Synthesis of camphor-derived chiral auxiliaries and their application in asymmetric Morita-Baylis-Hillman reactions

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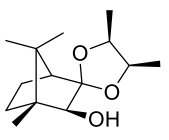
Abstract

N-Substituted 2-*exo*-hydroxybornyl-10-sulfonamides, prepared as potential chiral auxiliaries for use in asymmetric Morita-Baylis-Hillman (MBH) reactions, have been treated with acryloyl chloride to afford the corresponding 2-*exo*-acrylate esters as MBH substrates. Reaction of selected 2-*exo*-acrylate ester substrates with pyridine-4-carbaldehyde and 6-methylpyridine-2-carbaldehyde in the presence of DABCO gave the expected MBH adducts in > 91% yield and with diastereoselectivities of 7-33% d.e.

Keywords: Camphor, chiral auxiliaries, bornyl acrylates, Morita-Baylis-Hillman reactions

Introduction

The conformational rigidity and steric demands of the bicyclic camphor system account for its use in the construction of a wide range of chiral auxiliaries.[1] These include Oppolzer′s classic camphorsultams[2] and the sterically hindered systems developed by Helmchen.[3] In earlier studies, we have explored the application of camphor-derived chiral auxiliaries in the asymmetric α-benzylation of carboxylic esters prepared using the borneol derivative **1**,[4] Simmons-Smith asymmetric cyclopropanation of α,β-unsaturated acetals prepared using the chiral diol **2**,[5] and preliminary asymmetric Morita-Baylis-Hillman (MBH) reactions involving chiral acrylate esters.[6] The chiral auxiliary used in these preliminary MBH reactions was the *N*-adamantyl-2-*exo*-hydroxybornyl-10-sulfonamide (**3**), and the promising level of diastereoselectivity observed in one of these reactions prompted us to investigate the preparation of a series of *N*-substituted analogues as potential chiral auxiliaries for asymmetric MBH reactions.



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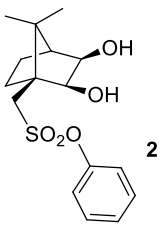

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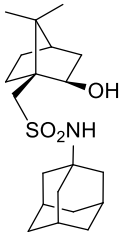

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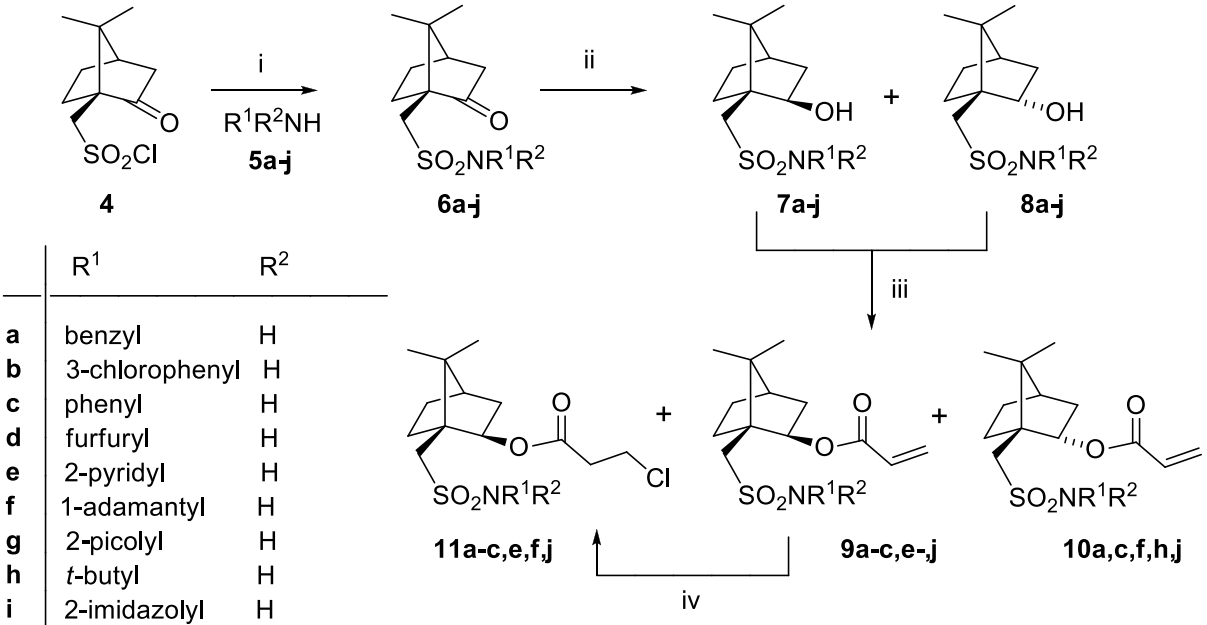
Results and Discussion

