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The asymmetric hetero-Diels–Alder reaction and addition of allylic organometallics to 10-*N*,*N*-dicyclohexylsulphamoyl-(2*R*)-isobornyl glyoxylate

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Abstract

The recent development of very effective chiral auxiliaries has led to the design of 10-*N*,*N*-dicyclohexylsulphamoyl-(*R*)-isoborneol, which is similar to Oppolzer's (2*R*)-bornane-10,2-sultam but less effective on account of a less rigid structure. 10-*N*,*N*-Dicyclohexylsulphamoyl-(*R*)-isobornyl glyoxylate was examined in Diels–Alder and organometallic addition reactions. The results obtained were compared with those achieved by application of *N*-glyoxyloyl-(2*R*)-bornane-10,2-sultam.

1. Introduction

In recent years, we have introduced a highly effective glyoxylic acid derivative **2**,[1,2] bearing Oppolzer's chiral auxiliary **1**[3] (Scheme 1). Compound **2** was shown to be the reagent of choice for the hetero-Diels–Alder reaction,[4] providing a straightforward route to enantiomerically pure deoxy and amino-deoxy sugars.[5,6] It was also successfully applied in an ene reaction[7] and an aldol-type addition to 2-trimethylsilyloxyfuran[8] furnishing the corresponding products with very high asymmetric induction. In organometallic additions, compound **2** has shown some limitations. Addition of allyltrimethylsilane to compound **2**, catalyzed by Lewis acids, provided the corresponding homoallylic alcohols with good to excellent diastereoselectivity,[9] but the labile nature of the amide bond in *N*-glyoxyloyl-(2*R*)-bornane-10,2-sultam **2** precludes use of classical organometallic reagents, e.g. Grignard compounds, in this type of reaction. To this end, we decided to prepare the glyoxylate bearing 10-*N*,*N*-dicyclohexylsulphamoyl-

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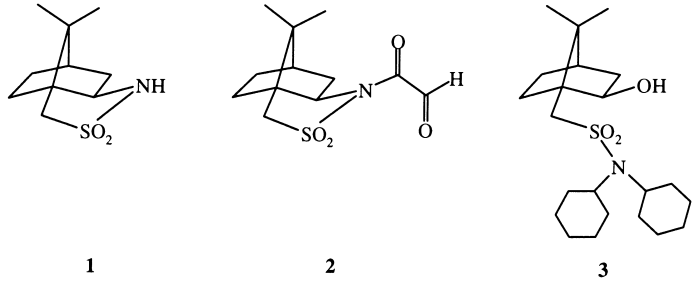
(*R*)-isoborneol **3**, another camphor-10-sulfonic acid-derived chiral auxiliary with a high diastereodifferentiating power, as shown by Oppolzer et al.[10,11]



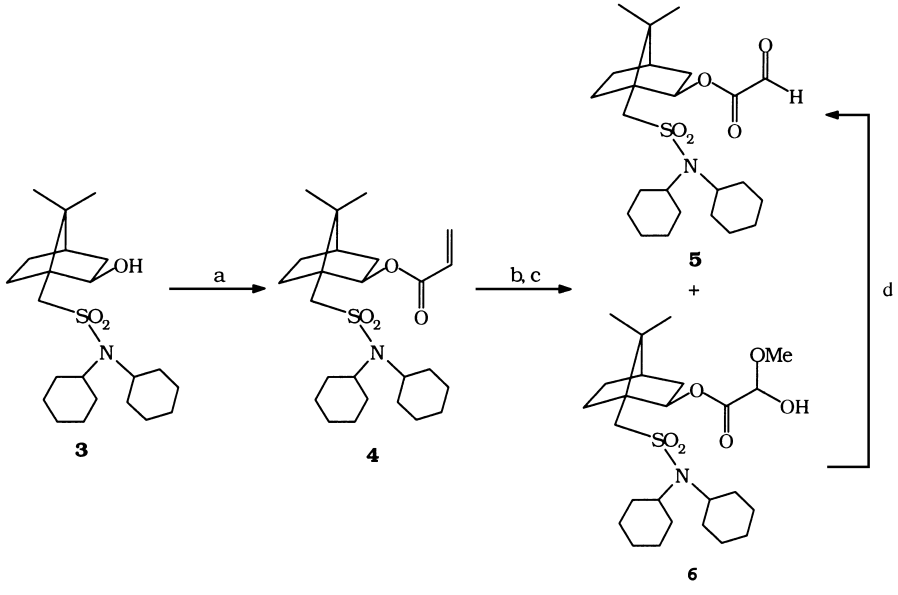
1 **2** **3**

Scheme 1.

