group proceeded readily using aluminum trichloride-anisole method.[6] In those cases it was possible to isolate the carboxylic acids although they were thermally unstable. Treatment of carboxylic acid **3a** or **3b** with ethyl chloroformate in the presence of triethylamine afforded mixed anhydride **4a** or **4b**. The purification of each compound from the reaction mixture failed because of their sensitivity to silica gel and polar solvents, but their formation was observed by ^{1}H NMR spectroscopy analysis of the crude products.

The use of bases such as triethylamine led the mixed anhydride **4a** or **4b** to the cyclization and formation of bicyclic compound **5a** or **5b**, but in relatively low yields. The structures of the new compounds were assigned from their spectroscopic data and were additionally confirmed by oxidation to the substituted sultam **5** (X = SO_2).[4] No systematic work was carried out to optimize the yields of **5**, but few experimental observations were made in adjusting the conditions for preparation and cyclization of **4a**. It should be noted that the one-pot procedure, without isolation of mixed anhydride, was also applied and afforded bicyclic products, but it was less successful.

It was assumed that in any case, a single diastereoisomer was formed resulting from retention of the configuration at sulfur in all steps. The stereochemical assignments for novel amides **2**, **3**, **4**, and **8** (compared

with sulfinates **7**) were deduced from ^{1}H NMR data summarized in Table 1. All diastereoisomers of **a** configuration compared with diastereoisomers of **b** configuration exhibit the downfield shifts for the 3β-H atoms and the upfield shifts for the methyl H atoms (Me$_I$), what was in concordance with our earlier observation.[3]

The absolute configuration of **5a** was determined by single crystal X-ray crystallographic analysis (Figure 1) and this firmly established 5*R*,6*R* configuration (oxygen at sulfur was β-positioned). The selected molecular geometry parameters are listed in Table 2.

Although **5a** or **5b** could be purified by careful crystallization, they were very unstable. Treatment with methanol resulted in opening of the heterocyclic ring *via* nucleophilic attack on the sulfur to give methylsulfinate **8b** or **8a**. Nucleophilic opening of the ring takes place with inversion of the configuration at the sulfur, what was confirmed by the chemical transformations. Thus the enantiomerically pure **8b** was also obtained by action of benzylamine on mixed anhydride **7b**, which was prepared starting from methylsulfinate **1b** by deprotection of benzyl ester group and followed by activation of carboxylic acid of **6b** with ethyl chloroformate in similar conditions as reported above.

In summary, this paper reports the stereocontrolled transformation of the sulfinamides **4** into sulfinates **8** that involve the migration of an amino group from sulfur to carbon atom. Substituted 2-aminocephams **5**, prepared and characterized in this synthetic course prove to be accessible and powerful intermediates for the new functionalized, well-defined chiral monocyclic β-lactams or useful precursors for novel 2-azacephams.

X-Ray Crystal Analysis

(5*R*,6*R*)-4-benzyl-2-isopropylidene-5-oxo-5-thia-1,4-diazabicyclo[4.2.0]octane-3,8-dione **5a**; Molecular formula $C_{15}H_{16}N_2O_3S$; Formula weight 304.36; Monoclinic $P2_1$; a = 6.259(3), b = 14.631(7), c = 8 .308 Å, β = 99.35(2)°, V = 750.7(6) Å^3; Z = 2; Dc = 1.35 g cm^{-3}; F_{000} = 320; Mo-Kα radiation; structure refined on F^2 to final $wR2$ = 0.191; $R1$ = 0.072 for 1985 reflections with $I > 2\sigma(I)$.

A suitable crystal of the dimension 0.32 x 0.39 x 0.45 mm was obtained by slow evaporation of diethyl ether-acetone solution at room temperature. Data collection performed with a four circle diffractometer Philips PW1100/20 modified by Stoe&Cie. A total of 3354 reflections was collected between 2-28° Θ. Lorentz and polarization effects were corrected.[7] The structure was solved by direct methods using the program SIR88[8] and refined on F^2 by SHELXL93[9] to final $wR2$ = 0.191 ($R1$ = 0.072) and Flack parameter[10] x = 0.11(13). The hydrogen atoms were placed geometrically. All the non-hydrogen temperature factors were refined anisotropically. Atomic coordinates for the compound have been deposited at the Cambridge Crystallographic Data Centre.[11]

The β-lactam ring is folded about diagonal. The N1 atom is 0.202(3) Å out of plane defined by the other three atoms within β-lactam ring (C6, C7 and C8). The thiadiazine ring is nearly planar except for S5 atom which is 0.849(1) Å out of best plane throw other five atoms within ring (N1, C2, C3, N4, C6). These two defined planes (rings) make angle of 33.0(2)°.