Synthetic access to the series of chiral auxiliaries **7** and **8** and the corresponding acrylate ester derivatives **9** and **10** is outlined in Scheme 1. Thus, each of primary or secondary amines **5a-j** was treated with (1*S*)-(+)-camphor-10-sulfonyl chloride (**4**) in the presence of a catalytic quantity of 4-(dimethylamino)pyridine (DMAP) in acetonitrile. Work-up and purification furnished the corresponding *N*-substituted camphor-10-sulfonamides **6a-j** in good to excellent yields (83-100%; Table 1). Reduction of the carbonyl group in each of the *N*-substituted camphor-10-sulfonamides **6a-j** was effected using $NaBH_4$ to afford the epimeric 2-hydroxybornyl-10-sulfonamides **7a-j** and **8a-h,j** in moderate to excellent yields (53-100%) and, generally, with high diastereoselectivity (100% in the case of the 2-imidazolyl derivative **7i**), as shown in Table 1. The dicyclohexyl derivative **7j** has been used previously as a chiral auxiliary by Oppolzer *et al*. in asymmetric Diels-Alder reactions[7] and in the asymmetric synthesis of aldols,[8] halohydrins and epoxides,[9] and α-amino acids.[10] Semi-preparative HPLC permitted isolation of analytical samples of the 2-*exo*- and 2-*endo*-hydroxy epimers, eight of which are new compounds. The C-2 configurations assigned to these epimeric products are supported by their ^{1}H NMR chemical shift and coupling constant data. Dominance of the 2-*exo*-hydroxy epimers **7** may be attributed to preferential hydride delivery to the less hindered *endo* face of the carbonyl group in the ketone precursors **6.**



	R^1	R^2
a	benzyl	H
b	3-chlorophenyl	H
c	phenyl	H
d	furfuryl	H
e	2-pyridyl	H
f	1-adamantyl	H
g	2-picolyl	H
h	*t*-butyl	H
i	2-imidazolyl	H
j	cyclohexyl	cyclohexyl

Scheme 1. *Reagents and conditions:* i) DMAP, CH_3CN, 0 °C; ii) $NaBH_4$, EtOH-H_2O, 0 °C; iii) Al_2O_3, CH_2=CHCOCl; and iv) *in situ* HCl.

Formation of the acrylate esters **9** and **10** was achieved as reported previously.[6] The alcohols **7** and **8** were added, generally as epimeric mixtures, to neutral Al_2O_3 (1.5 eq.), followed by acryloyl chloride (2 eq.). The resulting dispersions were allowed to stand at r.t. for 72 h without stirring. Flash chromatographic separation of the products, following work-up, proved impossible, necessitating the use of semi-preparative HPLC to obtain analytical samples; even then, the products, in some cases, remained slightly contaminated. The major products were, typically, the 2-*exo*-acryloyloxybornane-10-sulfonamides **9** and their 2-*exo*-[(3-chloropropanoyl)oxy]bornane-10-sulfonamide derivatives **11**, the latter arising from conjugate addition to the former by the HCl released as a by-product. [We have shown previously[6] that dehydrochlorination (**11** → **9**) can be readily achieved using triethylamine.] Minor products, isolated in some cases, included the 2-*endo*-[(3-chloropropanoyl)oxy]bornane-10-sulfonamide derivatives due to the presence of low concentrations of the 2-*endo* alcohols in the substrate mixtures.

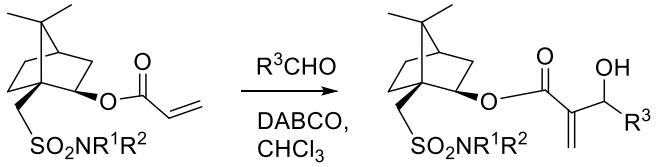
Table 1. Data for the preparation of the camphor-10-sulfonamides **6** and the diastereomeric bornyl alcohols **7** and **8**

R^1	R^2	Camphor-10-sulfonamide	Yield %	2-*exo*-alcohol	2-*endo*-alcohol	Yield[a] %	exo: endo %
benzyl	H	**6a**	99	**7a**	**8a**	95	78: 22
3-chlorophenyl	H	**6b**	99	**7b**	**8b**	53	93: 7
phenyl	H	**6c**	93	**7c**	**8c**	97	90: 10
furfuryl	H	**6d**	100	**7d**	**8d**	83	82: 18
2-pyridyl	H	**6e**	84	**7e**	**8e**	98	87: 13
1-adamantyl	H	**6f**	89	**7f**	**8f**	70	87: 13
2-picolyl	H	**6g**	90	**7g**	**8g**	93	90: 10
t-butyl	H	**6h**	94	**7h**	**8h**	92	79: 21
2-imidazolyl	H	**6i**	83	**7i**	**8i**	86	100: 0
cyclohexyl	cyclohexyl	**6j**	88	**7j**	**8j**	100	62: 38

[a]Total yield for both diastereomers.

In the present study, attention was focused on using the 2-*exo*-acryloyloxybornane-10-sulfonamides **9a,b,f** as chiral MBH substrates. Pyridinecarbaldehydes tend to react rapidly under MBH conditions,[11] and pyridine-4-carbaldehyde and 6-methylpyridine-2-carbaldehyde were selected as the electrophiles and the tertiary amine, DABCO, as the nucleophilic catalyst for these reactions (Scheme 2). The reactions were allowed to run for 90 h and the desired series of MBH adducts **12** and **13** were obtained with excellent conversion levels (91-100%) as determined by ^{1}H NMR analysis after preliminary flash chromatography of the reaction mixtures. The diastereoselectivities were determined by comparing the relative integrals of the signals