2. Results and discussion

*2.1. Synthesis of 10-*N,N*-dicyclohexylsulphamoyl-(*R*)-isobornyl glyoxylate **5***

10-*N*,*N*-Dicyclohexylsulphamoyl-(*R*)-isoborneol **3** was prepared according to a known procedure.[10] Reaction of **3** with acrylic acid in the presence of 2-chloro-*N*-methylpyridinium iodide furnished the corresponding acrylate **4**,[12] which was used in the synthesis of 10-*N*,*N*-dicyclohexylsulphamoyl-(*R*)-isobornyl glyoxylate **5**. Thus, ozonolysis of **4**, followed by quenching with dimethyl sulfide, gave a crystalline product which turned out to be a mixture of 10-*N*,*N*-dicyclohexylsulphamoyl-(*R*)-isobornyl glyoxylate **5** and its methyl hemiacetal **6** in a ratio of 1:2, as revealed by ^{1}H NMR. This mixture was converted to the pure glyoxylate **5** by heating at 100°C under high vacuum (Scheme 2).

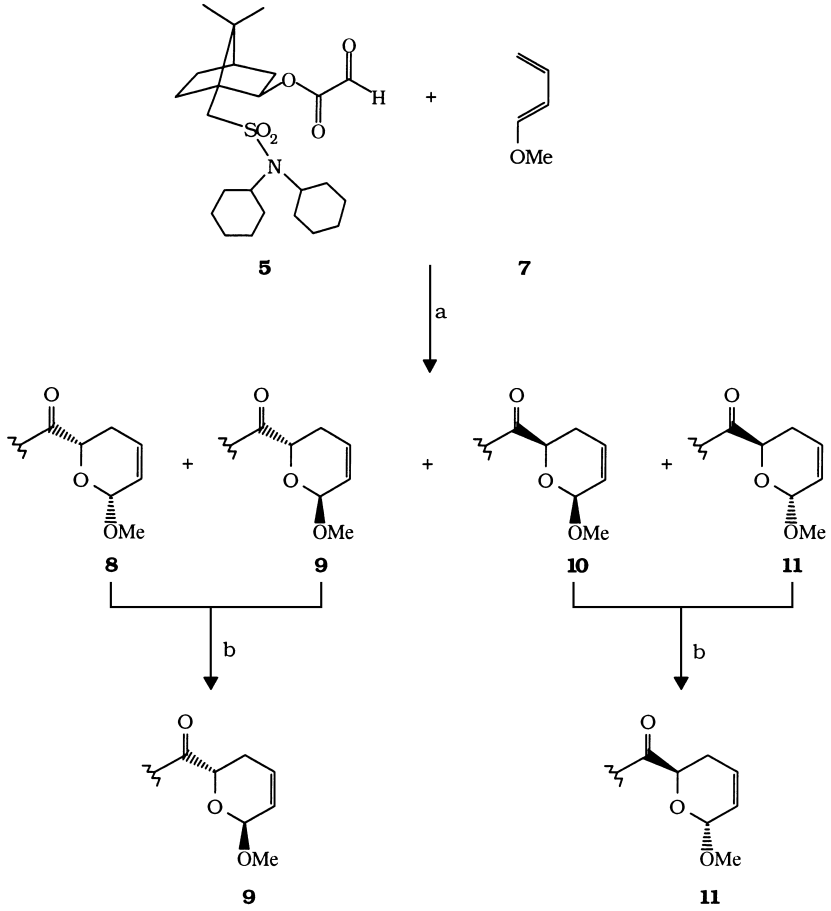


3 **4** **5** **6**

Scheme 2. Reagents and reaction conditions: (a) acrylic acid, 2-chloro-1-methylpyridinium iodide; (b) O_3, CH_2Cl_2:MeOH (6:8); (c) Me_2S, −78°C; (d) 100°C, 0.5 torr, 2 h

2.2. The hetero-Diels–Alder reaction of **5** with 1-methoxybuta-1,3-diene **7**

The properties of this new chiral glyoxylate were first checked in the hetero-Diels–Alder reaction with 1-methoxybuta-1,3-diene **7**. The high-pressure technique[13] and/or Eu(fod)$_3$ catalysis[14,15] were applied in order to improve the asymmetric induction. The cycloaddition of diene **7** to chiral dienophile **5** provided four cycloadducts: two *cis*-diastereoisomers **8** and **10** by *endo* addition, and two *trans*-diastereoisomers **9** and **11** by *exo* addition. The crude reaction mixture was subjected to acidic isomerization with pyridinium *p*-toluenesulphonate (PPTS),[16] which gave two *trans*-diastereoisomers **9** and **11** separable via flash chromatography (Scheme 3). The results of the [4+2] cycloaddition are presented in Table 1.



Scheme 3. Reagents and reaction conditions: (a) 20°C, CH_2Cl_2, the amounts of catalyst and the pressure are indicated in Table 1; (b) PPTS, MeOH, rt, overnight

According to the X-ray analysis of a single crystal obtained from the pure diastereoisomer **11** the *R*-configuration at C-2′ was established (Fig. 1).

