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Diastereoselective Synthesis of α-Bromo amides leading to Diastereomerically Enriched α-Amino-, α-Hydroxy- and α-Thiocarboxylic Acid Derivatives.

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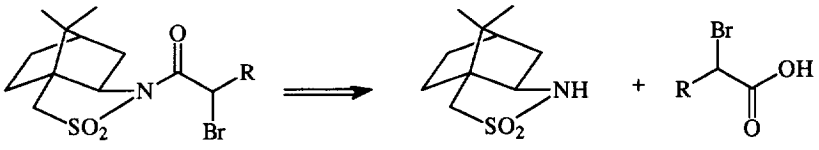
Abstract: α-Bromo amides derived from Oppolzer's camphorsultam can be prepared diastereoselectively starting from racemic α-bromo acids, and undergo epimerisation under appropriate conditions leading to an enhanced d.e.. By reacting the individual isomers or the mixture of diastereoisomers with a suitable nucleophile it is possible to obtain α-substituted carboxylic acids, including α-amino- α-hydroxy- and α-thiocarboxylic acid derivatives, in diastereomerically enriched form.

INTRODUCTION

The asymmetric synthesis of natural and unnatural α-amino acids has been the subject of extensive interest in recent years and several elegant procedures have been reported.[1] These include the asymmetric hydrogenation of dehydroamino acids, reactions of chiral enolates with nitrogen electrophiles and the asymmetric alkylation of heterocyclic nitrogen containing compounds. Likewise, various methods have been developed for the preparation of optically active α-hydroxy acids, including the asymmetric reduction of α-keto esters,[2,3] and asymmetric oxygenation of chiral imide enolates.[4] In an effort to develop a general approach to the asymmetric synthesis of α-substituted carboxylic acids we have studied the preparation and reactions of a series of N-(2-bromoalkanoyl) derivatives (**1**) of bornane-10,2-sultam (**2**).[5] These derivatives are formed diastereoselectively and undergo epimerisation in some solvents leading to an enhancement of the diastereomeric ratio. We have therefore investigated their nucleophilic displacement reactions and have found that in some cases they afford α-substituted carboxylic acid derivatives with high diastereomeric excess.[6]



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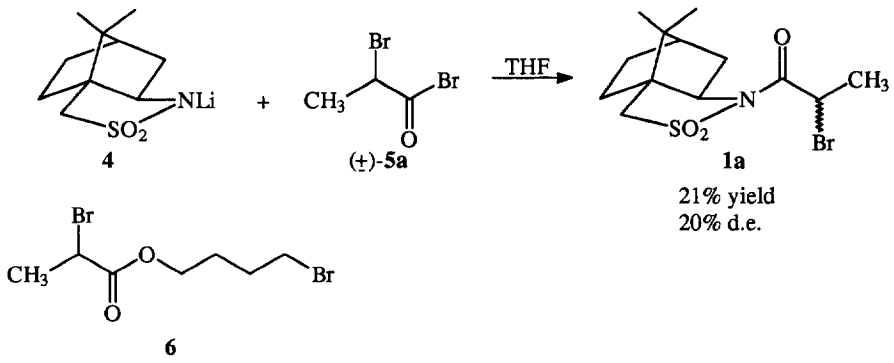
RESULTS AND DISCUSSION

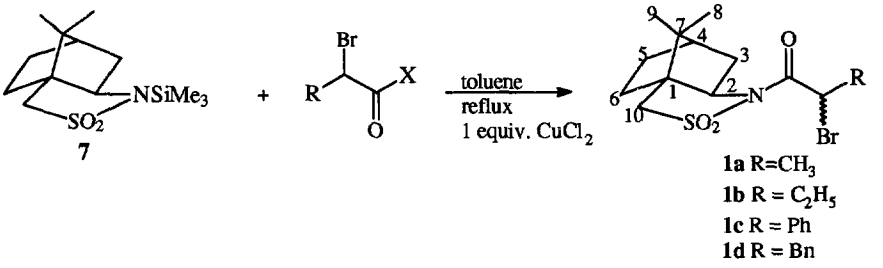
Preparation of N-(2-bromoalkanoyl) derivatives

The attempted preparation of the α-bromo amides (**1**) using the methods usually employed for the preparation of N-alkanoyl sultams[7-9] was largely unsuccessful. Reaction of the lithium derivative (**4**) of the sultam (**2**) with racemic 2-bromopropionyl bromide (**5a**) did however give a 21% yield of the required α-bromo amide (**1a**), as a mixture of diastereoisomers (20% d.e.) (Scheme 1). However no sultam was recovered and the main product was the α-bromo ester (**6**) formed by reaction of the α-bromo acid bromide with THF.



Scheme 1

The fact that (**1a**) was obtained as an unequal mixture of two diastereoisomers attracted our immediate attention and we therefore decided to seek a milder, more efficient method for the preparation of such compounds. We turned our attention to a recent method[10] which involves reacting the N-trimethylsilyl derivative (**7**) of the sultam with the acid chloride in the presence of a catalytic amount of $CuCl_2$ (equation 1). This method was applied to the preparation of the α-bromo amide derivatives (**1**) using either the racemic α -bromo acid chloride or the α-bromo acid bromide as the starting material. The acid bromide was found to give a much higher yield than the acid chloride (Table 1). For the preparation of the α-bromopropionyl and α-bromobutyryl derivatives (**1a**) and (**1b**) it was found that one equivalent of $CuCl_2$ was required and this was transformed into an insoluble brown deposit (presumably copper (0)) in the course of the reaction.



(eq. 1)

Table I. Preparation of α-bromo amides using Kocienski's method[10]

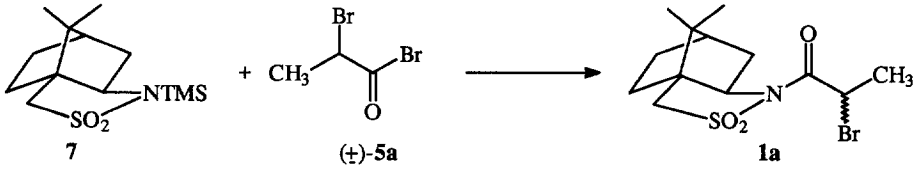
Product	R	X	Cryst. yield (%)	d.e. (%)	Recovered sultam (%)	Corrected yield (%)
1a	CH_3	Br	70	27	0	70
1b	C_2H_5	Cl	41	22	45	75
1b	C_2H_5	Br	75	40	0	75
1c	Ph	Cl	0	-	60	0
1c	Ph	Br	33	0	65	94
1d	Bn	Br	0	-	0	0*

*This reaction gave a complex mixture which contained some of the product as shown by HPLC but also contained many other components.

We therefore decided to investigate the preparation of the 2-bromopropionyl derivative (**1a**) using different solvents and different additives to bring about the reaction. We first examined the reaction (equation 2) in toluene at room temperature with various catalysts (Table II), and found that the d.e. in favour of the (*R*)-isomer‡ (assignment based on X-ray structure - see later) was identical for each of the additives employed. Furthermore the d.e. decreased with time showing that the (*R*)- and (*S*)-isomers are the kinetic and thermodynamic products respectively. The use of a catalyst increased the yield, NaF being the best catalyst for this reaction.

‡ the descriptors (*R*)/(*S*) refer to the α-bromo stereogenic centre, with those from the sultam being omitted for clarity.

We next examined the reaction in acetonitrile (Table III). In this case the use of a catalyst had no effect on the yield of the reaction. Once again the d.e. decreased with time.



7 (±)-5a 1a (eq. 2)

Table II. Preparation of α-bromo amide derivative ***1a*** *in toluene*

Catalyst	d.e. 1hr (%)	d.e. 3hrs (%)	d.e. 24hrs (%)	Ratio of **1a** : **2***
0.2 eq. $CuCl_2$	68	66	50	80 / 20
0.2 eq. $CuBr_2$	68	62	52	56 / 44
0.2 eq. NaF	70	68	52	90 / 10
0.15 eq. Cu	70	62	58	71 / 29
None	66	62	58	39 / 61

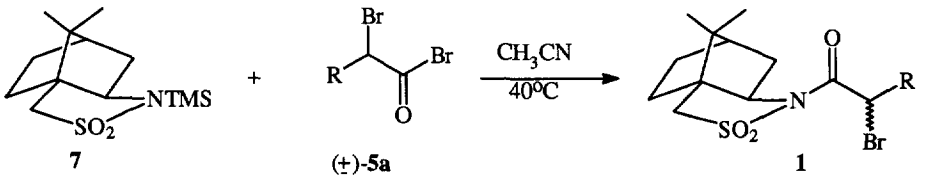
* determined by comparing the integration of the CH_2SO_2 signals for (**1a**) and (**2**) in the ^1H NMR spectrum of the crude product.

Table III. Preparation of α-bromo amide derivative ***1a*** *in* CH_3CN

Catalyst	d.e. 1hr (%)	d.e. 3hrs (%)	d.e. 24hrs (%)	Ratio of **1a** : **2***
0.2 eq. $CuCl_2$	82	78	66	87 / 13
0.2 eq. $CuBr_2$	80	78	70	87 / 13
0.2 eq. NaF	92	84	66	85 / 15
0.15 eq. Cu	92	84	68	88 / 12
None	90	80	58	90 / 10

*see footnote to Table II

We also studied the effect of temperature and found that at 60°C in acetonitrile a significant amount of by-products are formed. We therefore concluded that carrying out the reaction at 40°C without a catalyst gave the best compromise between yield, d.e., and ease of purification, particularly since the d.e. could be subsequently enhanced (see below). Results obtained under these conditions for a series of α-bromoalkanoyl bromides (equation 3) are shown in Table IV. It is noteworthy that in the case of the α-bromophenylacetyl derivative (R=Ph, Table IV) a 1:1 mixture of the two diastereomeric α-bromo amides was obtained.



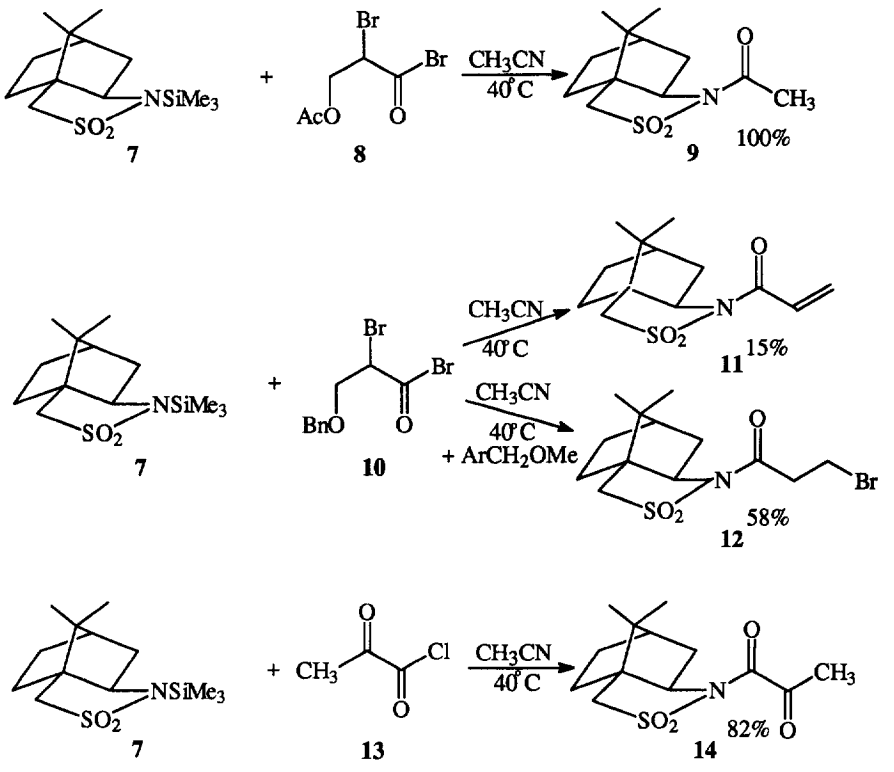
7 (±)-5a 1 (eq. 3)

Table IV. Optimised preparation of N-(2-bromoalkanoyl)bornane-10,2-sultams

Product	R	Time (hrs)	Conversion (%)	d.e. (%)	Crystallized yield (%)	Corrected yield (%)
1a	CH_3	48	100	58	75	75
1b	C_2H_5	48	100	66	72	72
1c	Ph	48	60	0	45	69
1d	Bn	48	100	50	48*	48

*N-(3-phenylpropenoyl)bornane-10,2-sultam also obtained in 30% yield.

Unfortunately the generality of this reaction is limited by the occurrence of side reactions in some cases (see, for example, R = Bn, Table IV). Two other cases in which unexpected products were obtained are illustrated in Scheme 2. Both involve substrates in which a β-alkoxy- or acyloxy- substituent is present. Although the formation of the N-acetyl derivative (**9**) from (**8**) can be readily explained, the formation of the N-acryloyl derivative (**11**) from (**10**) is less easily rationalised. Furthermore, when this reaction was carried out in the presence of p-methoxybenzyl methyl ether (to trap TMSBr) the 3-bromopropionyl derivative (**12**) was obtained. However the method has been successfully extended to the preparation of the pyruvyl derivative (**14**) in 82% yield.