Table 2 Fractional atomic coordinates and equivalent isotropic temperature factors [x 10^4] Ueq with standard deviation (in parenthesis) for (5*R*,6*R*)-4-benzyl-2-isopropylidene-5-oxo-5-thia-1,4-diaza-bicyclo[4.2.0]octane-3,8-dione **5a**

Atom	x/a	y/b	z/c	Ueq
S5	1.0096(2)	0.01758(6)	0.67341(12)	0.0500(3)
O3	0.9362(7)	0.1819(3)	0.3059(5)	0.0638(9)
O5	0.7963(8)	-0.0301(2)	0.6414(5)	0.0742(11)
O8	0.4349(5)	0.1358(4)	0.7882(6)	0.0792(13)
N1	0.7669(4)	0.1635(2)	0.6955(4)	0.0372(6)
N4	1.0398(5)	0.0798(2)	0.5050(5)	0.0430(7)
C2	0.7442(5)	0.1892(2)	0.5307(5)	0.0381(7)
C3	0.9088(6)	0.1501(3)	0.4367(5)	0.0418(8)
C6	0.9527(5)	0.1181(3)	0.7890(4)	0.0365(7)
C7	0.8153(6)	0.0948(3)	0.9213(5)	0.0479(9)
C8	0.6296(5)	0.1313(3)	0.8004(5)	0.0480(9)
C9	0.5894(7)	0.2502(3)	0.4665(6)	0.0478(9)
C10	0.4577(8)	0.2989(4)	0.5743(8)	0.0631(12)
C11	0.5371(11)	0.2746(5)	0.2902(8)	0.078(2)
C12	1.2192(7)	0.0523(4)	0.4214(6)	0.0563(11)
C13	1.1560(7)	-0.0123(3)	0.2783(5)	0.0445(8)
C14	1.2932(8)	-0.0146(4)	0.1607(6)	0.0580(11)
C15	1.2543(11)	-0.0765(5)	0.0323(7)	0.071(2)
C16	1.0826(12)	-0.1355(4)	0.0191(7)	0.072(2)
C17	0.9445(12)	-0.1322(3)	0.1335(7)	0.0675(14)
C18	0.9817(9)	-0.0714(3)	0.2627(6)	0.0560(10)

EXPERIMENTAL

M.p.s were determined by a Fisher-Johns apparatus and were uncorrected. IR spectra were recorded by using a Perkin-Elmer Model 257 G spectrometer. ^{1}H NMR (90 MHz) spectra were recorded by a Jeol FX 90Q spectrometer. Chemical shifts δ_H were in ppm downfield from Me_4Si, and *J*-value were given in Hz. Specific rotations were recorded at 589 nm [sodium D line] on a Jasco DIP-360 polarimeter using a 1 dm cell. TLC was run on Merck Kieselgel HF_{254} plates and were visualized under UV light or J_2 vapor adsorption. Column chromatography was performed on Merck Kieselgel 60 (70-230 mesh ASTM) activated at 105 °C. 4-Oxoazetidine-2-sulfinates **1a** and **1b** their carboxylic acids **6a** and **6b** and mixed anhydrides **7a** and **7b** were prepared previously.[1,3]

Benzyl 2-[(2*R*)-2-benzylsulfinamoyl-4-oxoazetidin-1-yl]-3-methylbut-2-enoate (2a) and (2b): Hydrogen chloride was bubbled through a stirred solution of methylsulfinate **1a** (337 mg, 1 mmol) in dry dichloromethane (15 mL) for 15 minutes. The reaction mixture was then stirred for a further 15 minutes and dichloromethane was removed by evaporation under reduced pressure to give a yellowish syrup. To a cooled solution (0 °C) of evaporated residue in dichloromethane (50 mL) benzylamine was added drop-by-drop until the pH was adjusted to 7.5. The resulting mixture was allowed to warm to room temperature. After being

stirred for 30 minutes, the mixture was treated with 1 mol/dm^{-3} hydrochloric acid (20 mL) and the aq. layer was extracted with dichloromethane (20 mL). The organic phase was washed and dried (Na_2SO_4). Evaporation of the organic layer under reduced pressure and purification of the residue by silica gel chromatography with dichloromethane-ethyl acetate (gradient eluation) gave the title compounds **2a** and **2b** (159 mg, 39%) in a ratio of 3:2, which showed spectroscopic properties identical to those described earlier.[3]