The Diels–Alder reaction was carried out under various conditions. In the beginning, when we examined the diastereomeric excess and chemical yield under ambient conditions, the products were obtained in rather low chemical yields and diastereomeric excesses (25% and 34% d.e., respectively) with the predomination of the (*R*)-diastereoisomer **11** (Table 1, entry 1). This indicates that the glyoxylate **5** is a less active dienophile than *N*-glyoxyloyl-(2*R*)-bornane-10,2-sultam **2**. The application of high pressure caused inversion of the direction of asymmetric induction and in this case the (*S*)-diastereoisomer **9**

Table 1
The asymmetric [4+2] cycloaddition of diene **7** to heterodienophile **5**

Entry	Pressure	Temp. [°C]	Time [h]	Catalyst	Yield [%]	Asymmetric induction [**11**]:[**9**]	Absolute configuration at C-2'
1	1 atm	20	72	-	25	67/33	*R*
2	20 kbar	20	20	-	28	22/78	*S*
3	1 atm	20	72	1%	38	66/34	*R*
4	1 atm	20	48	2%	31	71/29	*R*
5	1 atm	20	48	3%	39	71/29	*R*
6	1 atm	20	24	5%	85	73/27	*R*

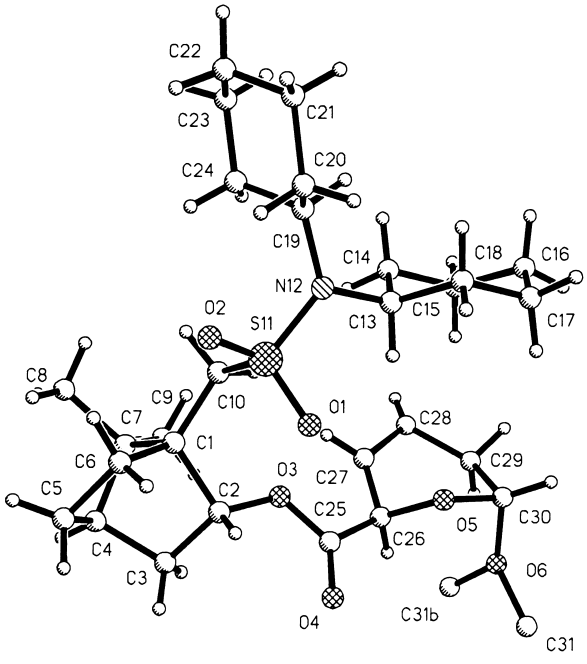
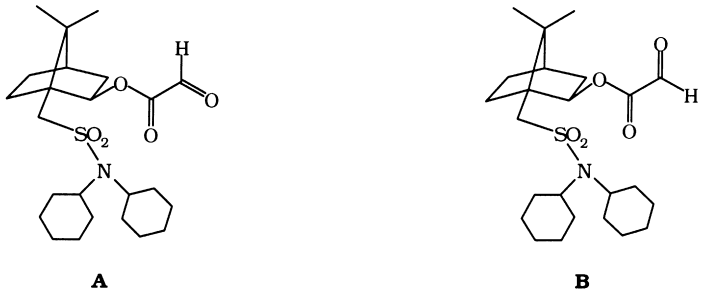


Figure 1. Molecular structure of compound **11**

was predominant (entry 2). We also studied the relationship between the molar equivalent of $Eu(fod)_3$ added and diastereoselectivity (entries 3–6). The best result in terms of both chemical yields and diastereoisomeric excess was obtained with 5% of the catalyst (entry 6).

For a rationalization of our results, we postulate two preferred conformations of heterodienophile. On account of the strain of the O–CO bond, and as suggested by X-ray analysis, the conformations **A** and **B** should predominate (Scheme 4). The approach of diene **7** to dienophile **5** should occur from the less hindered side of the sultam group.

The CO/CHO *s-trans*-conformation **B** is favoured under normal conditions, due to an unfavourable

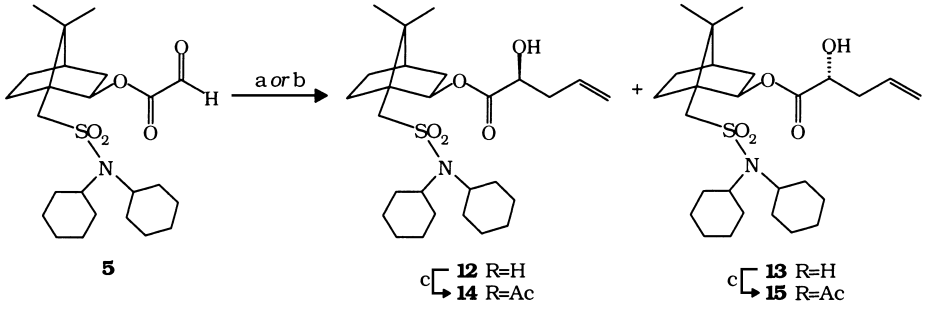


Scheme 4.

interaction of the CO/CHO in *s-cis* planar conformer **A**, as proposed by Oppolzer et al.[10,11] for [4+2] cycloaddition of cyclopentadiene to 10-*N*,*N*-dicyclohexylsulphamoyl-(*R*)-isobornyl acrylate **4** and confirmed by X-ray analysis.[12,17] When using $Eu(fod)_3$, the *s-trans*-conformer is also preferred; chelation involves the carbonyl group and one of the sulphonyl oxygen atoms, and similarly, as in the former case, unfavourable interaction of (Eu) O=C/CHO is eliminated.