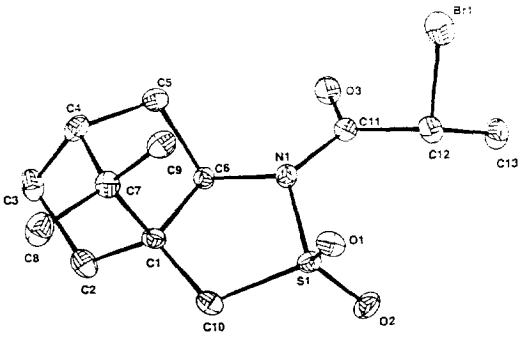


Scheme 2

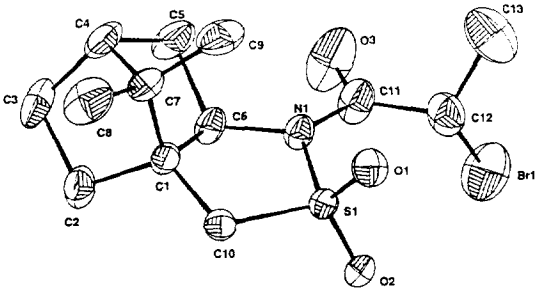
In each of the four cases listed in Table IV the two diastereoisomeric α-bromo amides (**1a-d**) could be clearly resolved on reverse phase HPLC. The two diastereomers could also be separated by flash chromatography on silica, and were fully characterised by ^{1}H and ^{13}C NMR spectroscopy. The relative configuration of the α-centre to the sultam was determined by X-ray crystallography (see, for example, Figure 1) and hence knowing the absolute configurations of the sultam, that of the α-bromo stereogenic centre was established.. In every case the major isomer after equilibration was the (*R*)-isomer.

Epimerisations of N-(2-bromoalkanoyl) derivatives (1)

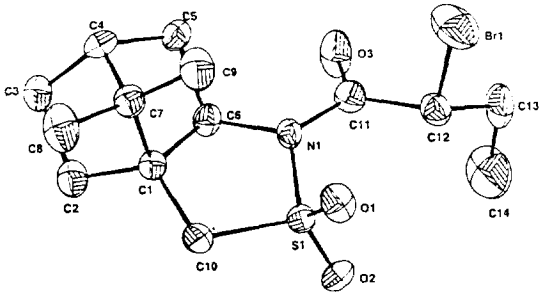
The fact that **1a** and **1b** were obtained in 70 - 75% yield and 58 - 66% d.e. (Table IV) and that the d.e. varied between 50 - 92% depending on the time of reaction (Tables II and III) prompted us to study the epimerisation of the N-(2-bromoalkanoyl) sultams.



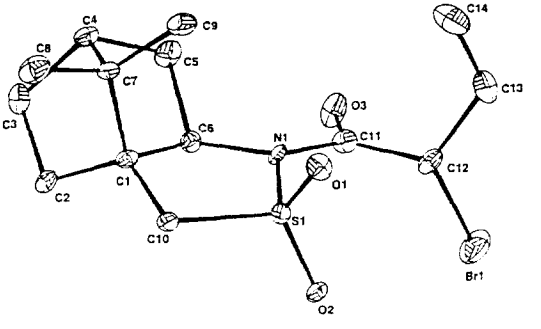
(R)-**1a**



(S)-**1a**



(R)-**1b**



(S)-**1b**

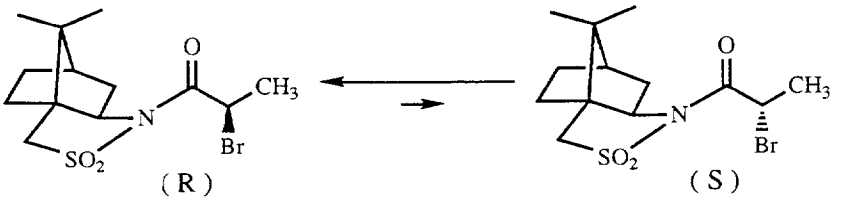
Figure 1. X-Ray analysis of the (R) and (S) isomers of the α-bromopropionyl and α-bromobutyryl derivatives ***1a*** *and* ***1b***

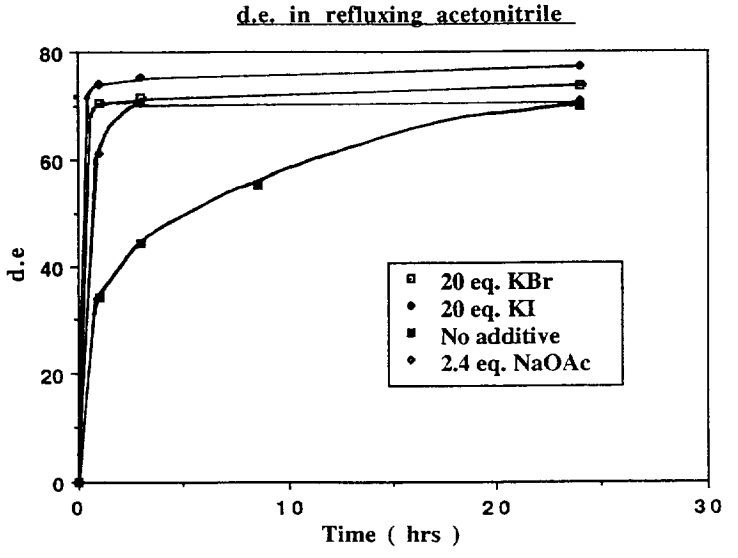
The epimerisation of **1a** was studied with various additives and in solvents of increasing polarity, of which polar aprotic solvents such as acetonitrile and DMSO were found to be the best (Figure 2). In these solvents addition of potassium bromide increased the d.e. from 0% to 70% in 1 hr, while the increase was much slower in the solvent alone. Sodium acetate gave the same result as potassium bromide in acetonitrile but gave quantitative displacement of bromide in DMSO. Potassium iodide gave the iodo compounds *in situ* and epimerisation was observed between the two iodo derivatives leading to a slightly higher d.e. value at equilibrium. However potassium iodide also led to extensive cleavage of the alkanoyl sultam. Similar results were obtained with the 2-bromobutyryl derivative (**1b**) and the 2-bromo-3-phenylpropionyl derivative (**1d**). In the case of the α-bromophenylacetyl derivative (**1c**) a 50/50 ratio was obtained at equilibrium in acetonitrile whatever additive was used, while in DMSO a displacement reaction occurred).

Two possible pathways for the epimerisation can be envisaged. The first involves keto-enol tautomerism. The second involves nucleophilic displacement of the bromide anion. We have no formal evidence in favour of either pathway although the facile displacement of the bromide by iodide or acetate (in DMSO) would tend to support a displacement. In the case of the α-bromopropionyl, the α-bromobutyryl and the α-bromo-3-phenylpropionyl derivatives (**1a**), (**1b**) and (**1d**) the (*R*)-isomer with the bromine located on the less hindered face is preferred. In the case of the α-bromophenylacetyl derivative (**1c**) the similar size of Br and Ph would explain the 50/50 mixture obtained.

Nucleophilic displacement reactions.

Starting from either the enantiomerically pure 2-bromoalkanoyl derivative or the diastereomeric mixture it is possible in principle to obtain enantiomerically enriched α-substituted carboxylic acids. Thus S_N2 displacement of bromide with a good, unhindered nucleophile should preclude epimerisation and give the pure (*S*)-product from the pure (*R*)-bromide, and *vice versa*. On the other hand, starting from a mixture of the diastereoisomers and displacing the bromide with a soft, quite hindered nucleophile should allow equilibration to occur giving mainly the (*R*)-product which would be formed from the more reactive (*S*)-isomer (Scheme 3).





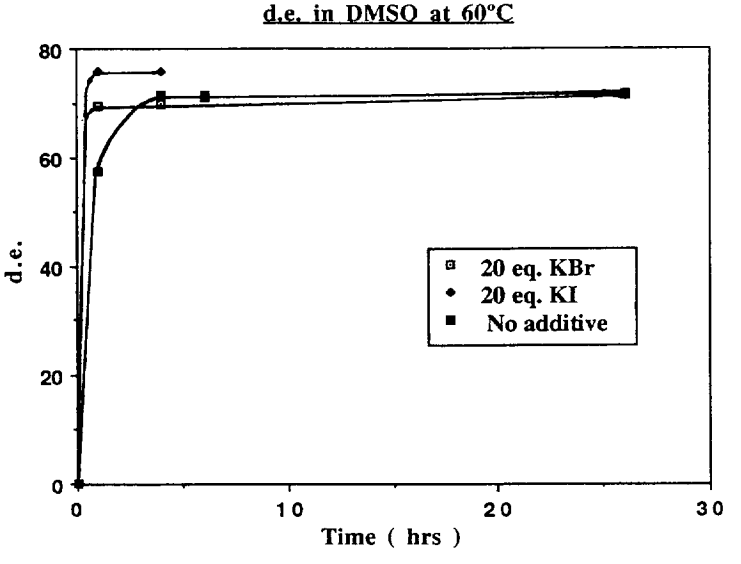
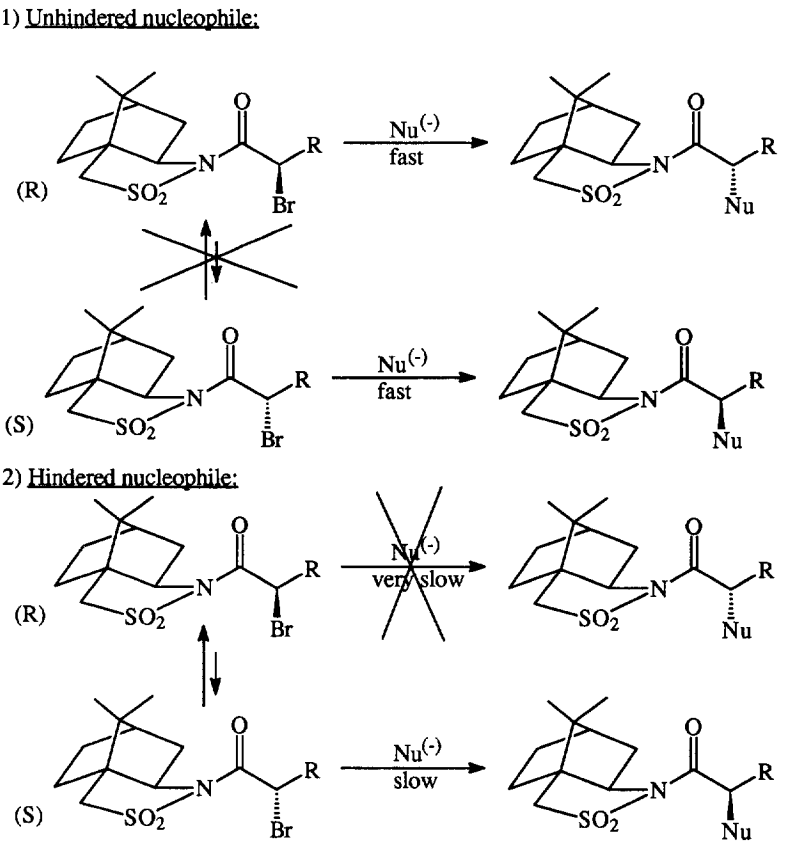
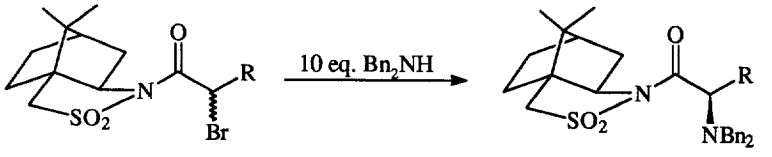


Figure 2. Epimerisation of α-bromoamide ***1a*** *in acetonitrile and DMSO*



Scheme 3

Table V shows the results obtained using dibenzylamine as nucleophile (equation 4). All of the reactions on the α-bromopropionyl derivative (**1a**) proceeded in essentially quantitative yield and gave 100% d.e. of the (*R*)-α-amino acid derivative (**15a**). Similar observations involving reactions of α-bromo esters of pantolactone and 2-oxoimidazolidine-4-carboxylate with benzylamine have been recently reported by Durst *et al*[11] and Nunami *et al.*[17] Unfortunately we have not been able to extend this method to the other members of the series since complex mixtures were obtained with the α-bromobutyryl and α-bromophenylacetyl derivatives (**1b** and **1c**).