2-[(2*R*,*R*$_S$)-2-Benzylsulfinamoyl-4-oxoazetidin-1-yl]-3-methylbut-2-enoic acid (3a) [12]: This compound was prepared under conditions similar to those described earlier.[6] To a cooled solution (0 °C) of 4-oxoazetidin-2-sulfinamide **2a** (217 mg, 0.53 mmol) in dry dichloromethane (10 mL) and anisole (342 mg, 3.17 mmol) the anhydrous aluminum trichloride (210 mg, 1.57 mmol) was added in one portion. The mixture was stirred at 0 °C for 1 hour and at 20 °C for the another hour, and then poured dropwise into a stirred mixture of ethyl acetate (20 mL) and ice (20 g). The layers were separated and the aq. layer was once more extracted with ethyl acetate (20 mL). The combined organic layers were extracted with aq. sodium hydrogen carbonate (10 cm^3). The aq. layer was acidified with 1 mol/dm^{-3} hydrochloric acid and extracted with ethyl acetate. Evaporation under reduced pressure of dried (Na_2SO_4) organic extract gave the title compound **3a** (94 mg, 61.5%) as a yellowish oil. R_f 0.24 [ethyl acetate-methanol (3:1 v/v)]; IR (film)ν_{max}/cm^{-1} 3215m, 2930m, 1770vs, 1720s, 1630m, 1360s, 1270m, 1210s, 1070s, and 1020s; ^{1}H NMR ($CDCl_3$) δ 2.01 and 2.16(each 3 H, s, CMe_2), 3.00(1H, dd, *J* 2.4 and 15.6, 3β-H), 3.37(1 H, dd, *J* 5.5 and 15.6, 3α-H), 3.32 and 4.39(2H, 2dd, *J* 5.3, 6.0 and 14.3, CH_2Ph), 5.42(1 H, 2d, *J* 2.4 and 5.5, 2-H), 5.56(1H, 2d, *J* 5.3 and 6.0, NH), 7.26-7.34(5H, m, C_6H_5).

2-[(2*R*,*S*$_S$)-2-Benzylsulfinamoyl-4-oxoazetidin-1-yl]-3-methylbut-2-enoic acid (3b): The same treatment of 4-oxoazetidin-2-sulfinamide **2b** as described for the preparation of **3a** gave carboxylic acid **3b** (58%) as a yellowish oil; R_f 0.24 [ethyl acetate-methanol (3:1 v/v)]; IR (film)ν_{max}/cm^{-1} 3210m, 2920m, 1775vs, 1720s, 1635m, 1215s, 1080s, and 1035s; ^{1}H NMR ($CDCl_3$) δ 1.81 and 2.20(each 3 H, s, CMe_2), 3.20-3.34(2 H, m, 3α- H and 3β-H), 4.21(2 H, s, CH_2Ph), 5.06(1 H, br, 2-H), 5.20(1 H, br, NH), 7.24-7.29(5 H, m, C_6H_5).

Ethoxycarbonyl 2-[(2*R*,*R*$_S$)-2-benzylsulfinamoyl-4-oxoazetidin-1-yl]-3-methylbut-2-enoate (4a): To a cooled solution (0 °C) of carboxylic acid **3a** (105 mg, 0.32 mmol), triethylamine (35 mg, 0.35 mmol) and dichloromethane (15 mL) the solution of ethyl chloroformate (69 mg, 0.64 mmol) in dichloromethane (1 mL) was added dropwise. The mixture was stirred for 1 h at 0 °C, and washed with cooled water. Evaporation under reduced pressure of dried (Na_2SO_4) organic layer gave a residue of the title compound **4a** (116 mg, 80%) as a yellowish oil; R_f 0.43 [dichloromethane ethyl acetate (4:2 v/v)]; IR (film)ν_{max}/cm^{-1} 3210m, 2980m, 1800vs, 1775vs, 1365s, 1240s, 1150, 1060s and 1020m; ^{1}H NMR ($CDCl_3$) δ 1.37(3 H, t, *J* 7.1, -CH_2-CH_3), 2.16 and 2.28(each 3 H, s, CMe_2), 3.08(1 H, dd, *J* 2.5 and 15.6, 3β-H), 3.26(1 H, dd, *J* 5.5, and 15.6, 3α-H), 4.15(1 H, dd, *J* 5.0 and 6.1, NH), 4.34(2 H, q, *J* 7.1, -CH_2-CH_3), 4.28 and 4.35(2H, 2dd, *J* 5.0, 6.1 and 14,1 NCH_2), 4.87(1 H, 2d, *J* 2.5 and 5.5, 2-H), 7.28-7.38(5H, m, C_6H_5).