*2.3. Organometallic addition to 10-*N,N*-dicyclohexylsulphamoyl-(*R*)-isobornyl glyoxylate **5***

The asymmetric effectiveness of 10-*N*,*N*-dicyclohexylsulphamoyl-(*R*)-isobornyl glyoxylate **5** was also examined in nucleophilic addition reactions (Scheme 5). Two approaches for obtaining the homoallylic alcohol were undertaken. Firstly, the addition of an allyl-Grignard reagent to 10-*N*,*N*-dicyclohexylsulphamoyl-(2*R*)-isobornyl glyoxylate **5** was studied (Table 2). The results were unsatisfactory (40% d.e.), but remarkably advantageous in comparison to those achieved by application of *N*-glyoxyloyl-(2*R*)-bornane-10,2-sultam **2**.[9] An addition of 1 equivalent of LiCl did not improve the stereoselectivity; however, a slight increase of chemical yield (50%) was observed.



Scheme 5. Reagents and reaction conditions: (a) allylmagnesium chloride, −78°C, THF; (b) allyltrimethylsilane, Lewis acid, CH_2Cl_2, the other conditions: see Table 2; (c) Ac_2O, py, rt, 3 h

Next, we examined the addition of allyltrimethylsilane to 10-*N*,*N*-dicyclohexylsulphamoyl-(2*R*)-isobornyl glyoxylate **5** in the presence of Lewis acids (Table 3). The diastereoisomeric ratio (**12**/**13**) was determined by ^1H NMR spectroscopy. The crude reaction mixture was subjected to acetylation; at this stage diastereoisomeric products **14** and **15** were easily separated into single diastereoisomers via flash chromatography and then **15** was recrystallized. The relative configuration within this diastereoisomer was established by X-ray analysis. The results are presented in Fig. 2.

Several aspects of the data shown in Table 3 are noteworthy. The enantiomeric excesses, as well as the chemical yields, were lower then those obtained with *N*-glyoxyloyl-(2*R*)-bornane-10,2-sultam **2** as the chiral substrate. The application of various catalysts failed to improve substantially either of these

Table 2
The asymmetric addition of allylmagnesium chloride to glyoxylate **5**

Catalyst [equiv]	Temp. [°C]	Time [h]	Yield [%]	Asymmetric induction [**12**] : [**13**]	Absolute configuration at C-2'
-	-78	1	40	30 : 70	*R*
LiCl [1]	-78	1.5	50	30 : 70	*R*

Table 3
The asymmetric addition of allyltrimethylsilane to glyoxylate **5**

Entry	Catalyst [equiv]	Temp. [°C]	Time [h]	Yield [%]	Asymmetric induction [**12**] : [**13**]	Absolute configuration at C-2'
1	$SnCl_4$ [0.5]	-20	3	20	61 : 39	*S*
2	$SnCl_4$ [1]	-20	3	55	61 : 39	*S*
3	$SnCl_4$ [2]	-20	3	80	67 : 33	*S*
4	$SnCl_4$ [10]	-78	2	70	82 : 18	*S*
5	$TiCl_4$ [0.5]	-20	3	40	30 : 70	*R*
6	$TiCl_4$ [1]	-20	3	74	82 : 18	*S*
7	$TiCl_4$ [2]	-20	3	76	72 : 28	*S*
8	BF_3*Et_2O[1]	0	92	30	60 : 40	*S*
9	$ZnBr_2$ [1]	7	24	58	51 : 49	*S*
10	$ZnCl_2$ [1]	7	24	78	52 : 48	*S*

experimental variables. The best results were obtained using strong Lewis acids, such as $TiCl_4$ and $SnCl_4$ (entries 4 and 6, respectively).

The results obtained for the reaction catalyzed by these Lewis acids could be explained by predominance of *s-cis* conformer **A** (Scheme 4), that leads to the product of *S*-absolute configuration. What is more, in the case of a deficiency of the catalyst (0.5 equiv. of $TiCl_4$) the product with the opposite absolute configuration was obtained, probably as a result of the predominance of *s-trans* conformer **B**. The use of Lewis acids such as $BF_3 \cdot Et_2O$, $ZnBr_2$ or $ZnCl_2$, that have weak chelating properties, results in very poor asymmetric induction, probably due to the presence of both conformers **A** and **B** in the transition state.