corresponding to the vinylic methylene and hydroxymethine protons (between 5 and 6 ppm) in the ^{1}H NMR spectra of the mixtures of the major and minor MBH products. The results, summarised in Scheme 2, reveal that while a measure of diastereoselectivity (7-33% d.e.) was observed in all cases, there is considerable room for improvement, and careful optimisation of the methodology is required to establish reproducibility of our encouraging, preliminary results (up to 95% d.e.) obtained earlier.[6] As observed previously, reactions with the more sterically hindered aldehyde, 6-methylpyridine-2-carbaldehyde exhibit significantly higher diastereo-selectivities than reactions with pyridine-4-carbaldehyde, confirming the expectation that steric effects play a major role in diastereocontrol. It is expected that future efforts will focus on using inter- and/or intramolecular coordination effects to increase transition-state rigidity and thus enhance diastereoselectivity in such MBH reactions.



9a,b,f

12a,b,f: R^3 = 4-pyridyl
13a,b,f: R^3 = 2-(6-methylpyridyl)

	R^1	R^2	R^3	Yield (%)[a]	% D.e.[b]
a	benzyl	H	4-pyridyl	91	8
			2-(6-methylpyridyl)	100	33
b	3-chlorophenyl	H	4-pyridyl	92	7
			2-(6-methylpyridyl)	98	21
f	1-adamantyl	H	4-pyridyl	93	8
			2-(6-methylpyridyl)	96	15

[a] Yields based on % conversion as determined by ^{1}H NMR analysis of the material isolated following work-up.
b As determined by ^{1}H NMR analysis of the diastereomeric products.

Scheme 2

Conclusions

A number of borneol derivatives have been prepared with the potential to serve as chiral auxiliaries in various transformations, and the use of three of these compounds has been explored in asymmetric MBH reactions. Future challenges include the optimisation of reaction conditions and structural modifications to enhance diastereoselectivity.

Experimental Section

General. Reagents and solvents were used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AMX400 or Avance II^{+} 600 MHz spectrometers, and were calibrated using solvent signals; coupling constants are given in Hertz (Hz). Melting points were determined using a hot-stage apparatus, and are uncorrected. IR spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR spectrometer. High-resolution mass spectra were recorded at the University of Stellenbosch Mass Spectrometry Unit. Flash chromatography was carried out using Merck silica gel 60 [230-240 mesh (particle size 0.040-0.063 mm)] and preparative layer chromatography was conducted using silica gel 60 PF_{254}.

Compounds **6a,b,c,e,f,g,h**,**j**, **7a,c,h,j**, **8a,c**, **12f** and **13f** are known.[14-17] General procedures and analytical data for new compounds are as follows.

Formation of the camphor-10-sulfonamides 6a-j

General procedure, exemplified by the preparation of *N*-benzylcamphor-10-sulfonamide (6a). A solution of (+)-camphor-10-sulfonyl chloride (**4**) (10.0 g, 39.9 mmol) in acetonitrile (100 mL) was added dropwise under N_2 to a stirred solution of the benzylamine (**5a**) (8.67 mL, 79.5 mmol) and DMAP (1.28 g, 10.5 mmol) in acetonitrile (50 mL) at 0 °C. The solution was stirred for 1 h and water (50 mL) was then added, followed by 10% HCl (10 mL), and the resulting mixture was extracted with EtOAc (3 × 125 mL). The organic layers were combined, washed with 5% aqueous NaOH (25 mL) and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* to afford the known *N*-benzylcamphor-10-sulfonamide (**6a**)[14,15] as colourless crystals (12.8 g, 39.8 mmol, 99%).

***N*-(2-Furfuryl)camphor-10-sulfonamide (6d).** Yellow crystals (100%), mp 42-44 °C (Found: MNa^{+}, 334.1085. $C_{15}H_{21}NO_4SNa$ requires, *M*+23: 334.1089); δ_H (600 MHz; $CDCl_3$) 0.78 (3H, s, 9-Me), 0.95 (3H, s, 8-Me), 1.42-2.88 (7H, series of m, H_2-3,5,6, H-4), 2.87 and 3.16 (2H, AB system, *J* 15.0 Hz, H_2-10), 4.31 and 4.42 (2H, two ddd, *J* 4.8, 7.2 and 15.6 Hz, furfuryl CH_2), 5.96 (1H, m, NH), 6.32 (2H, br s, ArH), 7.35 (1H, s, ArH); δ_C (150 MHz; $CDCl_3$) 19.4 (C-9), 19.9 (C-8), 27.0 and 27.2 (C-3,5), 40.4 (CH_2N), 42.8 (C-4), 42.9 (C-6), 48.8 (C-1), 51.3 (C-10), 59.4 (C-7), 108.6, 110.5, 142.6, and 150.4 (ArC), 216.8 (C-2).