Ethoxycarbonyl 2-[(2*R*,*S*$_S$)-2-benzylsulfinamoyl-4-oxoazetidin-1-yl]-3-methylbut-2-enoate (4b): The same treatment of carboxylic acid **3b** as described for the preparation of **4a** gave title compound **4b**

(78%) as a yellowish oil; R_f 0.32 [dichloromethane-methanol (4:2 v/v)]; IR (film)ν_{max}/cm^{-1} 3215w, 2990m, 1800vs, 1780vs, 1620w, 1360s, 1250m, 1150vs, 1060s, and 1025s; ^{1}H NMR ($CDCl_3$) δ 1.36(3 H, t, *J* 7.1, -CH_2-CH_3), 2.00 and 2.27(each 3 H, s, CMe_2), 3.24(1 H, dd, *J* 5.2, and 15.4, 3α-H), 3.43(1 H, dd, *J* 2.2, and 15.4, 3β-H), 4.21-4.27(2 H, 2dd, *J* 5.7, 6.0 and 13.5 NCH_2), 4.32(1 H, 2d, *J* 5.7 and 6.0, NH), 4.34(2 H, q, *J* 7.1, -CH_2.CH_3), 4.87(1 H, dd, *J* 2.2 and 5.2, 2-H), 7.26-7.35(5H, m, C_6H_5).

(5*R*,6*R*)-4-benzyl-2-isopropylidene-5-oxo-5-thia-1,4-diazabicyclo[4.2.0]octane-3,8-dione (5a): To a cooled solution (0 °C) of mixed anhydride **4a** (118 mg, 0.30 mmol) in dry dichloromethane (15 mL) triethylamine was added drop-by-drop until the pH was adjusted to 7.5. The mixture was allowed to warm to room temperature. After being stirred for 1 hr., the mixture was washed and then treated with 1 mol/dm^{-3} hydrochloric acid (10 mL). The organic phase was washed and dried (Na_2SO_4). Evaporation of the organic layer under reduced pressure and purification of the residue by silica gel chromatography with dichloromethane-ethyl acetate (gradient eluation) gave the title compounds **5a** (37 mg, 42%) as a crystalline solid; R_f 0.70 [dichloromethane-ethyl acetate (4:2) v/v]; m.p. 164-166 °C (diethyl ether-acetone); $[\alpha]_D^{20}$ = +179 (*c* 1, CH_2Cl_2); IR (film)ν_{max}/cm^{-1} 1775vs, 1670s, 1610m, 1390m, 1355s, 1270m, 1230s, 1140m, 1080s, 1020m; ^{1}H NMR ($CDCl_3$) δ 2.08 and 2.30(each 3H, s, CMe_2), 3.20(1 H, dd, *J* 1.0 and 15.3 7β-H), 3.39(1H, dd, *J* 4.3 and 15.3 7α-H), 4.65 and 5.21(2 H, 2d, J 15.0 CH_2), 4.78(1 H, dd, *J* 1.0 and 4.3 6-H), 7.33(5 H, s, C_6H_5). Found C, 58.90; H, 5.65; N, 9.05; S, 9.85; $C_{15}H_{16}N_2O_3S$ requires C, 59.19; H, 5.30; N, 9.21; S, 10.53.

(5*S*,6*R*-4-benzyl-2-isopropylidene-5-oxo-5-thia-1,4-diazabicyclo[4.2.0]octane-3,8-dione (5b): To a treatment of mixed anhydride **4b** as described for the preparation of **5a** gave title compound **5b** (32%) as yellowish oil; R_f 0.65 [dichloromethane-ethyl acetate (4:2) v/v ; $[\alpha]_D^{20}$ = +118 (*c* 0.4, CH_2Cl_2); IR (film)ν_{max}/cm^{-1} 1780vs, 1665s, 1610m, 1390m, 1350s, 1265m, 1230s, 1080s; ^{1}H NMR ($CDCl_3$) δ 2.06 and 2.33(each 3H, s, CMe_2), 2.91(1 H, dd, *J* 2.5 and 16.5 7β-H), 3.50(1 H, dd, *J* 5.0 and 16.5 7α-H), 4.35 and 5.30(2 H, 2d, *J* 14.9, CH_2Ph), 4.65(1 H, dd *J* 2.5 and 5.2, 6-H), 7.32(5 H, s, C_6H_5); Found C, 59.40; H, 5.55; N, 9.00; S, 9.70; $C_{15}H_{16}N_2O_3S$ requires C, 59.19; H, 5.30; N, 9.21; S, 10.53.