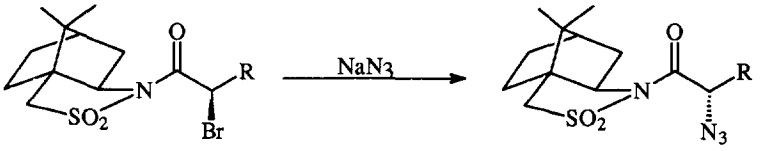


1 (*R*)-**15** (eq. 4)

Table V. Reactions of α-bromo amides with dibenzylamine

	R	Conditions	(*R*) / (*S*) Bromide	(*R*) / (*S*) Amine
1a	CH_3	Toluene/DMSO reflux	60 / 40	100 / 0
		DMSO 60°C	60 / 40	100 / 0
		Refluxing acetonitrile	100 / 0 or 55 / 45 or 0 / 100	100 / 0
1b	C_2H_5	Refluxing acetonitrile	100 / 0 or 33 / 67 or 0 / 100	Complex mixture
1c	Ph	Refluxing acetonitrile	50 / 50	Complex mixture

Tables VI and VII show the results obtained using sodium azide (equation 5). Epimerisation can be prevented in this case by carrying out the reaction at 60°C in DMSO (Table VI). The relative configuration of the α-stereogenic centre of the azide (**16a**) was determined by X-ray crystallography. Extending this reaction to other members of the series gave the same outcome (Table VII). In each case a small amount of cleavage of the amide occurred but, since the product and the parent sultam can be readily separated, this does not present a major problem.



(*R*)-**1** (*S*)-**16** (eq. 5)

*Table VI Reactions of α-bromo amide **1a** with 3 eq. NaN^3*

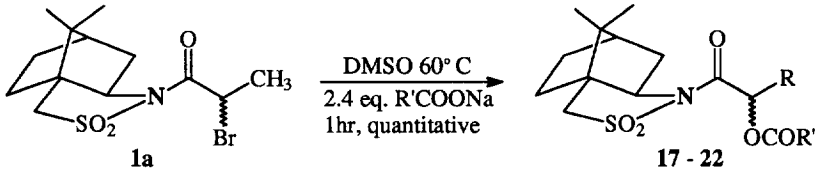
Conditions	(*R*) / (*S*) Bromide	(*R*) / (*S*) Azide	Sultam cleaved (%)
DMSO 20°C 5hrs	65 / 35	59 / 41	0
	84 / 16	30 / 70	0
DMSO 60°C 1hr	100 / 0	0 / 100	8
CH_3CN 20°C 3 days	85 / 15	28/ 72	0

Table VII Reactions of α-bromo amides with 1.5 eq. NaN_3 in DMSO at 60° C

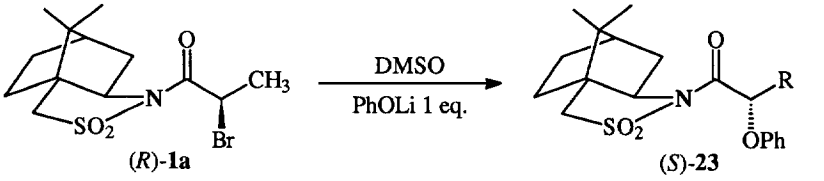
	R	(*R*) / (*S*) Bromide	(*R*) / (*S*) Azide	Yield (%)	Sultam cleaved (%)
1a	CH_3	100 / 0	0 / 100	91	3.5
1b	C_2H_5	100 / 0	0 / 100	94	2.5
1b	C_2H_5	0 / 100	100 / 0	95	3
1c	Ph	50 / 50	50 / 50	92	-

Tables VIII-X summarise results obtained with oxygen and sulphur nucleophiles on the α-bromopropionyl derivative (**1a**). When NaOAc is used (Table VII) some epimerisation is evident. Unfortunately more hindered carboxylate salts (equation 6) gave little or no improvement in the diastereoselectivity of the reaction. Similar results were obtained starting from the α-bromobutyryl and α-bromophenylacetyl derivatives (**1b**) and (**1c**).

Most alcoholates gave complex mixtures or led to cleavage of the alkanoyl sultam. However using lithium phenolate (equation 7) under carefully controlled conditions minimised such problems and lead to direct displacement with very little epimerisation (Table IX). Koh and Durst have studied similar reactions using α-bromo esters of pantolactone.[12] Similar results (Table X) were also obtained with thiophenolate (equation 8).



1a **17 - 22** (eq. 6)



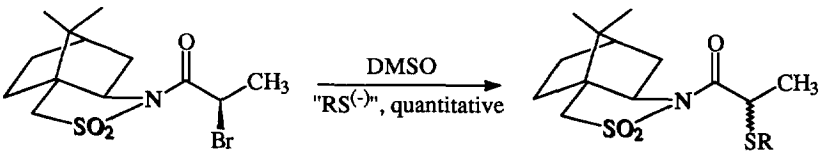
(*R*)-**1a** (*S*)-**23** (eq. 7)

*Table VIII. Reactions of α-bromo amides **1a-c** with carboxylate salts*

Product	R	(*R*) / (*S*) Bromide	(*R*) / (*S*) Ester	Yield (%)
17a	CH_3	65 / 35	60 / 40	87
17a	CH_3	100 / 0	6 / 94	87
17b	CH_3	60 / 40	60 / 40	89
17c	CH_3	50 / 50	50 / 50	93
18a	Ph_2CH	65 / 35	60 / 40	91
19a	^tBu	65 / 35	55 / 45	92
20a	Ph	68 / 32	40 / 60	88
21a	2,4,6 $(CH_3)_3Ph$	69 / 31	50 / 50	95
22a	H	100 / 0	17 / 83	91

*Table IX. Reactions of α-bromo amides **1a** and **1b** with PhOLi*

Product	Conditions	(*R*) / (*S*) Bromide	(*R*) / (*S*) Product	Sultam cleaved (%)	Yield (%)
23a	20°C, 10 mins	85 / 15	24 / 76	5	82
23a	20°C, 10 mins	100 / 0	5 / 95	5	74
23a	60°C, 5 mins	100 / 0	0 / 100	12	75
23b	60°C, 5 mins	100 / 0	0 / 100	18	77



(*R*)-**1a** **24,25a** (eq. 8)

*Table X. Reactions of α-bromo amide **1a** with $RS^{(-)}$*

Product	"$RS^{(-)}$"	Conditions	(*R*)/(*S*) Bromide	(*R*)/(*S*) Product	Yield (%)
24a	CH_3COSNa 2.3 eq.	DMSO 60°C, 1hr	79 / 21	50 / 50	81
25a	PhSLi 1 eq.	DMSO rt, 10 mins	100 / 0	0 / 100	98
25a	PhSLi 1 eq.	DMSO rt, 10 mins	100 / 0	0 / 100	98

CONCLUSION

We have shown that diastereomerically enriched α-amino-, α-hydroxy- and α-thiocarboxylic acid derivatives can be prepared by reacting diastereomeric α-bromo amides with appropriate nucleophiles. Furthermore the α-bromo amides can be prepared diastereoselectively in greater than 50% yield starting from racemic α-bromo acids. These transformations are made possible by interconversion of the diastereoisomeric α -bromo amides under carefully controlled conditions.

EXPERIMENTAL

Infrared spectra were obtained on a Perkin Elmer 1725X FTIR spectrometer equipped with Perkin Elmer's IR data manager. ^{1}H and ^{13}C NMR spectra were recorded on Bruker 250 WM and 400 WM spectrometers at 250 and 400 MHz for ^{1}H spectra and at 63 and 100 MHz for ^{13}C spectra. Tetramethylsilane was used as internal standard and deuteriochloroform as solvent. Mass spectra were obtained on a VG-12-250 low resolution quadrupole mass spectrometer, while accurate mass measurements were obtained on a ZAB-E high resolution double focussing instrument. Melting points were obtained on an Electrothermal digital melting point apparatus and are uncorrected. X-ray analyses were provided by the SERC X-ray service based at University College Cardiff.

HPLC analyses were carried out using a Milton Roy 3100 SpectroMonitor and 3100 ConstaMetric Pump, coupled to a CI-4100 integrator, and using a reverse-phase (methanol-water) Apex II ODS 5μ column. Flash chromatography was performed with silica gel (Merck 9385, Kieselgel 60, 230 - 400 mesh).

Tetrahydrofuran and ether were dried by stirring overnight over calcium hydride, passing down a dry alumina column, and distillation from sodium wire and benzophenone. Toluene and petroleum spirit (b.p. 60-80°) were dried by distillation from calcium hydride and stored over sodium wire. Acetonitrile was dried by distillation from calcium hydride. Chlorotrimethylsilane and triethylamine were also purified using the same procedure. Dimethylsulphoxide was distilled under vacuum from calcium hydride.

Preparation of α-bromo acids from the corresponding α-amino acids:

(DL)-Phenylalanine (10.0 g, 60.7 mmol) was suspended in H_2SO_4 (130 ml, 1.25 M) containing KBr (23.3 g, 195.5 mmol, 3.2 eq.) and the slurry stirred for 10 min at -8°C. Then $NaNO_2$ (4.3 g, 62.2 mmol, 1.0 eq.) was added portionwise at -8°C over 30 min, resulting in the immediate formation of red fumes. After complete

addition of $NaNO_2$, the foamy mixture was left for 1 hr at room temperature and then extracted with ethyl acetate. The ethyl acetate was dried ($MgSO_4$), filtered and evaporated to give 3-phenyl-2-bromopropanoic acid[13] (10.0 g, 72 %) as a yellow oil. ^1H NMR: 3.3 (dd(6,9), 2H, CH_2); 4.4(t(6), 1H, CHBr); 7.2(s, 5H, Ph) and 8.6 ppm (br, 1H, COOH).

3-Acetoxy-2-bromopropanoic acid was obtained as a yellow oil (9.8 g, 59 %) from (DL)-O-acetyl serine (14.5 g, 0.08 mole). ^1H NMR: 2.13 (s, 3H, CH_3); 4.45 - 4.68 (m, 3H, CH_2, CH) and 11.23 ppm (br, 1H, COOH). ^{13}C NMR: 20.63 (CH_3); 39.93 (CH); 64.09 (CH_2); 170.99 (CO) and 172.52 ppm (COOH). Mass Spec: CI (m/z %): 228/230 (65); 131 (100).

3-Benzyloxy-2-bromopropanoic acid was obtained as a brown oil (4.3 g, 65 %) from (DL)-O-benzyl serine (5.0 g, 0.026 mol). ^1H NMR: 3.79 (dd (5.72, 5.71), 1H); 3.95 (dd (8.27, 8.26), 1H, CHBr); 4.36 (dd (5.69, 5.68), 1H); 4.58 (s, 2H, CH_2); 7.25 - 7.36(m, 5H, Ph); 9.67 ppm (br, 1H, COOH), ^{13}C NMR: 41.53 (CH); 70.48 (CH_2); 73.67 (CH_2); 127.63 - 128.44 (Ar) and 173.77 ppm (COOH). Mass Spec: CI (m/z %): 276/278 (100); 198 (37); 179 (23); 108 (55).

Alternative Preparation of 3-benzyloxy-2-bromopropanoic acid:[14]

A freshly prepared solution of BnONa in benzyl alcohol (1.6 M, 30 ml, 48.6 mmols) was added at 0°C to ethyl 2,3-dibromopropionate (12.7g, 48.9 mmoles, 1.0 eq.) resulting in the immediate formation of a white slurry which was kept at 0°C for 1.5 hr. NaOH (15 ml, 5N) was then added with cooling and vigorous stirring and the resulting mixture stirred for 1 hr at r.t.. The reaction mixture was then extracted with ether and the aqueous layer acidified to pH 2 with 5N H_2SO_4 resulting in the formation of a white suspension. The suspension was then extracted with ether and the ether dried ($MgSO_4$), filtered and evaporated to give an oil which was submitted to high vacuum to remove the traces of BnOH. The product was obtained as a yellowish oil (9.7 g, 87.4 %) with ^1H NMR identical with the sample prepared above.

*Preparation of the α-bromo acid bromides (**5b - f**):*

To the stirred α-bromo acid under N_2 was added 2 eq. of PBr_3 and the slurry heated to 80°C. White fumes were then evolved and the slurry turned to an homogeneous orange solution which was kept at 80°C for 2 hrs. The solution was then allowed to cool down to r.t. and decanted from a white precipitate. The excess PBr_3 was then removed under vacuum and the acid bromide distilled as a colourless liquid. All had NMR spectra very similar to the starting acid apart from the absence of peaks due to COOH.

α-Bromophenylacetyl bromide (**5c**): bp = 140°C. ^1H NMR 5.8 (s, 1H, CH); 7.5 ppm (s, 5H, Ph).

3-Phenyl-2-bromopropanoyl bromide (**5d**): bp = 116°C (~ 3 mm Hg). ^{1}H NMR 3.0 (dd (6,9), 2H, CH_2); 4.4 (t (6), 1H, CHBr) and 6.9 ppm (s, 5H, Ph).

3-Acetoxy-2-bromopropanoyl bromide (**8**): bp = 120°C (~ 20 mm Hg). ^{1}H NMR 2.0 (s, 3H, CH_3) and 4.4 ppm (m, 3H, CH_2, CHBr).