***N*-(2-Imidazolyl)camphor-10-sulfonamide (6h).** Brown oily crystals (83%), m.p. 218-220 °C (Found: MH^{+}, 298.1225. $C_{13}H_{20}N_3O_3S$ requires, *M*+1: 298.1225); ν_{max} (ATR)/cm^{-1} 1675 (C=O); δ_H (400 MHz; $CDCl_3$) 0.86 (3H, s, 9-Me), 1.08 (3H, s, 8-Me), 1.44-2.55 (7H, series of m, H_2-3,5,6, H-4), 2.90 and 3.40 (2H, AB system, *J* 12.4 Hz, H_2-10), 6.56 and 7.23 (2H, two s, ArH), 11.6 (2H, s, 2 × NH); δ_C (100 MHz; $CDCl_3$) 19.8 (C-8), 19.9 (C-9), 24.7 and 27.1 (C-5,6), 42.7 (C-4), 43.0 (C-3), 48.2 (C-10), 48.5 (C-1), 59.3 (C-7), 112.6 (imidazolyl C-4',5'), 148.3 (C-2'), 216.5 (C-2).

Formation of *N*-substituted 2-hydroxybornane-10-sulfonamides 7 and 8. General procedure, exemplified by the preparation of *N*-benzyl-2-*exo*-hydroxybornane-10-sulfonamide (7a) and *N*-benzyl-2-*endo*-hydroxybornane-10-sulfonamide (8a). A solution of *N*-benzylcamphor-10-sulfonamide (**6a**) (12.0 g, 37.3 mmol) in EtOH/H_2O (5:1) (104 mL) was added drop-wise to a

stirred solution of $NaBH_4$ (10 eq.; 14.10 g, 372.7 mmol) in EtOH/H_2O 5:1 (121 mL) at r.t. The mixture was stirred overnight; the reaction was then quenched with 5% HCl (10 mL) and the resulting mixture extracted with EtOAc (3 × 25 mL). The organic layers were combined, washed with 5% brine (25 mL) and dried over anhydrous $MgSO_4$. Solvent was removed *in vacuo* to give light-yellow crystalline material (11.5 g), which was chromatographed (HPLC; elution with hexane/EtOAc 8:2) to afford two products.

Fraction 1. The known *N*-benzyl-2-*exo*-hydroxybornane-10-sulfonamide **7a**[14,17] as white crystals (78%).

Fraction 2. The known *N*-benzyl-*2-endo*-hydroxybornane-10-sulfonamide **8a**[14,17] as white crystals (22%).

Similar reaction of *N*-(3-chlorophenyl)-10-sulfonamide (**6b**) afforded two products:

Fraction 1. *N*-(3-Chlorophenyl)-2-*exo*-hydroxybornane-10-sulfonamide (7b). White crystals (93%), mp 108-110 ºC [Found: $(M-H)^-$, 342.0916. $C_{16}H_{21}ClNO_3S$ requires $(M-1)^-$: 342.0931]; ν_{max}(ATR)/cm^{-1} 3441 (OH); δ_H (600 MHz; $CDCl_3$) 0.78 (3H, s, 9-Me), 1.03 (3H, s, 8-Me), 1.14-1.83 (7H, series of m, H_2-3,5,6, H-4), 2.98 and 3.55 (2H, AB system, *J* 13.8 Hz, H_2-10), 3.05 (1H, s, OH), 4.14 (1H, m, H-2), 6.79 (1H, br s, NH), 7.12 (1H, ddd, *J* 0.7, 2.3 and 8.3 Hz, ArH), 7.16 (1H, ddd, *J* 1.1, 2.0 and 8.0 Hz, ArH), 7.23 (1H, t, *J* 2.1 Hz, ArH), 7.29 (1H, t, *J* = 8.1 Hz Hz, ArH); δ_C (150 MHz; $CDCl_3$) 19.9 (C-9), 20.5 (C-8), 27.3, 30.5, and 39.3 (C-3,5,6), 44.4 (C-4), 49.0 and 50.5 (C-1,7), 52.0 (C-10), 76.4 (C-2), 118.0, 120.1, 125.3, 130.8, 135.4, and 138.0 (ArC).

Fraction 2. *N*-(3-Chlorophenyl)-2-*endo*-hydroxybornane-10-sulfonamide (8b). White crystals (7%) [Found: $(M-H)^-$, 342.0946. $C_{16}H_{21}ClNO_3S$ requires, $(M-1)^-$: 342.0931]; δ_H (600 MHz; $CDCl_3$) 0.85 (6H, s, 8,9-Me), 1.06-2.44 (7H, series of m, H_2-3,5,6, H-4), 3.13 and 3.19 (2H, AB system, *J* 14.6 Hz, H_2-10), 4.32 (1H, dt, *J* 3.9 and 15.0 Hz, H-2), 7.12-7.28 (4H, series of m, ArH).

Similar reaction of *N*-(furfuryl)camphor-10-sulfonamide (**6d**) afforded two products:

Fraction 1. *N*-(Furfuryl)-2-*exo*-hydroxybornane-10-sulfonamide (7d). Yellow crystals (82%), mp 60-62 °C [Found: $(M-H)^-$, 312.1281. $C_{15}H_{22}NO_4S$ requires, $(M-1)^-$: 312.1270]; ν_{max} (ATR)/cm^{-1} 3493 (OH); δ_H (400 MHz; $CDCl_3$) 0.72 (3H, s, 9-Me), 0.97 (3H, s, 8-Me), 1.41-1.75 (7H, series of m, H_2-3,5,6, H-4), 2.97 and 3.26 (2H, AB system, *J* 15.0 Hz, H_2-10), 3.16 (1H, br s, OH), 4.04 (1H, m, H-2), 4.33 (2H, s, furfuryl CH_2), 4.87 (1H, br s, NH), 6.33 (2H, m, furfuryl H-3',4'), 7.40 (1H, br s, H-5'); δ_C (100 MHz; $CDCl_3$) 19.8 (C-9), 20.5 (C-8), 27.3 (C-3), 30.3 (C-5), 38.9 (furfuryl CH_2), 40.0 (C-6), 44.3 (C-4), 48.6 and 50.3 (C-1,7), 53.1 (C-10), 76.4 (C-2), 108.9 and 110.7 (furfuryl C-3',4'), 142.8 (C-5'), 150.0 (C-2').