3. Experimental

3.1. General

Optical rotations were recorded using a JASCO DIP-360 polarimeter with a thermally jacketed 10 cm cell. IR spectra were obtained on a Perkin–Elmer Spectrum 2000 and Perkin–Elmer 1640 FTIR spectrophotometers in KBr pellets. ^1H NMR and ^{13}C NMR spectra were recorded using a Bruker AM 500 spectrometer and Varian Unity Plus (200 MHz and 500 MHz). All chemical shifts are quoted in

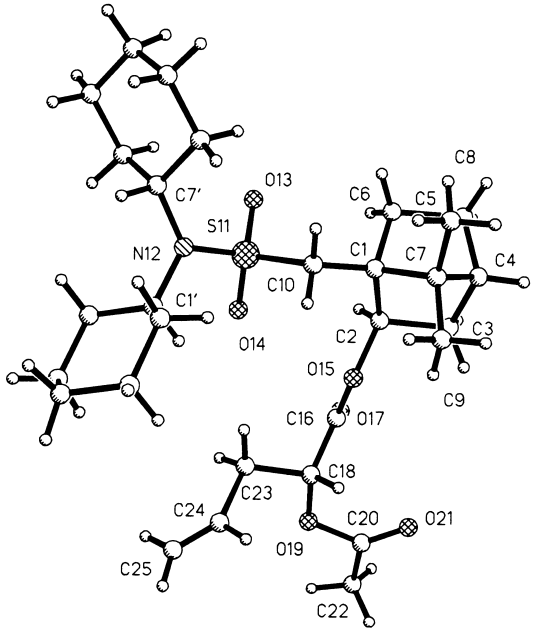


Figure 2. Molecular structure of compound **15**

parts per million relative to tetramethylsilane (δ, 0.00 ppm) and coupling constants (J) are given in hertz. Mass spectra were recorded on an AMD-604 Intectra instrument using the electron impact (EI) and LSIMS techniques. Flash column chromatography was performed according to Still et al.[18] on silica gel (Kieselgel-60, Merck, 200–400 mesh). 1-Methoxybuta-1,3-diene was prepared according to a literature procedure.[19] Reactions with Lewis acids were carried out under an argon atmosphere with anhydrous solvents that had been previously dried using standard laboratory methods.

*3.2. Preparation of 10-*N,N-*dicyclohexylsulphamoyl-(2*R*)-isobornyl acrylate **4***[10]

A mixture of alcohol **3** (0.56 mmol), N(*n*Pr)$_3$ (5.6 mmol) and acrylic acid (1.41 mmol) in toluene (3.8 mL) was added to α-chloro-*N*-methylpyridinium iodide (720 mg, 3.8 mmol). Heating of the mixture at reflux for 1 h, dilution with toluene, drying, evaporation and crystallization gave acrylate **4** (189 mg, 70%).

*3.3. Preparation of 10-*N,N-*dicyclohexylsulphamoyl-(2*R*)-isobornyl glyoxylate **5** and its methyl hemiacetal **6***

The solution of 10-*N*,*N*-dicyclohexylsulphamoyl-(2*R*)-isobornyl acrylate **4** (0.413 g, 0.91 mmol) in a 8:6 mixture of CH_2Cl_2:MeOH was cooled to −78°C and treated with ozone until the solution was blue. The dimethyl sulfide (2 mL) was then added at −78°C, and the mixture was stirred at room temperature over a period of 15 h. After careful evaporation of the solvents and an excess of dimethyl sulfide, a mixture of **5** and **6** was obtained (0.351 g, 85%).

3.4. Preparation of (2′S)-methoxy-(6′S)-[10-dicyclohexylsulphamoyl-(2R)-isobornyl]-carbonyl-5′,6′-dihydro-2H-pyran **9** and (2′R)-methoxy-(6′R)-[10-dicyclohexylsulphamoyl-(2R)-isobornyl]-carbonyl-5′,6′-dihydro-2H-pyran **11**

A solution of diene (1 mL, 10 mmol), heterodienophile (0.2 g, 0.44 mmol) and $Eu(fod)_3$ in CH_2Cl_2 (3 mL) was stirred. The reaction mixture was filtered through a short silica gel pad, then the filtrate was evaporated to dryness and the oily residue was dissolved in MeOH. To this solution PPTS (0.1 g, 0.4 mmol) was added. The *cis–trans* isomerization was carried out at room temperature over a period of 1 h. The solvent was evaporated and the residue was treated with Et_2O (5 mL). The precipitated inorganic salts were filtered off and the crude reaction mixture was purified by flash chromatography (hexane:ethyl acetate, 9:1) to afford the pure products **9** and **11**.