The 3-benzyloxy-2-bromopropanoyl derivative (**10**) was characterized as its methyl ester on quenching with MeOH: ^{1}H NMR of methyl 3-benzyloxy-2-bromopropionate: 3.77 (dd (5.86, 10.20), 1H, CH_2); 3.78 (s, 3H, CH_3); 3.79 (dd (8.36, 10.15), 1H, CH_2); 4.34 (dd (5.85, 8.35), 1H, CH); 4.58 (s, 2H, CH_2Ph), and 7.25-7.37 ppm (s, 5H, Ph). ^{13}C NMR: 41.65 (CH_3); 53.08 (CH); 70.73(CH_2); 73.54 (CH_2); 127.77 (Ar_p); 127.97 (Ar_m); 128.49 (Ar_o); 137.33 (Ar_i) and 168.98 ppm (CO).

Preparation of N-trimethylsilylbornane-10,2-sultam (7):[10]

To the bornane-10,2-sultam (1.0 g, 4.6 mmols) dissolved in toluene (20 ml) containing acetonitrile (2 ml) was added trimethylsilyl chloride (3 ml, 2.6g, 23.6 mmols, 5.0 eq.) and the clear solution cooled down to 0°C under N_2 prior to the quick addition of triethylamine (2 ml, 1.45g, 14.4 mmols, 3.1 eq.) which resulted in the immediate formation of a white precipitate and of white fumes. The slurry was kept for 5 min at 0°C and then allowed to warm up to room temperature where it was kept for 2hr. It was then evaporated under vacuum until dry and the white residue was triturated with toluene (20 ml) under N_2. The precipitated salt was removed by filtration under N_2 and washed with toluene (30 ml). The mother liquor was thereafter evaporated to dryness and the residual white crystals dissolved in acetonitrile (10 ml). The solution was used in the next stage of the reaction.

*Preparation of N-(2-bromoalkanoyl)bornane-10,2-sultams (**1a - d**):*

The solution of (**7**) was reacted with 2-bromopropionyl bromide (4.1 g, 19.1 mmol, 4.1 eq.) at 40°C for 2 days, by which time it had turned red. The mixture was then quenched by addition of a 0.1 M solution of sodium carbonate and extracted with ether. The combined ether layers were dried ($MgSO_4$), filtered and evaporated to give an oil which was purified by chromatography on silica to give *N-(2-bromopropionyl) bornane-10,2-sultam* (**1a**) as a white crystalline solid (1.2 g, 75.2 %) (58 % d.e.). Careful elution (pet spirit → 5% ether in pet spirit) allowed the separation of the major (*R*)-diastereoisomer (more polar) from the minor (*S*)-diastereoisomer.

(R)-isomer: m.p. 132-134°C. ^{1}H NMR: 0.99 (s, 3H, CH_3) 1.20 (s, 3H, CH_3); 1.32-1.47 (m, 2H, H_5); 1.82 (d (6.60), 3H, CH_3); 1.86-2.10 (m, 5H, H_4, H_6, H_3); 3.45 and 3.54 (ABq (13.77), 2H, H_{10}); 3.93 (dd (5.57, 6.98),

1H, H_2) and 4.98 ppm (q (6.59), 1H, CH). ^{13}C NMR: 19.91 (CH_3); 20.47 (CH_3); 20.67 (CH_3); 26.50 (C_5); 32.76 (C_6); 37.58 (C_3); 39.44 (CH); 44.49 (C_4); 47.87 (C_7); 48.79 (C_1); 52.99 (C_{10}); 64.96 (C_2) and 168.79 ppm (CO). Mass Spec: EI (m/z %): 206 (33), 134 (100), 41 (93). CI (m/z %): 369 (30), 367 (30), 352 (10), 350 (10) and 289 (100). Acc Mass M+NH_4^+: Calc. 367.0691, Found 367.0691. IR (KBr): 3070-2830 (CH), 1697 (CO), 1330-1190 cm^{-1} (SO_2).

(S)-isomer: ^1H NMR: 0.98 (s, 3H, CH_3); 1.20 (s, 3H, CH_3); 1.31-1.47 (m, 2H, H_5); 1.87 (d (6.83), 3H, CH_3); 1.90-2.12 (m, 5H, H_4, H_6, H_3); 3.52 (s, 2H, H_{10}); 3.93 (m, 1H, H_2) and 5.04 ppm (q (6.83), 1H, CH). ^{13}C NMR: 19.85 (CH_3); 20.82 (CH_3); 23.02 (CH_3); 26.35 (C_5); 32.81 (C_6); 38.14 (C_3); 41.05 (CH); 44.52 (C_4); 47.87 (C_7); 48.78 (C_1); 52.78 (C_{10}); 65.58 (C_2) and 168.38 ppm (CO). Acc Mass M+NH_4^+: Calc. 367.0691, Found 367.0691.

N-(2-Bromobutyryl)bornane-10,2-sultam (**1b**) was obtained as a white crystalline solid (1.2 g, 72.2 %) (66 % d.e.) starting from 2-bromobutyryl bromide (4.3 g, 18.8 mmol, 4.05 eq.).

(R)-isomer: m.p. 198-202°C. ^1H NMR: 0.99 (s, 3H, CH_3): 1.06 (t (7.37), 3H, CH_3) 1.20 (s, 3H, CH_3); 1.23-1.47 (m, 2H, H_5); 1.91-2.21 (m, 7H, H_4, H_6, H_7, CH_2); 3.46 and 3.55 (ABq (13.79), 2H, H_{10}); 3.94 (dd (5.44, 5.48), 1H, H_2) and 4.77 ppm (t (7.26), 1H, CH). ^{13}C NMR: 11.91 (CH_3); 19.98 (CH_3); 20.64 (CH_3); 26.47 (C_5); 27.23 (CH_2); 32.70 (C_6); 37.55 (C_3); 44.46 (C_4); 46.46 (CH); 47.85 (C_7); 48.70 (C_1); 53.05 (C_{10}); 64.88 (C_2) and 168.24 ppm (CO). Mass Spec: EI (m/z %): 366 (5), 364 (5). CI (m/z %): 383 (60), 381 (55). Acc Mass M+NH_4^+: Calc. 381.0848, Found 381.0848. IR (KBr): 3060-2880 (CH), 1693 (CO) and 1330-1170 cm^{-1} (SO_2).

(S)-isomer: ^1H NMR: 0.98 (s, 3H, CH_3); 1.03 (t (7.33), 3H, CH_3); 1.13 (s, 3H, CH_3); 1.15-1.48 (m, 2H, H_5); 1.89-2.21 (m, 7H, H_4, H_6, H_3, CH_2); 3.48 and 3.56 (ABq (14.02), 2H, H_{10}), 3.94 (t (6.36), 1H, H_2) and 4.86 ppm (t (6.99), 1H, CH). ^{13}C NMR: 11.79 (CH_3); 19.88(CH_3); 20.79(CH_3); 26.35 (C_5); 29.85 (CH_2); 32.85 (C_6); 38.26 (C_3); 44.58 (C_4); 47.58 (CH); 47.81 (C_7); 48.67 (C_1); 52.85 (C_{10}); 65.33 (C_2) and 168.00 ppm (CO). Acc Mass M+NH_4^+: Calc. 381.0848, Found 381.0848.

N-(2-Bromo-2-phenylacetyl)bornane-10,2-sultam (**1c**) was obtained as an oil which hardened on standing (432 mg, 45.2 %) (0 % d.e.) starting from 2-bromo-2-phenylacetylbromide (2.6 g, 10.0 mmol, 4.3 eq.). ^1H NMR: 0.76 (s, 1.5H, CH_3); 0.88 (s, 1.5H, CH_3), 0.98 (s, 1.5H, CH_3); 1.24 (s, 1.5H, CH_3); 1.26-1.44 (m, 2H, H_5); 1.76-2.16 (m, 5H, H_4, H_6, H_3); 3.47 (s, 1H, H_{10}); 3.45 and 3.57 (ABq (13.76), 1H, H_{10}); 3.86-3.95 (m, 1H, H_2); 6.03 (s, 0.5H, CH); 6.09 (s, 0.5H, CH); 7.20-7.38 (m, 3H, $Ar_{m/p}$) and 7.54-7.67 ppm (m, 2H, Ar_o). ^{13}C

NMR: 19.76 (CH_3); 19.85 (CH_3); 20.23 (CH_3); 20.73 (CH_3); 26.31 (C_5); 26.38 (C_5); 32.58 (C_6); 32.67 (C_6); 37.64 (C_3); 37.70 (C_3); 44.40 (C_4); 44.46 (C_4); 47.23 (C_7); 47.64 (C_1); 48.67 (C_1); 52.78 (C_{10}); 52.97 (C_{10}); 65.18 (C_2); 65.29 (CH); 65.37 (CH); 128.18-129.69 (Ar); 134.24 (Ar_i); 135.12 (Ar_i); 166.03 (CO) and 166.79 ppm (CO). Mass Spec: EI (m/z %): 333 (12), 135 (45), 118 (40), 91 (100). CI (m/z %): 431 (20), 429 (20), 414 (8), 412 (8) and 334 (100). Acc Mass: M+NH_4^+: Calc. 429.0848, Found 429.0848. IR (film): 3140 - 2840 (CH), 1703 (CO) and 1330 - 1170 cm^{-1} (SO_2).

N-(2-Bromo-3-phenylpropionyl)bornane-10,2-sultam (**1d**) was obtained as an oil which hardened on standing (473 mg, 48 %) (50 % d.e.) along with the N-(3-phenylpropenoyl) derivative[10] (236 mg, 30%), starting from 2-bromo-3-phenylpropionylbromide (2.6 g, 9.6 mmol, 4.15 eq.).

(R)-isomer: ^{1}H NMR: 0.96 (s, 3H, CH_3); 1.18 (s, 3H, CH_3); 1.30-1.41 (m, 2H, H_5); 1.87-1.92 (m, 3H, H_4, H_6); 2.02-2.09 (m, 2H, H_3); 3.25 (dd (7.41, 14.24), 1H, CH_2); 3.49 and 3.27 (ABq (13.62), 2H, H_{10}); 3.53 (dd (7.43, 14.18), 1H, CH_2); 3.88 (dd (5.09, 7.53), 1H, H_2); 5.07 (t (7.34), 1H, CHBr) and 7.23-7.32 ppm (m, 5H, Ph). ^{13}C NMR: 19.87 (CH_3); 20.67 (CH_3); 26.45 (C_5); 32.68 (C_6); 37.54 (C_3); 39.83 (CH_2Ph); 44.51 (C_4); 44.85 (CHBr); 47.85 (C_7); 48.74 (C_1); 64.88 (C_2); 127.17 (Ar_p); 128.50 (Ar_m); 129.60 (Ar_o); 136.53 (Ar_i) and 167.76 ppm (CO). Mass Spec: EI (m/z %): 428 (5), 426 (5), 346 (80), 131 (100), 91 (55). CI (m/z %): 445 (100), 443 (95), 428 (10), 426 (10), 365 (60). Acc Mass M+NH_4^+: Calc. 443.1004, Found 443.1004. IR (KBr): 3100-2800 (CH), 1698 (CO) and 1320-1170 cm^{-1} (SO_2).

(S)-isomer: ^{1}H NMR: 0.48 (s, 3H, CH_3); 0.85 (s, 3H, CH_3); 1.25-1.39 (m, 2H, H_5); 1.89-2.08 (m, 5H, H_4, H_6, H_3); 3.31 (dd (5.95, 13.25), 1H, CH_2); 3.39 (s, 2H, H_{10}); 3.50 (dd (6.11, 13.11), 1H, CH_2); 3.82 (br dd, 1H, H_2); 5.12 (dd (5.97, 9.84), 1H, CHBr) and 7.21-7.32 ppm (m, 5H, Ph). ^{13}C NMR: 19.74 (CH_3); 20.20 (CH_3); 26.80 (C_5); 32.74 (C_6); 37.90 (C_3); 42.22 (CH_2Ph); 43.63 (C_4); 44.83 (CHBr); 47.57 (C_7); 48.36 (C_1); 52.73 (C_{10}); 65.37 (C_2); 127.41 (Ar_p); 128.54 (Ar_m); 129.67 (Ar_o); 135.97 (Ar_i) and 167.33 ppm (CO). Acc Mass M+NH_4^+: Calc. 443.1004, Found 443.1004.

Attempted formation of N-(2-bromo-3-acetoxypropanoyl) bornane-10,2-sultam:

Following the method described above, treatment of the NTMS sultam (**7**) with 3-acetoxy-2-bromopropanoyl bromide (**8**) (2.5 g, 9.2 mmol, 4.0 eq.) gave the N-acetyl derivative (**9**) (580 mg, 97.4 %). Mp (MeOH): 130 - 132°C (lit:[15] 132 - 134°C). ^{1}H NMR: 0.98 (s, 3H, CH_3); 1.16 (s, 3H, CH_3); 1.21 - 1.46 (m, 2H, H_5); 1.88 - 2.20 (m, 5H, H_4, H_6, H_3); 2.41 (s, 3H, CH_3); 3.42 and 3.51 (ABq (13.84), 2H, H_{10}) and 3.86 ppm (dd (5.04, 7.43), 1H, H_2). ^{13}C NMR (100 MHz/$CDCl_3$): 19.88 (CH_3); 20.82 (CH_3); 23.17 (CH_3); 26.43 (C_5); 32.82 (C_6);

38.38 (C_3); 44.64 (C_4); 47.76 (C_7); 48.40 (C_1); 52.76 (C_{10}); 65.19 (C_2) and 168.94 ppm (CO). Mass Spec: EI (m/z %): 193 (5); 178 (10); 134 (60); 43 (100). CI (m/z %): 275 (60); 258 (100). IR (film): 3060 - 2020 (CH); 1690 (CO) and 1330 - 1140 cm^{-1} (SO_2). $[\alpha]_D^{22}$ -161.7 (c = 3.20, CH_2Cl_2).