Fraction 2. *N*-(Furfuryl)-2-*endo*-hydroxybornane-10-sulfonamide (8d). Brown oil (trace amounts); δ_H (400 MHz; $CDCl_3$) 0.81 (6H, br s, 8,9-Me), 1.41-1.75 (7H, series of m, H_2-3,5,6, H-4), 2.92 and 2.97 (2H, AB system, *J* 14.0 Hz, H_2-10), 3.10 (1H, br s, OH), 4.16 (1H, m, H-2), 4.34 (2H, m, furfuryl CH_2), 5.17 (1H, br s, NH), 6.34 and 6.36 (2H, m, furfuryl H-3',4'), 7.41 (1H, m, H-5').

Similar reaction of *N*-(2-pyridyl)camphor-10-sulfonamide (**6e**) afforded two products:

Fraction 1. 2-*exo*-Hydroxy-*N*-(2-pyridyl)bornane-10-sulfonamide (7e). White crystals (87%), mp 230-232 °C (Found: MH^+, 311.1423. $C_{15}H_{23}N_2O_3S$ requires, *M*+1: 311.1429); ν_{max}(ATR)/cm^{-1} 3413 (OH); δ_H (400 MHz; $CDCl_3$) 0.81 (3H, s, 9-Me), 1.10 (3H, s, 8-Me), 1.60-1.89 (7H, series of m, H-4, H_2-3,5,6), 3.12 and 3.74 (2H, AB system, *J* 14.1 Hz, H_2-10), 4.17 (1H, dd, *J* 8.2 and 4.0 Hz, H-2), 6.84 (2H, br s, NH and OH), 6.87 (1H, t, *J* 6.5 Hz, pyridyl H-5'), 7.65 (1H, d, *J* 8.8 Hz, H-3'), 7.78 (1H, t, *J* 7.5 Hz, H-4'), 8.18 (1H, d, *J* 5.9 Hz, H-6'); δ_C (150 MHz; $CDCl_3$) 20.0 (C-9), 20.5 (C-8), 27.3, 30.5, and 39.4 (C-3,5,6), 44.5 (C-4), 49.1 and 50.7 (C-1,7), 53.5 (C-10), 75.9 (C-2), 115.1 (pyridyl C-3'), 116.3 (C-5'), 140.1 (C-4'), 143.4 (C-6'), 152.1 (C-2').

Fraction 2. 2-*endo*-Hydroxy-*N*-(2-pyridyl)bornane-10-sulfonamide (8e). Yellow oil (13%) (Found: MH^+, 311.1430. $C_{15}H_{23}N_2O_3S$ requires, *M*+1: 311.1429); ν_{max}(ATR)/cm^{-1} 3413 (OH); δ_H (400 MHz; $CDCl_3$) 0.85 (3H, s, 9-Me), 1.15 (3H, s, 8-Me), 1.60-1.85 (7H, series of m, H-4, H_2-3,5,6), 2.94 and 3.45 (2H, AB system, *J* 13.9 Hz, H_2-10), 4.40 (1H, d, *J* 9.3 Hz, H-2), 6.84 (2H, br s, NH and OH), 6.74 (1H, t, *J* 6.8 Hz, H5'), 6.97 (1H, d, *J* 8.8 Hz, .H-3') and 7.69-7.74 (2H, series of m, H-4',6'); δ_C (150 MHz; $CDCl_3$) 20.7 (C-8,9), 23.6, 28.2, and 38.4 (C-3,5,6), 44.2 (C-4), 48.2 and 51.6 (C-1,7), 54.5 (C-10), 75.1 (C-2), 115.1 (pyridyl C-3'), 116.3 (C-5'), 140.1 (C-4'), 143.4 (C-6'), 152.1 (C-2').

Similar reaction of *N*-(2-picolyl)camphor-10-sulfonamide **6g** afforded two products.

Fraction 1. 2-*exo*-Hydroxy-*N*-(2-picolyl)camphor-10-sulfonamide 7g, as a colourless oil (90%); δ_H (400 MHz; $CDCl_3$) 0.76 (3H, s, 9-Me), 1.01 (3H, s, 8-Me), 1.08-1.78 (7H, series of multiplets, 3-, 5- and 6-CH_2 and 4-H), 2.83 and 3.43 (2H, 2 x d, *J* 14.0 Hz, 10-CH_2), and 4.09 (1H, dd, *J* 4.0 and 8.0 Hz, 2-H), 4.46 (2H, br s, NCH_2),5.46 (1H, br s, NH), 7.24 (1H, m, ArH), 7.31 (1H, d, *J* 8.0 Hz, ArH), 7.71 (1H, t, *J* 7.6 Hz, ArH) and 8.53 (1H, d, *J* 4.0 Hz, ArH); δ_C (100 MHz; $CDCl_3$) 19.9 (C-8), 20.5 (C-9), 27.4, 30.4 and 39.3 (C-5, C-6 and C-3), 44.4 (C-4), 47.7 (C-1), 48.7 (C-7), 50.4 (C-11), 52.5 (C-10), 76.1 (C-2), 122.2, 122.9, 137.2, 149.3 and 155.3 (ArC).