Diastereoisomer **9**. Mp: 172–173°C; $[\alpha]_D^{20}$ −39.2 (*c* 0.85, $CHCl_3$); IR (KBr) ν_{max}=3441, 2932, 2855, 1729, 1691, 1399, 1324, 1289, 1143, 1110, 1051, 981, 893, 820, 773, 719, 645, 575, 525 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.1–5.5 (m, 1H, C*H*=C), 5.8–5.7 (m, 1H, C=C*H*), 5.05 (dd, J=7.7, 3.0 Hz, 1H, OC*H*C=O), 4.95 (m, 1H, OC*H*OCH_3), 4.47 (dd, J=10.1, 5.5 Hz, 1H, CH_2C*H*O), 3.43 (s, 3H, OCH_3), 3.4–3.2 (m, 3H, C*H*SO_2 and 2×C*H*N), 2.65 ($^1/_2$ABq, J=13.3 Hz, 1H, C*H*′SO_2), 2.4–2.3 (m, 2H, C*H*$_2$CH=C), 2.1–1.0 (m, 27H, 13×CH_2 and CH), 0.99 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.4 (C=O), 127.7 (C=CH), 125.8 (C=CH), 96.0 (O*C*HOMe), 65.5 (CHO), 57.5 (CHN), 55.5 (O*C*HC=O), 53.6 (CH_2SO_2), 49.5 (C), 49.1 (C), 44.5 (CH), 44.4 (CH), 39.6 (CH_2), 32.9 (CH_2), 32.8 (CH_2), 30.1 (CH_2), 27.5 (CH_2), 26.9 (CH_2), 26.4 (CH_2), 25.2 (CH_2), 20.4 (CH_3), 20.0 (CH_3); m/z (EIMS): 537 (M^+) (9.4), 505 (4.6), 494 (1.1), 442 (1.1), 380 (56), 316 (4), 298 (51), 292 (100), 254 (9), 244 (34), 228 (31), 180 (50), 157 (12), 135 (80), 111, (91), 93 (24), 81 (30), 55 (25); m/z (EIHR) calcd for $C_{29}H_{47}NO_6S$ (M^+): 537.3124; found: 537.31204.

Diastereoisomer **11**. Mp: 163–164°C; $[\alpha]_D^{20}$ −32.9 (*c* 1.1, $CHCl_3$); IR (KBr) ν_{max}=3475, 2931, 2855, 1748, 1447, 1402, 1322, 1242, 1142, 1109, 1047, 980, 894, 854, 772, 717, 644, 579, 525 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.1–6.0 (m, 1H, C*H*=C), 5.8–5.6 (m, 1H, C=C*H*), 5.2–5.1 (m, 1H, OC*H*OCH_3), 5.07 (dd, J=7.8, 2.9 Hz, 1H, OC*H*C=O), 3.49 (s, 3H, OC*H*$_3$), 3.5–3.2 (m, 3H, C*H*SO_2 and 2×C*H*N), 2.70 ($^1/_2$ABq, J=13.4 Hz, 1H, C*H*′SO_2), 2.6–2.5 (m, 1H, C*H*CH=C), 2.4–2.3 (m, 1H, C*H*′CH=C), 2.05–1.07 (m, 27H, 13×CH_2 and CH), 1.05 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.9 (C=O), 128.4 (C=CH), 126.9 (C=CH), 98.3 (O*C*HOMe), 70.7 (CHO), 57.6 (CHN), 55.1 (O*C*HC=O), 53.8 (CH_2SO_2), 49.6 (C), 49.2 (C), 44.4 (CH), 39.6 (CH), 39.4 (CH_2), 33.0 (CH_2), 32.8 (CH_2), 32.7 (CH_2), 32.6 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 27.0 (CH_2), 26.9 (CH_2), 26.5 (CH_2), 26.48 (CH_2), 26.4 (CH_2), 25.2 (CH_2), 25.1 (CH_2), 20.4 (CH_3), 20.0 (CH_3); m/z (EIMS): 537 (M^+) (19), 505 (10), 380 (51), 298 (60), 292 (57), 244 (44), 228 (34), 180 (52), 157 (18), 135 (100), 111 (90), 93 (30), 81 (35), 55 (26); m/z (EIHR) calcd for $C_{29}H_{47}NO_6S$: 537.31240; found: 537.31257.

3.5. Preparation of 10-dicyclohexylsulphamoyl-(2R)-isobornyl-2′(S)-hydroxy-pent-4-enoate **12** and 10-dicyclohexylsulphamoyl-(2R)-isobornyl-2(R)-hydroxy-pent-4-enoate **13**

A solution of glyoxylate **6** (117 mg, 0.258 mmol) in dry THF (5 mL) was cooled under argon (−78°C), and then allylmagnesium chloride was added (2 M solution in THF, 0.2 mL, 0.4 mmol). The reaction was stirred for 1 h, then poured into a saturated solution of NaCl. The reaction mixture was allowed to warm up to room temperature. It was extracted with ether (3×30 mL). Flash chromatography (hexane:ethyl acetate, 9:1) of the residue afforded a mixture of two diastereoisomers **12** and **13** (51 mg, 40%). The asymmetric induction was assessed by ^1H NMR analysis.