Methyl (2*R*,*R*$_S$)-1-(1-benzylcarbamoyl-2-methylpropenyl)-4-oxoazetidine-2-sulfinate [13,14] **(8b)**:

(*a*) Solution of 5-thia-1,4-diazabicyclo[4.2.0]octane **5a** (100 mg, 0.33 mmol) in dry methanol (10 mL) was stirred at r.t. for 2 hrs., and methanol removed by evaporation under reduced pressure. Nonvolatile residue was dissolved into dichloromethane (20 mL) and treated with 1 mol/dm^3 hydrochloric acid (20 mL) and aq. layer was extracted with dichloromethane (20 mL). The organic phase was washed and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure and purification of the residue by silica gel chromatography with dichloromethane-ethyl acetate (gradient eluation) gave compound **8b** as a white foam (95 mg, 87 %); R_f 0.32 [dichloromethane-methanol (4:2 v/v)]; $[\alpha]_D^{20}$ = -11.9 (*c* 1, CH_2Cl_2); IR (film)ν_{max}/cm^{-1} 3300m, 1775vs, 1650s, 1520s, 1450m, 1430m, 1355s, 1290m, 1130s, 980s; ^{1}H NMR ($CDCl_3$) δ 1.85 and 2.03(each 3 H, s, CMe_2), 3.14(1 H, dd, *J* 5.2, and 15.7, 3α-H), 3.47(1 H, dd, *J* 2.3, and 15.7, 3β-H), 3.80(3 H, s, OCH_3), 4.49(2 H, d, *J* 5.8, NCH_2), 4.67(1 H, dd, *J* 2.3 and 5.2, 2-H), 6.47(1 H, t, *J* 5.8, NH), 7.33(5H, m, C_6H_5); Found: C, 57.47; H, 5.86; N, 8.02; S, 8.70; $C_{16}H_{20}N_2O_4S$ requires C, 57.12; H, %.6.00; N, 8.33; S, 9.53.

(*b*) To a cooled solution (0 °C) of mixed anhydride **7b** (157 mg, 0.50 mmol) in dry dichloromethane (15 mL), benzylamine was added drop-by-drop until pH was adjusted to 7.5. The resulting mixture was allowed to warm to room temperature and then stirred for 30 min. After work-up as described above, the title compound **8a** (90 mg; 54 %) was obtained.

Methyl (2*R*,*S*S)-1-(1-benzylcarbamoyl-2-methylpropenyl)-4-oxoazetidine-2-sulfinate (8a):

(*a*) The same treatment of 4-thia-1,4-diazabicyclo[4.2.0]octane **5b** as described for the preparation of **8b** (procedure a) gave compound **8a** (80 %) as yellowish oil; R_f 0.21 [dichloromethane-methanol (4:2 v/v)]; $[\alpha]_D^{20}$ = +1.8 (*c* 1, CH_2Cl_2); IR (film) ν_{max}/cm^{-1} 3300m, 1775vs, 1650s, 1525s, 1355s, 1115s, 995m 960s; ^1H NMR ($CDCl_3$) δ 1.87 and 2.05(each 3 H, s, CMe_2), 3.12(1 H, dd, *J* 3.2, and 15.0, 3β-H), 3.15(1 H, dd, *J* 4.7, and 15.0, 3α-H), 3.68(3 H, s, OCH_3), 4.49(2 H, d, *J* 5.9, NCH_2), 4.67(1 H, dd, *J* 3.2 and 4.7, 2-H), 6.96(1 H, t, *J* 5.9, NH), 7.30(5H, m, C_6H_5).

(*b*) The same treatment of mixed anhydride **7a** as described for the preparation of **8b** (procedure b) gave compound **8a** (28 %).

References and Notes

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12. The symbol (R_S) given in this text indicates that the chirality of the sulfur is *R*.
13. The S_S configuration of sulfinates corresponds to R_S configuration of sulfinamides.
14. The isomers of sulfinates with higher R_f and isomers of sulfinamides with lower R_f have the same configuration.

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