Fraction 2. 2-*endo*-Hydroxy-*N*-(2-picolyl)camphor-10-sulfonamide 8g, as a colourless oil (10%) (Found: MH^+, 325.1592. $C_{16}H_{25}N_2O_3S$ requires, *M*+1: 325.1586); ν_{max}(ATR)/cm^{-1} 3524 (OH); δ_H (400 MHz; $CDCl_3$) 0.76 (3H, s, 9-Me), 1.01 (3H, s, 8-Me), 1.08-1.78 (7H, series of multiplets, 3-, 5- and 6-CH_2 and 4-H), 2.83 and 3.43 (2H, 2 x d, *J* 14.0Hz, 10-CH_2), and 4.09 (1H, dd, *J* 4.0 and 7.8 Hz, 2-H), 4.46 (2H, br s, NCH_2),5.46 (1H, br s, NH), 7.24 (1H, m, ArH), 7.31 (1H, d, *J* 8.0 Hz, ArH), 7.71 (1H, t, *J* 7.6 Hz, ArH) and 8.53 (1H, d, J 4.0 Hz, ArH); δ_C (100 MHz; $CDCl_3$) 18.9 (C-8), 20.4 (C-9), 26.7, 30.2 and 38.5 (C-5, C-6 and C-3), 44.0 (C-4), 47.6 (C-1), 47.9 (C-7), 51.1 (C-11), 51.5 (C-10), 75.1 (C-2), 122.9, 122.9, 137.1, 149.2 and 154.9 (ArC).

Similar reaction of *N*-(2-imidazolyl)camphor-10-sulfonamide (**6i**) afforded **2-*exo*-hydroxy-*N*-(2-imidazolyl)bornane-10-sulfonamide (7i)** as a black oil (86%) (Found: MH^+, 300.1395. $C_{13}H_{22}N_3O_3S$ requires, *M*+1: 300.1382); ν_{max} (ATR)/cm^{-1} 3378 (OH); δ_H (400 MHz; $CDCl_3$) 0.83 (3H, s, 9-Me), 1.09 (3H, s, 8-Me), 1.22-1.80 (6H, series of m, H_2-3,5,6), 2.17 (1H, s, H-4), 2.87 and 3.42 (2H, AB system, *J* 13.6 Hz, H_2-10), 3.25 (1H, s, OH), 3.93 (1H, m, H-2), 6.53 (2H, br s, imidazolyl H-4',5'), 11.60 (2H, s, NH); δ_C (100 MHz; $CDCl_3$) 19.8 (C-8), 20.4 (C-9), 27.1, 30.7,

and 30.9 (C-3,5,6), 44.1 (C-4), 47.3 (C-7), 50.1 (C-1), 50.6 (C-10), 75.8 (C-2), 106.7 and 113.5 (imidazolyl C-4',5'), 147.6 (C-2').

Similar reaction of *N*,*N*-dicyclohexylcamphor-10-sulfonamide (**6j**) afforded two products:

Fraction 1. The known *N*,*N*-dicyclohexyl-2-*exo*-hydroxybornane-10-sulfonamide (**7j**)[7] as white crystals (62%).

Fraction 2. *N*,*N*-Dicyclohexyl-2-*endo*-hydroxybornane-10-sulfonamide (8j). White crystals (38%), mp 162-164 °C (Found: MH^+, 398.2725. $C_{22}H_{40}NO_3S$ requires, *M*+1: 398.2729); ν_{max} (ATR)/cm^{-1} 3503 (OH); δ_H (400 MHz; $CDCl_3$) 0.87 and 0.88 (6H, two s, 8,9-Me), 1.11-3.27 (31H, m, H_2-3,5,6,10, 2 x cyclohexyl), 3.82 (1H, m, OH), 4.29 (1H, m, H-2); δ_C (100 MHz; $CDCl_3$) 20.0 and 20.6 (C-8,9), 44.0 (C-4), 57.8 (2 × CHN), 75.5 (C-2), 25.1, 26.4, 32.7, and 32.8 (cyclohexyl CH_2), 27.4, 33.5, 38.1, and 59.2 (C-3,5,6,10), 49.7 and 51.6 (C-1,7).