A mixture of diastereoisomers **12** and **13** ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.9–5.7 (m, 1H, C*H*=CH_2 for **12** and **13**), 5.3–5.1 (m, 2H, CH=C*H*$_2$ for **12** and **13**), 5.07 (dd, J=7.9, 3.2 Hz, 0.5H, C*H*OH for **12**), 5.01 (dd, J=7.8, 3.0 Hz, 0.5H, C*H*OH for **13**), 4.2–4.1 (m, 1H, C*H*O for **12** and **13**), 3.3–3.1 (m, 3H, C*H*SO_2 and 2×C*H*N for **12** and **13**), 3.0 (bs, 0.5H, O*H* for **12**), 2.84 (bs, 0.5H, O*H* for **13**), 2.67 ($^1/_2$ABq, J=13.3 Hz, 0.5H, C*H*SO_2 for **12**), 2.66 ($^1/_2$ABq, J=13.3 Hz, 0.5H, C*H*SO_2, for **13**), 2.6–2.3 (m, 2H, CH_2 for **12** and **13**), 2.1–1.0 (m, 27H, 13×CH_2 and CH for **12** and **13**), 1.00 (s, 1.5H, CH_3 for **13**), 0.99 (s, 1.5H, CH_3 for **12**), 0.89 (s, 1.5H, CH_3 for **13**), 0.88 (s, 1.5H, CH_3 for **12**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.2 (C=O for **12**), 172.6 (C=O for **13**), 132.8 (=CH for **13**), 132.5 (=CH for **12**), 119.1 (=CH_2 for **13**), 118.4 (=CH_2 for **12**), 80.1 (CHO for **12**), 79.9 (CHO for **13**), 57.6 (CHN for **12**), 57.5 (CHN for **13**), 54.1 (CH_2SO_2 for **13**), 53.9 (CH_2SO_2 for **12**), 49.7 (C for **13**), 49.6 (C for **12**), 49.3 (C for **13**), 49.2 (C for **12**), 44.5 (CH for **12**), 44.4 (CH for **13**), 39.7 (CH_2), 39.4 (CH_2), 38.9 (CH_2), 38.1 (CH_2), 33.3 (CH_2), 32.9 (CH_2), 32.8 (CH_2), 32.4 (CH_2), 30.8 (CH_2), 30.3 (CH_2), 27.0 (CH_2), 27.0 (CH_2), 26.5 (CH_2), 26.5 (CH_2), 26.4 (CH_2), 26.4 (CH_2), 25.2 (CH_2), 25.2 (CH_2), 20.4 (CH_3), 20.3 (CH_3), 20.1 (CH_3), 20.0 (CH_3); m/z (HRLSIMS) calcd for $(M+Na)^+$ $C_{27}H_{45}N_1O_5S_1Na$: 518.2916; found: 518.2902. When using allyltrimethylsilane, the solution of glyoxylate **6** (78 mg, 0.17 mmol) in CH_2Cl_2 (5 mL) was cooled under argon to −78°C. The Lewis acid was then added, followed by the allyltrimethylsilane (71 μL, 0.45 mmol). The workup procedure was the same as above.

*3.6. Preparation of 10-dicyclohexylsulphamoyl-(2*S*)-isobornyl-2′ (*S*)-acetoxy-pent-4-enoate **14** and 10-dicyclohexylsulphamoyl-(2*R*)-isobornyl-2′ (*S*)-acetoxy-pent-4-enoate **15***

The mixture of diastereoisomers **13** and **14** (558 mg, 1.13 mmol) was dissolved in 4 mL of pyridine and then treated with acetic anhydride (4 mL). The solution was stirred for 1 h at room temperature. The post-reaction mixture was washed with aqueous $CuSO_4$ (3×50 mL), and finally diluted with Et_2O (2×70 mL) and dried ($MgSO_4$). After evaporation in vacuo, the residue (97%) was subjected to flash chromatography (hexane:ethyl acetate, 9:1) in order to separate the two diastereoisomers.

Diastereoisomer **14** (oil). $[\alpha]_D^{20}$ −39.7 (*c* 1, $CHCl_3$); IR (KBr) ν_{max}=3464, 2936, 2857, 1746, 1644 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.9–5.6 (m, 1H, C*H*=CH_2), 5.2–5.0 (m, 3H, CH=C*H*$_2$ and C*H*O), 5.0–4.9 (m, 1H, C*H*OAc), 3.4–3.1 (m, 3H, C*H*SO_2 and 2×C*H*N), 2.9–2.5 (m, 3H, C*H′*SO_2 and CH_2), 2.1 (s, 3H, O=CC*H*$_3$), 2.1–1.0 (m, 27H, 13×CH_2 and CH), 0.93 (s, 3H, CH_3), 0.87 (s, 3H, CH_3); ^{13}C NMR (200 MHz, $CDCl_3$): δ 169.9 (C=O), 168.0 (C=O), 132.2 (=CH), 118.4 (=CH_2), 79.7 (CH–O), 71.7 (CHAc), 57.4 (CHN), 53.5 (CH_2SO_2), 49.3 (C), 49.0 (C), 44.3 (CH), 39.2 (CH_2), 35.3 (CH_2), 32.9 (CH_2), 32.5 (CH_2), 30.3 (CH_2), 26.9 (CH_2), 26.3 (CH_2), 25.0 (CH_2), 20.5 (CH_3), 20.3 (CH_3), 19.6 (CH_3); m/z (LSIMS, NBA) 560 $(M+Na)^+$ (15), 538 $(M+H)^+$ (10), 380 (80), 298 (15), 228 (30), 149 (37), 135 (100), 133 (20); m/z (HRLSIMS) calcd for $C_{29}H_{47}NO_6SNa$: 560.3018; found: 560.3018.