Attempted formation of N-(2-bromo-3-benzyloxypropanoyl) bornane-10,2-sultam

Following the method described above, treatment of the NTMS sultam (**7**) with 3-benzyloxy-2-bromopropanoyl bromide (**10**) (3.0 g, 9.4 mmole, 4.1 eq.) gave, after chromatography on silica, the corresponding acryloyl derivative (**11**)[10] (116 mg, 18.5 %) and recovered sultam (388 mg, 77.6 %). ^1H NMR: 0.98 (s, 3H, CH_3); 1.18 (s, 3H, CH_3); 1.31 - 1.48 (m, 2H, H_5); 1.87 - 1.98 (m, 3H, H_4, H_6); 2.02 - 2.20 (m, 2H, H_3); 3.45 and 3.52 (ABq (13.79), 2H, H_{10}); 3.95 (dd (5.24, 5.04), 1H, H_2); 5.86 (dd (1.56, 10.36), 1H, H_c); 6.51 (dd (1.6, 16.67), 1H, H_b) and 6.87 ppm (dd (10.36, 16.66), 1H, H_a). ^{13}C NMR: 19.88 (CH_3); 20.84 (CH_3); 26.47 (C_5); 32.87 (C_6); 38.40 (C_3); 44.68 (C_4); 47.80 (C_7); 48.55 (C_1); 53.11 (C_{10}); 65.12 (C_2); 127.75 (CH); 131.35 (CH_2) and 163.83 ppm (CO). Mass Spec: EI (m/z %): 162 (5); 134 (20); 108 (15). CI (m/z %): 287 (100). IR (film) 3100 - 2850 (CH), 1683 (CO) and 1330 - 1110 cm^{-1} (SO_2).

When the above reaction was repeated in the presence of 4-methoxybenzyl methyl ether (2.5 g, 16.5 mmole, 7.1 eq.) to remove TMSBr, the N-3-bromopropionyl bornane-10,2-sultam (**12**) (468 mg, 58%) was obtained. ^1H NMR: 0.98 (s, 3H, CH_3); 1.16 (s, 3H, CH_3); 1.34 - 1.45 (m, 2H, H_5); 1.86 - 1.94 (m, 3H, H_4, H_6); 2.06 - 2.19 (m, 2H, H_3); 3.28 (dt (17.18, 6.54)) and 3.36 (ddd (6.56, 7.15, 17.17), 2H, CH_2); 3.45 and 3.52 (ABq (13.82), 2H, H_{10}); 3.61 (dt (10.14, 6.38) and 3.66 (ddd (6.76, 7.16, 10.15), 2H, CH_2Br) and 3.89 ppm (dd (4.98, 7.7), 1H, H_2). ^{13}C NMR: 19.89 (CH_3); 20.81 (CH_3); 25.25 (CH_2); 26.45 (C_5); 32.82 (C_6); 38.37 (C_3); 44.65 (C_4); 47.83 (C_7); 48.67 (C_1); 52.91 (C_{10}); 65.23 (C_2) and 168.78 ppm (CO). IR (film): 3100 - 2870 (CH); 1692 (CO) and 1320 - 1100 cm^{-1} (SO_2). Mass Spec: CI (m/z %): 369 (100), 367 (100). Acc Mass: M + NH_4^+: Calc. 367.0691, Found 367.0691. $[\alpha]_D^{22}$ -79.94 (c =1.675, CH_2Cl_2).

Preparation of pyruvyl chloride:[16]

Freshly distilled α,α-dichloromethyl methyl ether (6.8g, 0.056 mol) was added dropwise to stirred, freshly distilled, pyruvic acid (5.1g, 0.058 mol, 1.0 eq.) at room temperature under N_2. Evolution of hydrogen chloride started within 5 min after which the mixture was heated at 50°C for 30 min and the methyl formate removed by distillation (bp = 34°C). NMR analysis of the crude product showed only one peak at 2.6 ppm (CH_3) and no signal above 10 ppm. The acid chloride (**13**) was used in the next step without any further purification.

Preparation of N-(pyruvyl)bornane-10,2-sultam:

To a solution of (**7**) (670 mg, 2.3 mmol) in dry acetonitrile (5 ml) at 40°C under N_2 was added pyruvyl chloride (1.1 g, 10.6 mmol, 4.6 eq.) and the mixture stirred at 40°C for 24 hrs. The solution was then poured onto ice and 0.1 N sodium bicarbonate solution and extracted with ether. The combined organic layers were dried ($MgSO_4$), filtered and evaporated to yield the title compound (**14**) (546 mg, 1.92 mmol, 82 %) as a gum. ^1H NMR: δ = 1.01 (s, 3H, CH_3); 1.19 (s, 3H, CH_3); 1.26 - 1.48 (m, 2H, H_5); 1.88 - 2.06 (m, 5H, H_4, H_6, H_3); 2.44 (s, 3H, CH_3); 3.48 and 3.50 (ABq (13.78), 2H, H_{10}) and 4.03 ppm (t (6.23), 1H, H_2). ^{13}C NMR): δ = 19.85 (CH_3); 21.35 (CH_3); 26.16 (CH_3 and C_5); 33.18 (C_6); 38.31 (C_3); 45.26 (C_4); 47.76 (C_7); 49.58 (C_1); 52.90 (C_{10}); 65.12 (C_2) and 194.19 ppm (CO). IR (neat): 3100 - 2070 (CH); 1731 (CO); 1682 (CO) and 1350 - 1180 cm^{-1} (SO_2). Mass Spec: CI (m/z %): 303 (100); 286 (3). Acc Mass: M + NH_4^+: Calc. 303.1379, Found 303.1379.

Preparation of N-[2-(N',N'-dibenzylamino)propionyl] bornane-10,2-sultam (**15a**):

To N-(2-bromopropionyl) bornane-10,2-sultam (**1a**) (323mg, 0.9 mmol) dissolved in toluene/DMSO (10/1) or DMSO or CH_3CN (14 ml) was added dibenzylamine (1.4 ml) and the clear solution brought either to the boil (toluene/DMSO or CH_3CN) or to 60°C (DMSO) for 24 hrs. The brownish solution was quenched with 5% citric acid solution to give a turbid mixture which was extracted with ether. The ether was dried ($MgSO_4$), filtered and evaporated to give (**15a**) as a yellow oil (426mg, 99% yield).

^1H NMR: 0.93 (s, 3H, CH_3); 1.10 (s, 3H, CH_3); 1.13-1.40 (m, 2H, H_5); 1.47 (d (7.21), 3H, CH_3); 1.86-2.04 (m, 5H, H_4, H_3, H_6); 3.38 (d (1.28), 2H, H_{10}); 3.88 and 3.97 (ABq (14.64), 4H, $N(CH_2Ph)_2$); 3.93 (m overlapped, 1H, H_2); 4.22 (q (7.19), 1H, CH) and 7.14-7.35 ppm (m, 10H, $N(CH_2Ph)_2$). ^{13}C NMR: 16.14 (CH_3); 18.79 (CH_3); 19.56 (CH_3); 25.46 (C_5); 31.64 (C_6); 37.26 (C_3); 43.46 (C_4); 46.70 (C_7); 47.37 (C_1); 51.84 (C_{10}); 54.02 ($N(CH_2Ph)_2$); 57.55 (CH); 63.55 (C_2); 125.63 (Ar_p); 126.99 (Ar_o); 127.51 (Ar_m); 139.30 (Ar_i) and 174.74 ppm (CO). Mass Spec: EI (m/z %): 91 (100); 224 (83). CI (m/z %): 91 (20); 198 (47); 224 (50); 403 (20); 467 (100). Acc Mass: $M+H^+$: Calc. 467.2368 Found: 467.2368. IR (film): 3120-2780 (CH); 1696 (CO) and 1330-1170 cm^{-1} (SO_2). $[\alpha]_D^{22}$ -62.00 (c = 1.10, CH_2Cl_2).

Preparation of N-(2-azidoalkanoyl) bornane-10,2-sultams (**16**):

To the N-(2-bromopropionyl) bornane-10,2-sultam (**1a**) (103 mg, 0.29 mmole) preheated at 60°C was added a solution of sodium azide (28mg, 0.43 mmol, 1.47 eq.) in DMSO (6 ml) preheated at 60°C, and the final solution kept at 60°C for 1 hr. The reddish solution was then poured into water to give a white turbid solution

which was extracted with ether. The ether was dried ($MgSO_4$), filtered and evaporated to give *N-(2-azidopropionyl)bornane-10,2-sultam* (**16a**) as oily crystals which were purified by chromatography on silica.

The *(S)-isomer* (83 mg, 91 %) was obtained as an oil which hardened on standing (crude d.e. = 100%, purified d.e. = 100%). ^{1}H NMR: 0.98 (s, 3H, CH_3); 1.13(s, 3H, CH_3); 1.26 - 1.47 (m, 2H, H_5); 1.56 (d (7.06), 3H, CH_3); 1.86 - 1.98 (m, 3H, H_4, H_6); 2.04 - 2.17 (m, 2H, H_3); 3.47 and 3.53 (ABq (13.85), 2H, H_{10}); 3.94 (dd (5.26, 5.25), 1H, H_2) and 4.43 ppm (q (6.95), 1H, CH). ^{13}C NMR: 17.62 (CH_3); 19.81 (CH_3); 20.68 (CH_3); 26.37 (C_5); 32.71 (C_6); 38.01 (C_3); 44.52 (C_4); 47.83 (C_7); 48.80 (C_1); 52.89 (C_{10}); 56.90 (CH); 65.08 (C_2) and 170.80 ppm (CO). Mass spec: EI (m/z %): 242 (5); 135 (50); 93 (50). CI (m/z %): 330 (100); 313 (30); 285 (35); 135 (20). Acc Mass: M+NH_4^+ Calc. 330.1600, Found: 330.1600. IR (Neat): 3100 - 2800 (CH); 2119 (N_3); 1694 (C=O) and 1340 - 1180 cm^{-1} (SO_2). $[\alpha]_D^{22}$ -43.67 (c = 2.05, CH_2Cl_2).

The *(R)-isomer* was obtained as a mixture with the *(S)*-isomer (11 mg, 100 %) starting from the *(R)/(S)*-bromide (12 mg, 0.034 mmol). ^{1}H NMR: 0.98 (s, 3H, CH_3); 1.18 (s, 3H, CH_3); 1.34 - 1.44 (m, 2H, H_5); 1.56 (d (6.89), 3H, CH_3); 1.90 - 2.17 (m, 5H, H_4, H_6, H_3); 3.49 and 3.51 (ABq (13.78), 2H, H_{10}); 3.94 (dd (5.41, 7.38), 1H, H_2) and 4.44 ppm (q (6.89), 1H, CH). ^{13}C NMR: 17.62 (CH_3); 19.84 (CH_3); 20.68 (CH_3); 26.37 (C_5); 32.73 (C_6); 38.01 (C_3); 44.54 (C_4); 47.86 (C_7); 48.80 (C_1); 52.89 (C_{10}); 56.92 (CH); 65.09 (C_2) and 170.79 ppm (CO). Acc Mass: M+NH_4^+: Calc. 330.1600, Found 330.1600.

N-(2-Azidobutyryl)bornane-10,2-sultam (**16b**): The *(S)-isomer* (87 mg, 93.6 %) was obtained as a crystalline product starting from N-(2-bromobutyryl)bornane-10,2-sultam (104 mg, 0.285 mmol) (crude d.e. = 100%, purified d.e. = 100%). ^{1}H NMR: 0.98 (s, 3H, CH_3); 1.05 (t (7.38), 3H, CH_3); 1.13 (s, 3H, CH_3); 1.26 - 1.47 (m, 2H, H_5); 1.82 - 2.17 (m, 7H, H_4, H_6, H_3, CH_2); 3.48 and 3.53 (ABq (13.83), 2H, H_{10}); 3.96 (dd (5.01, 7.62), 1H, H_2) and 4.28 ppm (dd (5.30, 8.34), 1H, CH). ^{13}C NMR: 10.31 (CH_3); 19.87 (CH_3); 20.73 (CH_3); 25.90 (CH_2); 26.42 (C_5); 32.81 (C_6); 38.17 (C_3); 44.60 (C_4); 47.85 (C_7); 48.71 (C_1); 53.00 (C_{10}); 62.63 (CH); 65.18 (C_2) and 170.28 ppm (CO). Mass Spec: EI (m/z %): 216 (2); 41 (100). CI (m/z /%): 344 (70); 327 (35); 299 (70); 233 (100); 216 (30). Acc Mass: M+NH_4^+: Calc. 344.1757, Found 344.1756. IR (neat): 3100 - 2800 (CH); 2106 (N_3); 1696 (CO) and 1330 - 1180 cm^{-1} (SO_2). $[\alpha]_D^{22}$ -46.82 (c = 2.00, CH_2Cl_2).