Formation of the *N*-substituted 2-(acryloyloxy)bornane-10-sulfonamides 9-11. General procedure, exemplified by the preparation of 2-*exo*-acryloyloxy-*N*-benzylbornane-10-sulfonamide (9a) and 2-*endo*-acryloyloxy-*N*-benzylbornane-10-sulfonamide (10a). Neutral Al_2O_3 (0.244 g, 2.4 mmol) was added to the mixture of the diastereomeric alcohols **7a** and **8a** (0.50 g, 1.5 mmol), followed by acryloyl chloride (0.30 g, 3.3 mmol). The resulting dispersion was shaken, sealed and kept unstirred at r.t. for 72 h. The mixture was then taken up in $CHCl_3$ (3 × 1 mL), filtered and the filtrate dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* to give an oil which was then treated with triethylamine (0.46 g, 4.5 mmol). The resulting mixture was stored under N_2 and stirred at 25 °C for 1 h and then taken up in EtOAc (5 mL); the organic solution was washed with brine and dried over anhydrous $MgSO_4$. Solvent was removed *in vacuo* to give an oil which was chromatographed [HPLC; elution with hexane-EtOAc (8: 2)] to afford three products.

Fraction 1. 2-*exo*-Acryloyloxy-*N*-benzylbornane-10-sulfonamide (9a). White crystals (0.39 g, 1.0 mmol, 67%), mp 82-84 °C (Found: MH^+, 378.1747. $C_{20}H_{28}NO_4S$ requires, *M*+1: 378.1747); ν_{max} (ATR)/cm^{-1} 1706 (C=O); δ_H (400 MHz; $CDCl_3$) 0.82 and 0.99 (6H, two s, 8,9-Me), 1.18-2.03 (7H, series of m, H_2-3,5,6, H-4), 2.81 and 3.43 (2H, AB system, *J* 14.0 Hz, H_2-10), 4.25 (2H, d, *J* 6.0 Hz, PhC$\underline{H_2}$), 4.57 (1H, br s, NH), 5.04 (1H, m, H-2), 5.79 (1H, d, J_{cis} 10.4 Hz, H_E-3'), 6.09 (1H, dd, *J* 10.2 and 17.4 Hz, H-2'), 6.33 (1H, d, J_{trans} 17.6 Hz, H_Z-3'), 7.33 (5H, overlapping signals, ArH); δ_C (100 MHz; $CDCl_3$) 19.9 and 20.3 (C-8,9), 27.0, 29.8, and 39.5 (C-3,5,6), 44.4 (C-4), 47.2 (Ph$\underline{C}H_2$), 49.2 and 49.4 (C-1,7), 51.9 (C-10), 77.9 (C-2), 128.9 (C-2′), 130.3 (C-3′), 127.97, 128.0, 128.8, and 137.0 (ArC),164.8 (C-1').

Fraction 2. *N*-Benzyl-2-*exo*-[(3-chloropropanoyl)oxy]bornane-10-sulfonamide (11a). White crystals (0.13 g, 0.3 mmol, 20%), mp 92-94 °C (Found: MH^+, 414.1498. $C_{20}H_{29}ClNO_4S$ requires, *M*+1: 414.1506); ν_{max} (ATR)/cm^{-1}1728 (C=O); δ_H (400 MHz; $CDCl_3$) 0.79 and 0.96 (6H, two s, 8,9-Me), 1.18-1.96 (7H, series of m, H_2-3,5,6, H-4), 2.74 (2H, m, H_2-2'), 2.76 and 3.55 (2H, AB system, *J* 14.0 Hz, H_2-10), 3.71 (2H, m, H_2-3'), 4.29 (2H, d, *J* 6.0 Hz, PhC$\underline{H_2}$), 4.66 (1H, s, NH), 4.98 (1H, m, H-2), 7.36 (5H, overlapping signals, ArH); δ_C (100 MHz; $CDCl_3$) 19.9 and 20.2 (C-8,9), 27.0, 30.0, and 39.4 (C-3,5,6), 37.9 (C-2′), 39.2 (C-3′), 44.4 (C-4), 47.2 (Ph$\underline{C}H_2$), 49.1 and 49.4 (C-1,7), 52.2 (C-10), 78.5 (C-2), 128.0, 128.1, 128.9, and 137.0 (ArC), 169.0 (C-1').

Fraction 3. 2-*endo*-Acryloyloxy-*N*-benzylbornane-10-sulfonamide (10a) as a solid isolated in trace amounts as a mixture with compound **11a**; δ_H (400 MHz; $CDCl_3$) 0.85 and 0.86 (6H, two s, 8,9-Me), 1.19-1.98 (7H, series of m, H_2-3,5,6, H-4), 2.92 (2H, AB system, *J* 14.4 Hz, H_2-10), 4.27 (2H, d, *J* 6.0 Hz, PhC$\underline{H_2}$), 5.16 (1H, d, *J* 6.0Hz, NH), 5.16 (1H, d, J_{cis} 10.4 Hz, H_E-3'), 5.79 (1H, m, H-2), 6.10 (1H, dd, *J* 10.4 and 17.2 Hz, H-2'), 6.42 (1H, d, J_{trans} 17.2 Hz, H_Z-3'), 7.31-7.37 (5H, overlapping signals, ArH).