Diastereoisomer **15**. Mp: 127°C (from methanol/hexane); $[\alpha]_D^{20}$ −19.0 (*c* 1.6, $CHCl_3$); IR (KBr) ν_{max}=3484, 2856, 1757, 1746, 1644 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.0–5.7 (m, 1H, C*H*=CH_2), 5.3–5.0 (m, 3H, CH=C*H*$_2$ and C*H*O), 5.1–4.9 (m, 1H, C*H*OAc), 3.4–3.1 (m, 3H, C*H*SO_2 and 2×C*H*N), 2.8–2.5 (m, 3H, C*H′*SO_2 and CH_2), 2.13 (s, 3H, O=CC*H*$_3$), 2.0–1.0 (m, 27H, 13×CH_2 and CH), 1.04 (s, 3H, CH_3), 0.9 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.4 (C=O), 168.1 (C=O), 132.4 (=CH), 118.5 (=CH_2), 79.6 (CH–O), 71.5 (CHAc), 57.5 (CHN), 53.8 (CH_2SO_2), 49.5 (C), 49.2 (C), 44.3 (CH), 39.4 (CH_2), 34.9 (CH_2), 33.2 (CH_2), 32.4 (CH_2), 30.5 (CH_2), 27.0 (CH_2), 26.4 (CH_2), 25.2 (CH_2), 20.6 (CH_3), 20.4 (CH_3), 19.9 (CH_3); m/z (EIMS) 537 (190) M^+, 298 (100), 244 (75), 180 (37), 135 (37); m/z (EIHR) calcd for $C_{29}H_{47}NO_6S$: 537.3124; found: 537.3134.

Table 4
Crystal data and structural refinement for compounds **11** and **15**

Identification code	**11**	**15**
Empirical formula	$C_{29}H_{49}NO_6S$	$C_{29}H_{47}NO_6S$
Formula weight M_r	539.75	537.74
Temperature [K]	293(2)	293(2)
Wavelength [Å]	1.54178	1.54178
Crystal system	orthorhombic	orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
Unit cell dimensions [Å]	a = 8.7459(5) b = 15.7260(10) c = 21.455(2)	a = 7.7346(5) b = 19.511(2) c = 20.281(2)
Volume [$Å^3$]	2950.9(4)	3060.6(4)
Z	4	4
Density (calculated) [Mg/m^{-3}]	1.215	1.167
Absorption coefficient [mm^{-1}]	0.302	1.255
F(000)	1176	1168
Crystal size [mm]	0.21 x 0.34 x 0.38	0.14 x 0.14 x 0.35
Range for data collection	3.48 to 74.10	3.14 to 64.33
Index ranges	$0\le h\le 10$, $0\le k\le 19$, $-26\le l\le 0$	$-9\le h\le 0$, $-21\le k\le 0$, $0\le l\le 22$
Reflections collected	2384	1853
Independent reflections	2202 [R(int) = 0.0001]	1853 [R(int) = 0.0000]
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2202 / 0 / 305	1853 / 0 / 335
Goodness-of-fit on F^2	1.128	1.114
Final R indices [$I>2\alpha(I)$]	$R_1 = 0.0812$, $wR_2 = 0.2148$	$R_1 = 0.0446$, $wR_2 = 0.1139$
R indices (all data)	$R_1 = 0.0864$, $wR_2 = 0.2224$	$R_1 = 0.0472$, $wR_2 = 0.1167$
Absolute structure parameter	0.09(6)	-0.01(4)
Extinction coefficient	0.0020(6)	0.0009(2)
Largest diff. peak and hole [e $Å^{-3}$]	0.517 and -0.244	0.173 and -0.143.

*3.7. X-Ray structure determination of compounds **11** and **15***

Suitable crystals were grown from ethyl acetate/hexane **11** and methanol/hexane **15** solutions. The measurements were done on a Nonius MACH3 diffractometer with Express package. No absorption correction was applied. Table 4 shows details of data collection and structure refinement. Positions for the hydrogen atoms were calculated and refined in the riding mode with isotropic thermal parameters 20% higher than that of the parent atoms.

In the case of compound **11**, both disorder and large thermal vibrations were detected at the newly generated asymmetric centres at carbons C26 and C30. Therefore, special attention has been paid during the structural elucidation and refinement processes. Careful refinement of different structural models taking into account both geometrical parameters and the relative electron densities of particular peaks in electron density maps brought us to the model shown in Fig. 1. The six-membered sugar ring has two locations (occupancy factors 0.7:0.3) obtained by parallel displacement of all atoms. After completing the ring with 0.7 population of atoms, the highest peak on the difference electron density maps was assigned to the O5a atom, which confirms the fact that rotation about O3–C25 was not observed and the compound is a single isomer.

The structures were solved by the SHELXS86[20] and refined by SHELXL93[21] programs. Crystallo-

graphic data have been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, England, as supplementary publication No. CCDC 114 322 for compound **11** and No. CCDC 114 321 for compound **15**.

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