The *(R)-isomer* (17 mg, 94.8 %) was obtained as an oil starting from the *(S)*-bromide (**1b**) (20 mg, 0.055 mmol) (crude d.e. = 100%). ^{1}H NMR: 0.98 (s, 3H, CH_3); 1.04 (t (7.40), 3H, CH_3); 1.19 (s, 3H, CH_3); 1.33 - 1.46 (m, 2H, H_5); 1.81 - 2.01 (m, 5H, H_4, H_6, CH_2); 2.07 - 2.18 (m, 2H, H_3); 3.45 and 3.55 (ABq (13.80), 2H, H_{10}); 3.91 (dd (4.98, 7.77), 1H, H_2) and 4.20 ppm (dd (5.71, 8.48), 1H, CH). ^{13}C NMR: 10.22 (CH_3); 19.85

(CH_3); 20.81 (CH_3); 23.59 (CH_2); 26.40 (C_5); 32.83 (C_6); 38.27 (C_3); 44.55 (C_4); 47.86 (C_7); 48.74 (C_1); 53.00 (C_{10}); 62.30 (CH); 65.26 (C_2) and 169.05 ppm (CO). Acc Mass: M+NH_4^+: Calc. 344.1757, Found 344.1756.

N-(2-Azido-2-phenylacetyl)bornane-10,2-sultam (**16c**) was obtained as a 50/50 mixture of (R) and (S)-isomers (25 mg, 92 % crude yield) starting from the (R)/(S)-bromide (**1c**) (30 mg, 0.073 mmole). ^{1}H NMR: 0.72 (s, 1.5H, CH_3); 0.88 (s, 1.5H, CH_3); 0.98 (s, 1.5H, CH_3); 1.20 (s, 1.5 H, CH_3); 1.25 - 1.45 (m, 2H, H_5); 1.78 - 2.17 (m, 5H, H_4, H_6, H_3); 3.40 and 3.42 (ABq (13.77), 1H, H_{10}); 3.46 and 3.53 (ABq (13.81), 1H, H_{10}); 3.89 (dd (4.96, 7.89), 0.5H, H_2); 3.96 (br m, 0.5H, H_2); 5.51 (s, 0.5H, CH); 5.54 (br s, O.5H, CH) and 7.36 - 7.53 ppm (m, 5H, Ph). ^{13}C NMR: 19.78 (CH_3); 19.85 (CH_3); 20.05 (CH_3); 20.81 (CH_3); 26.38 (C_5); 32.59 (C_6); 32.79 (C_6), 37.59 (C_3); 38.26 (C_3); 44.40 (C_4); 44.50 (C_4); 47.30 (C_7); 47.71 (C_1); 48.74 (C_1); 52.87 (C_{10}); 52.90 (C_{10}); 63.86 (C_2); 64.79 (C_2); 64.93 (CH); 65.55 (CH), 128.08, 128.62, 128.76, 129.00, 129.30 and 129.35 (Ar); 134.31 (Ar_i); 135.20 (Ar_i); 167.04 (CO) and 167.82 ppm (CO). IR: (Neat): 3070 - 2800 (CH), 2103 (N_3), 1696 (CO) and 1340 - 1180 cm^{-1} (SO_2).

Preparation of the carboxylate sodium salts RCOONa:

A solution of the carboxylic acid (10 mmols) and sodium hydroxide (340 mg, 8.5 mmols, 0.85 eq.) in MeOH (15 ml) was refluxed for 2 hrs. The solution was then cooled down and a precipitate appeared in most cases. The precipitate was filtered and then recrystallized from MeOH/ether. If the precipitate did not appear, the solution was concentrated until it did, and the work-up carried out as above. The powder was eventually dried in a vacuum dessicator (Typical yield ~ 75 %).

Preparation of N-(2-acyloxyalkanoyl)bornane-10,2-sultam (**17 - 22a**):

To the N-(2-bromopropionyl)bornane-10,2-sultam (**1a**) (51 mg, 0.15 mmol) dissolved in DMSO (5 ml) was added HCOONa (24 mg, 0.35 mmole, 2.4 eq.) as a solution in DMSO (1.6 ml) and the solution stirred for 1 hr at 60°C. The solution was then poured into water to give a white turbid mixture which was extracted with ether. The ether was dried ($MgSO_4$), filtered and evaporated to give *N-(2-hydroxypropionyl)bornane-10,2-sultam formate* (**22a**) (42 mg, 91 %) as an oil which hardened on standing (d.e. = 66% starting from bromide d.e. = 100%) $[\alpha]_D^{22}$ -110.9 (c = 0.85, CH_2Cl_2).

(S)-isomer: ^{1}H NMR: 0.98 (s, 3H, CH_3); 1.14 (s, 3H, CH_3); 1.33 - 1.49 (m, 2H, H_5); 1.59 (d, (6.86), 3H, CH_3); 1.87 - 1.98 (m, 3H, H_4, H_6); 2.01 - 2.09 (m, 2H, H_3); 3.52 (s, 2H, H_{10}); 3.96 (t (6.33), 1H, H_2); 5.64; (q (6.93), 1H, CH) and 8.06 ppm (s, 1H, H). ^{13}C NMR: 17.50 (CH_3); 19.84 (CH_3); 20.67 (CH_3); 26.35 (C_5); 32.68 (C_6); 37.98 (C_3); 44.50 (C_4); 47.82 (C_7); 48.94 (C_1); 52.82 (C_{10}); 65.00 (C_2); 69.16 (CH); 159.53 (HCO) and 169.23

(NCO) ppm. IR (neat): 3070 - 2810 (CH), 1733 (COO), 1706 (NCO) and 1300 - 1180 cm^{-1} (SO_2). Mass Spec: CI (m/z %): 333 (100), 316 (10), 303 (70), 233 (50). Acc Mass: M + NH_4^+: Calc. 333.1484, Found 333.1484.

(R)-isomer: ^1H NMR: 0.98 (s, 3H, CH_3); 1.24 (s, 3H, CH_3); 1.33 - 1.49 (m, 2H, H_5); 1.57 (overlapped d, 3H, CH_3); 1.87 - 1.98 (m, 3H, H_4, H_6); 2.01 - 2.09 (m, 2H, H_3); 3.46 and 3.55 (ABq (13.80), 2H, H_{10}); 3.90 (dd (4.95, 7.78), 1H, H_2); 5.50 (q (6.62), 1H, CH) and 8.00 ppm (s, 1H, CHO). ^{13}C NMR: 16.25 (CH_3); 19.95 (CH_3); 20.38 (CH_3); 26.43 (C_5); 32.76 (C_6); 37.84 (C_3); 44.50 (C_4); 47.82 (C_7); 49.14 (C_1); 52.90 (C_{10}); 65.29 (C_2); 69.35 (CH); 159.97 (CHO) and 169.23 ppm (NCO). Acc Mass M+NH_4^+: Calc. 333.1484, Found 333.1484.

N-(2-Acetoxypropionyl)-bornane-10,2-sultam (**17a**) was obtained using the same procedure in 87% yield.

(S)-isomer: ^1H NMR: 0.98 (s, 3H, CH_3); 1.13 (s, 3H, CH_3); 1.35 - 1.45 (m, 2H, H_5); 1.54 (d(6.93), 3H, CH_3); 1.88 - 1.93 (m, 3H, H_4, H_6); 2.07 - 2.09 (m, 2H, H_3); 2.12 (s, 3H, CH_3); 3.50 (s, 2H, H_{10}); 3.94 (t (6.35), 1H, H_2) and 5.48 ppm (q (6.94), 1H, CH). ^{13}C NMR: 17.33 (CH_3); 19.97 (CH_3); 20.47 (CH_3); 20.67 (CH_3); 26.38 (C_5); 32.73 (C_6); 38.02 (C_3); 44.52 (C_4); 47.81 (C_7); 49.11 (C_1); 52.84 (C_{10}); 65.02 (C_2); 69.73 (CH) and 170.15 ppm (NCO). Mass Spec: EI (m/z %): 115 (100), 87 (97). CI (m/z %): 347 (100), 330 (58), 289 (20). Acc Mass: M+NH_4^+: Calc. 347.1641, Found 347.1641. IR (neat): 3060 - 2880 (CH); 1746 (COO); 1706 (NCO) and 1330 - 1170 cm^{-1} (SO_2).

(R)-isomer: ^1H NMR: 0.98 (s, 3H, CH_3); 1.26 (s, 3H, CH_3); 1.30 - 1.47 (m, 2H, H_5); 1.53 (d (6.66), 3H, CH_3); 1.81 - 2.23 (m, 5H, H_4, H_6, H_3); 2.09 (s, 3H, CH_3); 3.43 and 3.54 (ABq (13.72), 2H, H_{10}); 3.92 (m, 1H, H_2) and 5.34 ppm (q (6.66), 1H, CH). ^{13}C NMR: 16.23 (CH_2); 19.88 (CH_3); 20.38 (CH_3); 20.67 (CH_3); 26.46 (C_5); 32.79 (C_6); 37.90 (C_3); 44.52 (C_4); 47.87 (C_7); 49.11 (C_1); 52.96 (C_{10}); 65.34 (C_2); 69.40 (CH) and 169.97 ppm (NCO). Acc Mass M+NH_4^+: Calc. 347.1641, Found 347.1641.

N-(2-Hydroxypropionyl)bornane-10,2-sultam diphenylacetate (**18a**) was obtained using the same procedure in 91% yield.

(S)-isomer: ^1H NMR: 0.89 (s, 3H, CH_3); 1.04 (s, 3H, CH_3); 1.19 - 1.41 (m, 2H, H_5); 1.45 (d (7.29), 3H, CH_3); 1.78 - 2.04 (m, 5H, H_4,H_6, H_3); 3.40 (s, 2H, H_{10}); 3.89 (t (6.4), 1H, H_2); 5.04 (s, 1H, *CH*Ph_2); 5.46 (q (6.9), 1H, CH) and 7.14 - 7.28 ppm (m, 10H, Ph). ^{13}C NMR: 17.33 (CH_3); 19.83 (CH_3); 20.69 (CH_3); 26.35 (C_5); 32.72 (C_6); 38.02 (C_3); 44.55 (C_4); 47.78 (C_7); 48.87 (C_1); 52.82 (C_{10}); 56.63 (CH); 64.96 (C_2); 70.25 (*CH*Ph_2); 127.06 - 128.76 (Ar); 138.15 (Ar_i); 138.33 (Ar_i); 169.70 (NCO) and 171.40 ppm (COO). Mass Spec EI (m/z %): 266 (5); 194 (5); 167 (100). CI (m/z %): 499 (100); 482 (5); 267 (30); 194 (25); 167 (60). Acc

Mass: M+NH_4^+ Calc. 499.2267, Found. 499.2267. IR (neat): 3100 - 2900 (CH); 1740 (COO); 1706 (NCO) and 1350 - 1170 cm^{-1} (SO_2).

(R)-isomer: ^{1}H NMR: 0.89 (s, 3H, CH_3); 1.12 (s, 3H, CH_3); 1.19 - 1.41 (m, 2H, H_5); 1.43 (d (6.82), 3H, CH_3); 1.78 - 2.04 (m, 5H, H_4, H_6, H_3); 3.34 and 3.43 (ABq (13.69), 2H, H_{10}); 3.81 (dd (5.0, 7.81), 1H, H_2); 5.00 (s, 1H, *CH*Ph_2); 5.38 (q (6.5), 1H, CH) and 7.14 - 7.28 ppm (m, 10H, Ph). ^{13}C NMR: 16.11 (CH_3); 19.95(CH_3); 20.58 (CH_3); 26.46 (C_5); 32.77 (C_6); 37.89 (C_3); 44.49 (C_4); 47.84 (C_7); 49.04 (C_1); 52.92 (C_{10}); 56.43 (CH); 65.30 (C_2); 70.20 (*CH*Ph_2); 127.06 - 128.76 (Ar); 138.38 (Ar_i); 138.47 (Ar_i); 169.57 (NCO) and 171.58 ppm (COO). Acc Mass M+NH_4^+: Calc. 499.2267, Found 499.2267.

N-(2-Hydroxypropionyl)bornane-10,2-sultam pivalate (**19a**) was obtained using the same procedure in 92% yield.

(S)-isomer: ^{1}H NMR: 0.97 (s, 3H, CH_3); 1.14 (s, 3H, CH_3); 1.24 (s, 9H, ^{t}Bu); 1.27 - 1.45 (m, 2H, H_5); 1.54 (d (6.94), 3H, CH_3); 1.88 - 1.92 (m, 3H, H_4, H_6); 1.99 - 2.17 (m, 2H, H_3); 3.50 (s, 2H, H_{10}); 3.96 (t (6.32), 1H, H_2) and 5.42 ppm (q (6.94), 1H, CH). ^{13}C NMR: 17.17 (CH_3); 19.98 (CH_3); 20.69 (CH_3); 26.52 (C_5); 27.00 (CH_3); 32.73 (C_6); 38.05 (C_3); 38.37 ($C(CH_3)_3$); 44.53 (C_4), 47.79 (C_7); 48.86 (C_1); 52.82 (C_{10}); 64.89 (C_2); 69.35 (CH); 170.25 (NCO) and 177.51 ppm (COO). Mass Spec: EI (m/z %): 372 (5); 244 (5); 157 (60); 85 (40); 57 (100). CI (m/z %): 389 (60); 372 (15); 157 (100). Acc Mass: M+NH_4^+: Calc. 389.2110, Found 389.2110. IR (neat): 3110 - 2880 (CH); 1736 (COO); 1708 (NCO) and 1340 - 1180 cm^{-1} (SO_2).

(R)-isomer: ^{1}H NMR: 0.97 (s, 3H, CH_3); 1.20 (s, 9H, ^{t}Bu); 1.26 (s, 3H, CH_3); 1.27 - 1.45 (m, 2H, H_5); 1.51 (d (6.61), 3H, CH_3); 1.88 - 1.92 (m, 3H, H_4, H_6); 1.99 - 2.17 (m, 2H, H_3); 3.43 and 3.52 (ABq (13.74), 2H, H_{10}); 3.89 (dd (4.93, 7.83), 1H, H_2) and 5.35 ppm (q (6.60), 1H, CH). ^{13}C NMR: 16.04 (CH_3); 19.87 (CH_3); 20.55 (CH_3); 26.39 (C_5); 27.00 (CH_3); 32.73 (C_6); 37.94 (C_3); 38.40 ($C(CH_3)_3$); 44.46 (C_4); 47.86 (C_7); 49.03 (C_1); 52.91 (C_{10}); 65.24 (C_2); 69.18 (CH); 169.86 (NCO) and 177.51 ppm (COO). Acc Mass M+NH_4^+: Calc. 389.2110, Found 389.2110.

N-(2-Hydroxypropionyl)bornane-10,2-sultam benzoate (**20a**) was obtained using the same procedure in 88% yield.

(S)-isomer: ^{1}H NMR: 0.98 (s, 3H, CH_3); 1.16 (s, 3H, CH_3); 1.35 - 1.46 (m, 2H, H_5); 1.69 (d (6.86), 3H, CH_3); 1.86 - 1.97 (m, 3H, H_4, H_6); 2.01 - 2.11 (m, 2H, H_3); 3.53 (s, 2H, H_{10}); 3.99 (dd (5.31, 7.42), 1H, H_2); 5.73 (q (6.93), 1H, CH); 7.40 - 7.48 (m, 2H, Ar_m); 7.53 - 7.60 (m, 1H, Ar_p) and 8.04 -8.11 ppm (m, 2H, Ar_o). ^{13}C NMR: 17.43 (CH_3); 19.87 (CH_3); 20.69 (CH_3); 26.37 (C_5); 32.71 (C_6); 38.03 (C_3); 44.52 (C_4); 47.82 (C_7);

48.91 (C_1); 53.85 (C_{10}); 65.05 (C_2); 70.07 (CH); 128.30 (Ar_p); 128.82 (Ar_m); 129.92 (Ar_o); 133.19 (Ar_i); 166.83 (NCO) and 169.99 ppm (COO). Mass Spec: EI (m/z %): 283 (2), 177 (30), 105 (100). CI (m/z %): 409 (35), 392 (5), 194 (5), 177 (100), 105 (20). Acc Mass M+NH_4^+: Calc. 409.1797, Found 409.1797. IR: (neat): 3100 - 2800 (CH), 1726 (COO), 1708 (NCO) and 1300 - 1800 cm^{-1} (SO_2).

(R)-isomer: ^1H NMR: 0.98 (s, 3H, CH_3); 1.32 (s, 3H, CH_3); 1.35 - 1.46 (m, 2H, H_5); 1.67 (d (6.45), 3H, CH_3); 1.86 - 1.97 (m, 3H, H_4 H_6); 2.01 - 2.11 (m, 2H, H_3); 3.46 and 3.55 (ABq (13.79), 2H, H_{10}); 3.93 (dd (4.92, 7.86), 1H, H_2); 5.60 (q (6.63), 1H, CH); 7.40 - 7.48 (m, 2H, Ar_m); 7.53 - 7.60 (m, 1H, Ar_p) and 8.04 - 8.11 ppm (m, 2H, Ar_o). ^{13}C NMR: 16.39 (CH_3); 19.97 (CH_3); 20.53 (CH_3); 26.47 (C_5); 32.77 (C_6); 37.97 (C_3); 44.52 (C_4); 47.82 (C_7); 48.91 (C_1); 52.94 (C_{10}); 65.35 (C_2); 70.00 (CH); 128.27 (Ar_p); 128.82 (Ar_m); 130.02 (Ar_o); 133.19 (Ar_i); 166.77 (NCO) and 169.99 ppm (COO). Acc Mass M+NH_4^+: Calc. 409.1797, Found 409.1797.

N-(2-Hydroxypropionyl)bornane-10,2-sultam 2,4,6-trimethylbenzoate (**21a**) was obtained using the same procedure in 95% yield.

(S)-isomer: ^1H NMR: 0.99 (s, 3H, CH_3); 1.16 (s, 3H, CH_3); 1.33 - 1.47 (m, 2H, H_5); 1.62 (d (6.97), 3H, CH_3); 1.87 - 1.94 (m, 3H, H_4, H_6); 2.03 - 2.12 (m, 2H, H_3); 2.26 (s, 3H, CH_{3Ar}); 2.31 (s, 6H, CH_{3Ar}); 3.53 (s, 2H, H_{10}), 4.02 (dd (5.83, 6.83), 1H, H_2); 5.70 (q (6.96), 1H, CH) and 6.83 ppm (d (0.48), 2H, Ar). ^{13}C NMR: 17.58 (CH_3); 19.75 (CH_3); 20.00 (CH_{3Ar}); 20.77 (CH_3); 21.14 (CH_{3Ar}); 26.41 (C_5); 32.77 (C_6); 38.11 (C_3); 44.60 (C_4); 47.85 (C_7); 48.95 (C_1); 52.89 (C_{10}); 65.03 (C_2); 70.08 (CH); 128.45 (Ar_p); 129.41 (Ar_m); 135.84 (Ar_o); 139.57 (Ar_i); 169.49 (NCO) and 169.86 ppm (COO). Mass Spec: EI (m/z/%): 218 (5), 147 (95), 146 (100). CI (m/z %): 451 (10), 289 (2) 233 (2), 219 (10), 147 (100). Acc. Mass: M+NH_4^+: Calc. 451.2267, Found 451.2267. IR (neat): 3100 - 2800 (CH), 1730 (COO), 1708 (NCO) and 1300 - 1180 cm^{-1} (SO_2).

(R)-isomer: ^1H NMR: 0.98 (s, 3H, CH_3); 1.31 (s, 3H, CH_3); 1.33 - 1.47 (m, 2H, H_5); 1.61 (d (6.68), 3H, CH_3); 1.87 - 1.94 (m, 3H, H_4, H_6); 2.03 - 2.12 (m, 2H, H_3); 2.27 (s, 3H, CH_{3Ar}); 2.36 (s, 6H, CH_{3Ar}); 3.46 and 3.56 (ABq (13.73), 2H, H_{10}), 3.93 (dd (4.93, 7.84), 1H, H_2); 5.59 (q (6.68), 1H, CH) and 6.84 ppm (d (6.84), 2H, Ar). ^{13}C NMR: 16.32 (CH_3); 19.89 (CH_3); 20.18 (CH_{3Ar}); 20.44 (CH_3); 21.14 (CH_{3Ar}); 26.55 (C_5); 32.77 (C_6); 37.85 (C_3); 44.50 (C_4), 47.85 (C_7); 49.20 (C_1); 52.97 (C_{10}); 65.29 (C_2); 69.89 (CH); 128.43 (Ar_p); 129.60 (Ar_m); 136.11 (Ar_o); 139.60; (Ar_i), 168.60 (NCO) and 169.92 ppm (COO). Acc Mass: M+NH_4^+: Calc. 451.2267, Found 451.2267.

N-(2-Acetoxybutyryl)bornane-10,2-sultam (**17b**) was obtained using the same procedure in 89% yield.

(S)-isomer ^{1}H NMR: 0.97 (s, 3H, CH_3), 1.02 (t (7.58), 3H, CH_3); 1.13 (s, 2H CH_3); 1.30 - 1.46 (m, 2H, H_5); 1.83 - 2.17 (m, 7H, H_4, H_6, H_3, CH_2); 2.13 (s, 3H, CH_3); 3.49 (s, 2H, H_{10}); 3.93 (t (6.32), 1H, H_2) and 5.36 ppm (dd (3.68, 8.27), 1H, CH). ^{13}C NMR: 8.60 (CH_3); 18.87 (CH_3); 19.31 (CH_3); 19.63 (CH_3); 22.64 (C_5); 25.45 (CH_2); 31.72 (C_6); 37.16 (C_3); 43.51 (C_4); 46.86 (C_7); 47.80 (C_1); 51.83 (C_{10}); 64.01 (C_2); 73.21 (CH) and 169.84 ppm (NCO). Mass Spec: EI (m/z %): 55 (100). CI (m/z %): 361 (77), 344 (40), 129 (100). Acc Mass: M+NH_4^+: Calc. 361.1798, Found 361.1797. IR (neat): 3060 - 2880 (CH), 1746 (COO), 1706 (NCO) and 1330 - 1170 cm^{-1} (SO_2).

(R)-isomer: ^{1}H NMR: 0.97 (s, 3H, CH_3); 1.04 (t (7.32), 3H, CH_3); 1.26 (s, 3H, CH_3); 1.30 - 1.46 (m, 2H, H_5); 1.83 - 2.17 (m, 7H, H_4, H_6, H_3, CH_2); 2.11 (s, 3H, CH_3); 3.43 and 3.53 (ABq (13.76), 2H, H_{10}); 3.89 (dd (5.05, 7.76), 1H, H_2); and 5.15 ppm (dd (3.09, 9.03), 1H, CH). ^{13}C NMR: 8.67 (CH_3); 18.95 (CH_3); 19.31 (CH_3); 19.40 (CH_3); 23.93 (C_5); 25.45 (CH_2); 31.72 (C_6); 36.86 (C_3); 43.42 (C_4); 46.86 (C_7); 48.09 (C_1); 51.90 (C_{10}); 64.27 (C_2); 73.62 (CH) and 168.16 ppm (NCO). Acc Mass: M+NH_4^+: Calc. 361.1798, Found 361.1797.

N-(2-Acetoxy-2-phenylacetyl)bornane-10,2-sultam (**17c**) was obtained using the same procedure in 93% yield as a 50/50 mixture of diastereoisomers. ^{1}H NMR: 0.61 (br s, 1.5H, CH_3); 0.86 (s, 3H, CH_3); 0.97 (s, 1.5H, CH_3); 1.21 - 1.40 (m, 2H, H_5); 1.74 - 2.06 (m, 5H, H_4, H_6, H_3); 2.13 (s, 1.5H, CH_3); 2.16 (s, 1.5H, CH_3); 3.34 and 3.43 (ABq (13.79), 1H, H_{10}); 3.40 and 3.49 (ABq (13.70), 1H, H_{10}); 3.75 - 3.90 (m, 1H, H_2); 6.29 (s, 0.5H, CH); 6.42 (br s, 0.5H, CH); 7.35 - 7.42 (m, 3H, $Ar_{m/p}$) and 7.52 - 7.57 ppm (m, 2H, Ar_o). ^{13}C NMR: 18.80 (CH_3); 18.95 (CH_3); 19.28 (CH_3); 19.52 (CH_3); 25.39 (C_5); 24.45 (C_5); 31.48 (C_6); 31.66 (C_6); 36.44 (C_3); 36.92 (C_3); 43.28 (CH_3); 43.38 (CH_3); 46.65 (C_4); 46.89 (C_4); 47.80 (C_7); 48.19 (C_1); 51.71 (C_{10}); 51.83 (C_{10}); 63.68 (C_2); 64.37 (C_2); 73.94 (CH); 127.46 (Ar); 127.62 (Ar); 127.67 (Ar); 128.41 (Ar); 128.63 (Ar); 128.67 (Ar); 131.11 (Ar_i); 165.50 (NCO); 168.86 (NCO); 169.01 (COO) and 169.63 ppm (COO). Mass Spec: EI (m/z %): 149 (72); 107 (100). CI (m/z %): 409 (40); 349 (100); 332 (45). Acc Mass: M +NH_4^+: Calc. 409.1797, Found 409.1797. IR (neat): 3060 - 2880 (CH), 1745 (COO), 1703 (NCO) and 1340 - 1170 cm^{-1} (SO_2).

Alternative preparation of N-(2-acetoxy-2-phenylacetyl) bornane-10,2-sultam (**17c**):

(i) *N-(2-Hydroxy-2-phenylacetyl)bornane-10,2-sultam:*

(**1c**) (d.e. = 0%, 92mg, 0.22 mmol) was dissolved in DMSO (9ml) and the solution brought to 64°C for 1hr, at which time the bromide peaks on HPLC had vanished. The reaction was then poured into water to give a white turbid mixture which was extracted with ether. The ether was dried ($MgSO_4$), filtered and evaporated to give

an oil (68 mg, 0.195 mmole, 87 %) whose structure was assigned to be the N-(2-hydroxy-phenylacetyl) bornane-10,2-sultam (d.e. ≠ 0 but difficult to assign due to overlapping and broadness of peaks). Major signals underlined. ^{1}H NMR : 0.69 (br s, CH_3); 0.88 (s, 3H, CH_3); 0.97 (s, CH_3); 1.12 - 1.44 (m, 2H, H_5); 1.72 - 2.11 (m, 5H, H_4, H_6, H_3); 3.37 - 3.50 (m + s, 2H, H_{10}); 3.54 - 3.86 (br, 1H, OH); 3.90 (m + dd (5.01, 7.85), 1H, H_2); 5.68 (br s, CH); 5.71 (br s, CH) and 7.22 - 7.47 ppm (m, 5H, Ph). ^{13}C NMR: 19.83 (CH_3); 19.97 (CH_3); 20.53 (CH_3); 20.67 (CH_3); 26.41 (C_5); 32.67 (C_6); 32.76 (C_6); 37.52 (C_3); 38.05 (C_3); 44.43 (C_4); 44.56 (C_4); 47.73 (C_7); 48.93 (C_1); 52.76 (C_{10}); 52.84 (C_{10}); 64.69 (C_2); 65.31 (C_2); 73.04 (CH); (73.40 (CH); 127.13 - 129.77 (Ar); 136.56 (Ar_i); 137.87 (Ar_i); 171.29 (NCO) and 173.20 ppm (NCO). Mass Spec: EI (m/z %): 332 (5); 304 (5); 107 (70); 49 (100). CI (m/z %): 367 (65); 350 (100); 332 (55). Acc Mass: M +NH_4^+: Calc. 367.1692, Found 367.1691. IR (neat): 3700 - 3050 (br OH); 1710 (NCO) and 1330 - 1180 cm^{-1} (SO_2).

(ii) *N-(2-Acetoxy-2-phenylacetyl)bornane-10,2-sultam*:

The hydroxy sultam was dissolved in CH_2Cl_2 (2 ml) and treated with DMAP (24 mg, 0.20 mmol, 1.0 eq) and Ac_2O (0.1 ml, 0.11g, 1.1 mmol, 5.4 eq) under N_2 at rt. The solution was stirred at r.t. for 6 hrs, then quenched with water and extracted with ether. The ether was dried ($MgSO_4$), filtered and evaporated to give a brown oil (75mg, 0.19 mmole, 98 %). Data for (**17c**) identical to those given above (de = 60%, major signals underlined).

Preparation of N-(2-thioacetylpropionyl)bornane-10,2-sultam (**24a**)

This was prepared by reacting (**1a**) (25 mg, 0.07 mmole, d.e. = (62%) with CH_3COSNa (16 mg, 0.16 mmol, 2.9 eq.) in DMSO (2 ml) at 60°C for 1 hr. The product was obtained as a 50/50 mixture of diastereoisomers in 81% yield. ^{1}H NMR: 0.98 (s, 3H, CH_3); 1.15 (s, 1.5H, CH_3); 1.26 (s, 1.5H, CH_3); 1.35 - 1.48 (m, 2H, H_5); 1.52 (d (6.92), 1.5H, CH_3); 1.57 (d (7.21), 1.5H, CH_3); 1.88 - 1.96 (m, 3H, H_4, H_6); 2.01 - 2.12 (m, 2H, H_3); 2.31 (s, 1.5H, CH_3); 2.32 (s, 1.5H, CH_3); 3.45 and 3.53 (ABq (13.79), 1H, H_{10}); 3.51 (s, 1H, H_{10}); 3.91 (t (5.57), 0.5H, H_2); 3.93 (t (5.88), 0.5H, H_2); 4.72 (q (6.94), 0.5H, CH) and 4.81 ppm (q (7.17), 0.5H, CH). ^{13}C NMR: 16.85 (CH_3); 18.74 (CH_3); 19.87 (CH_3); 20.00 (CH_3); 20.63 (CH_3); 20.78 (CH_3); 26.39 (C_5); 26.49 (C_5); 29.83 (CH_3); 30.01 (CH_3); 32.79 (C_6); 32.91 (C_6); 38.11 (C_3); 38.19 (C_3); 41.00 (CH); 41.92 (CH); 43.50 (C_4); 44.62 (C_4); 47.82 (C_7); 48.65 (C_1); 52.87 (C_{10}); 53.03 (C_{10}); 65.40 (C_2); 64.43 (C_2); 170.46 (NCO); 170.98 (NCO) and 193.80 ppm (SCO). Mass Spec: EI (m/z %): 346 (2); 131 (50); 43 (100). CI (m/z /%): 363 (50); 346; (100); 233 (60); 148 (40); 131 (60). Acc Mass: M + H^+: Calc. 346.1147, Found 346.1147. IR (neat): 3100 - 2800 (CH); 1749 (SCO); 1691 (NCO) and 1320 - 1190 cm^{-1} (SO_2).

Preparation of lithium phenolate:

A solution of phenol in toluene was azeotroped in a Dean & Stark apparatus for 4 hr and the distillate discarded from time to time and replaced with new dry solvent. An aliquot was then transferred to a dry vessel and evaporated to dryness. The dry phenol was then dissolved in ether (0.5 ml/mmole) and cooled down to 0°C prior to the addition of an equimolar amount of ^{n}BuLi in hexane which resulted in the immediate formation of a yellow precipitate. The slurry was kept for 1 hr at 0°C and the precipitate collected by filtration under N_2. The white precipitate was then thoroughly washed with dry pet spirit and eventually dissolved in either CH_3CN or DMSO. (2.5 ml/mmol) (Typical yield ~ 70 %).

Preparation of N-(2-hydroxyalkanoyl)bornane-10,2-sultam phenyl ether (**23**):

To the N-(2-bromoalkanoyl)bornane-10,2-sultam (**1a**) (33 mg, 0.09 mol, d.e. = 100%) preheated to 60°C was added a preheated solution of lithium phenolate in DMSO (1 ml, 0.097 M, 0.097 mmole, 1.0 eq.) and the clear solution stirred at 60°C for 5 mins. It was then poured into water to give a white turbid mixture which was extracted with ether. The ether was dried ($MgSO_4$), filtered and evaporated to give the product (**23a**) as an oil (29 mg) which contained 12% of the sultam (corrected yield 75%).

(S)-isomer: ^{1}H NMR: 0.98 (s, 3H, CH_3); 1.16 (s, 3H, CH_3); 1.26 - 1.47 (m, 2H, H_5); 1.69 (d (6.64), 3H, CH_3); 1.78 - 2.06 (m, 5H, H_4, H_6, H_3) 3.50 and 3.55 (ABq (13.83), 2H, H_{10}); 3.94 (t (6.29), 1H, H_2); 5.37 (q (6.74), 1H, CH); 6.91 - 7.02 (m, 3H, $Ar_{m/p}$) and 7.20 - 7.27 ppm (m, 2H, Ar_o). ^{13}C NMR: 19.41 (CH_3); 19.87 (CH_3); 20.63 (CH_3); 26.39 (C_5); 32.67 (C_6); 38.02 (C_3); 44.49 (C_4); 47.86 (C_7); 48.99 (C_1); 53.00 (C_{10}); 65.09 (C_2); 72.24 (CH); 115.07 (Ar_p); 121.38 (Ar_m); 129.47 (Ar_o); 157.04 (Ar_i) and 171.36 ppm (CO). Mass Spec: EI (m/z %): 121 (100); 77 (75); 49 (80). CI (m/z %): 381 (35); 364 (50); 260 (60); 233 (100). Acc Mass: M + H^+: Calc. 364.1583, Found 364.1583. IR (film): 3100 - 2800 (CH); 1708 (CO) and 1310 - 1180 cm^{-1} (SO_2).

The (R)-isomer was obtained as a mixture with the *(S)-isomer* starting from the *(R)/(S)*-bromide (10 mg). ^{1}H NMR: 0.97 (s, 3H, CH_3); 1.26 (s, 3H, CH_3); 1.26 - 1.47 (m, 2H, H_5); 1.64 (d (6.37), 3H, CH_3); 1.78 - 2.06 (m, 5H, H_4, H_6, H_3); 3.47 and 3.56 (ABq (13.62), 2H, H_{10}); 3.91 (dd (5.38, 7.40), 1H, H_2); 5.41 (q (6.34), 1H, CH); 6.91 - 7.02 (m, 3H, $Ar_{m/p}$) and 7.20 - 7.27 ppm (m, 2H, Ar_o). ^{13}C NMR: 18.05 (CH_3); 19.84 (CH_3); 20.51 (CH_3); 26.31 (C_5); 32.92 (C_6); 38.25 (C_3); 44.69 (C_4); 47.80 (C_7); 48.99 (C_1); 53.10 (C_{10}); 65.60 (C_2); 71.92 (CH); 115.58 (Ar_p); 121.68 (Ar_m); 129.45 (Ar_o); 156.93 (Ar_i) and 171.07 ppm (CO). Acc Mass M + H^+: Calc. 364.1583, Found 364.1583.

N-(2-Hydroxybutyryl)bornane-10,2-sultam phenyl ether (**23b**): This was prepared starting from (**1b**) (21 mg, 0.058 mol) as described above and obtained along with 18% of the sultam as an oil (corrected yield 77%): *(S)-isomer:* ^{1}H NMR: 0.99 (s, 3H, CH_3); 1.12 (t (7.30), 3H, CH_3); 1.16 (s, 3H, CH_3); 1.17 - 1.48 (m, 2H, H_5); 1.86 - 2.17 (m, 7H, H_4, H_6, H_3, CH_2); 3.51 and 3.56 (ABq (13.84), 2H, H_{10}); 3.95 (dd (5.39, 7.2), 1H, H_2); 5.18 (dd (3.12, 8.19), 1H, CH); 6.84 - 7.02 (m, 3H, $Ar_{m/p}$) and 7.20 - 7.34 ppm (m, 2H, Ar_o). ^{13}C NMR: 9.80 (CH_3); 19.84 (CH_3); 20.60 (CH_3); 26.40 (C_5); 26.94 (CH_2); 32.65 (C_6); 38.14 (C_3); 44.45 (C_4); 47.85 (C_7); 48.93 (C_1); 53.00 (C_{10}); 65.06 (C_2); 77.11 (CH); 115.10 (Ar_p); 121.30 (Ar_m); 129.43 (Ar_o); 157.46 (Ar_i) and 170.75 ppm (CO). Mass Spec: EI (m/z %): 377 (2); 284 (2); 135 (100). CI (m/z %): 395 (10); 378 (25); 233 (40), 96 (80); 79 (100). Acc Mass: M + H$^+$: Calc. 378.1739, Found 378.1739. IR (film): 3120 - 2810 (CH); 1710 (CO) and 1310 - 1190 cm^{-1} (SO_2).

Preparation of N-(2-thiopropionyl) bornane-10,2-sultam phenyl ether (**25a**):

To (**1a**) (30 mg, 0.086 mmol, d.e. = 100%)) was added a solution of lithium thiophenolate in DMSO at r.t. (1 ml, 0.086 M, 0.086 mmol, 1 eq.) and the clear solution was stirred for 10 mins. It was then poured into water to give a white turbid emulsion which was extracted with ether. The ether was dried ($MgSO_4$), filtered and evaporated to give (**25a**) as oily crystals (32 mg, 98.5%).

(S)-isomer: ^{1}H NMR: 0.97 (s, 3H, CH_3); 1.13 (s, 3H, CH_3); 1.29 - 1.44 (m, 2H, H_5); 1.55 (d (7.03), 3H, CH_3); 1.81 - 1.95 (m, 3H, H_4, H_6) 2.06 - 2.09 (m, 2H, H_3); 3.46 and 3.51 (ABq (13.8), 2H, H_{10}); 3.91 (t (6.36), 1H, H_2); 4.52 (q (7.02), 1H, CH); 7.24 - 7.32 (m, 3H, $Ar_{m/p}$) and 7.48 - 7.51 ppm (m, 2H, Ar_o). ^{13}C NMR: 19.40 (CH_3); 19.84 (CH_3); 20.80 (CH_3); 26.36 (C_5); 32.74 (C_6); 38.22 (C_3); 44.53 (C_4); 46.96 (CH); 47.79 (C_7); 48.56 (C_1); 52.93 (C_{10}); 65.41 (C_{7a}); 127.72 (Ar_p); 128.88 (Ar_m); 132.96 (Ar_o); 133.11 (Ar_i) and 171.19 (CO). Mass Spec: EI (m/z %): 379 (10); 206 (15); 137 (100). CI (m/z %): 397 (60); 380 (100); 369 (40); 289 (50). Acc Mass: M + H$^+$: Calc. 380.1355, Found 380.1354. IR (film): 3130 - 2800 (CH), 1709 (CO) and 1300 - 1180 cm^{-1} (SO_2).

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