Similar reaction of crude *N*-(3-chlorophenyl)-2-*exo*-hydroxybornane-10-sulfonamide (**7b**) afforded two products:

Fraction 1. 2-*exo*-Acryloyloxy-*N*-(3-chlorophenyl)bornane-10-sulfonamide (9b) as white crystals (0.420 g, 1.1 mmol, 73%), mp 150-152 °C (Found: MH^+, 398.1195. $C_{19}H_{25}ClNO_4S$ requires, *M*+1: 398.1193); ν_{max} (ATR)/cm^{-1} 1710 (C=O); δ_H (400 MHz; $CDCl_3$) 0.86 and 1.00 (6H, two s, 8,9-Me), 1.26-2.02 (7H, series of m, H_2-3,5,6, H-4), 3.03 and 3.62 (2H, AB system, *J* 14.0 Hz, H_2-10), 5.07 (1H, m, H-2), 5.75 (1H, d, J_{cis} 10.4 Hz, H_E-3'), 5.98 (1H, dd, *J* 10.4 and 17.2 Hz, H-2'), 6.24 (1H, d, J_{trans} 17.2 Hz, Hz-3'), 7.05-7.21 (5H, overlapping signals, ArH and NH); δ_C (100 MHz; $CDCl_3$) 19.9 and 20.3 (C-8,9), 27.1, 30.1, and 39.5 (C-3,5,6), 44.4 (C-4), 49.2 and 49.7 (C-1,7), 50.7 (C-10), 77.7 (C-2), 117.0, 119.1, 124.5, 130.6, 135.3, and 138.5 (ArC), 128.5 and 130.4 (C-2′,3′), 164.8 (C-1').

Fraction 2. *N*-(3-Chlorophenyl)-2-*exo*-[(3-chloropropanoyl)oxy]bornane-10-sulfonamide (11b), white crystals (0.100 g, 0.2 mmol, 13%), mp 120-122 °C; ν_{max} (ATR)/cm^{-1} 1698 (C=O); δ_H (400 MHz; $CDCl_3$) 0.84 and 0.99 (6H, two s, 8,9-Me), 1.67-1.99 (7H, series of m, H_2-3,5,6, H-4), 2.68 (2H, t, *J* 6.6 Hz, H_2-2'), 3.01 and 3.55 (2H, AB system, *J* 14.0 Hz, H_2-10), 3.66 (2H, m, H_2-3'), 5.02 (1H, m, H-2), 6.69 (1H, br s, NH), 7.06 (1H, ddd, *J* 0.9, 2.1 and 8.1 Hz, ArH), 7.14 (1H, ddd, *J* 0.8, 2.0 and 8.0 Hz, ArH), 7.23 (1H, t, *J* 2.0 Hz, ArH), 7.28 (1H, t, *J* 8.0 Hz, ArH); δ_C (100 MHz; $CDCl_3$) 19.9 and 20.3 (C-8,9), 27.0, 30.2, and 39.5 (C-3,5,6), 37.7 (C-2′), 39.1 (C-3′), 44.4 (C-4), 49.1 and 49.7 (C-1,7), 50.9 (C-10), 78.4 (C-2), 117.7, 119.6, 125.0, 130.7, 135.4, and 138.3 (ArC), 168.9 (C-1').

Similar reaction of crude 2-*exo*-hydroxy-*N*-phenylbornane-10-sulfonamide (**7c**) afforded two fractions:

Fraction 1. **2-*exo*-Acryloyloxy-*N*-phenylbornane-10-sulfonamide (9c)** (36%, contaminated with compound **11c**); δ_H (400 MHz; $CDCl_3$) 0.82 and 0.96 (6H, two s, 8,9-Me), 1.20-2.03 (7H, series of m, H_2-3,5,6, H-4), 3.01 and 3.54 (2H, AB system, *J* 14.0 Hz, H_2-10), 5.01 (1H, d, *J* 6.4 Hz, H-2), 5.73 (1H, d, J_{cis} 12.0 Hz, H_E-3'), 5.97 (1H, dd, *J* 10.4 and 17.2 Hz, H-2'), 6.22 (1H, d, J_{trans} 17.2 Hz, H_Z-3'), 7.10-7.34 (5H, m, ArH); δ_C (100 MHz; $CDCl_3$) 19.8 and 20.2 (C-8,9), 27.0, 30.0, and 39.4 (C-3,5,6), 44.3 (C-4), 49.0 and 49.6 (C-1,7), 50.1 (C-10), 78.3 (C-2), 128.6 and 130.3 (C-2′,3′), 119.1, 119.2, 120.1, 124.9, 129.6, and 137.1 (ArC), 169.0 (C-1').

Fraction 2. *2-exo*-[(3-Chloropropanoyl)oxy]-*N*-phenylbornane-10-sulfonamide (11c) (64%, contaminated with compound **9c**); δ_H (400 MHz; $CDCl_3$) 0.83 and 1.00 (6H, two s, 8,9-Me), 1.20-2.03 (7H, series of m, H_2-3,5,6, H-4), 2.58 (1H, t, *J* 6.8 Hz, CO.H_a), 3.01 (1H, m, *J* 6.8 Hz, CO.H_b), 3.03 and 3.54 (2H, AB system, *J* 14.0 Hz, H_2-10), 3.61 (2H, d, *J* 7.0 Hz, H_2-3'), 5.08 (1H, d, *J* 6.4 Hz, H-2), 7.10-7.34 (5H, m, ArH); δ_C (100 MHz; $CDCl_3$) 19.9 and 20.2 (C-8,9), 27.0, 29.9, and

39.5 (C-3,5,6), 37.6 and 39.0 (C-2′,3′), 44.4 (C-4), 49.1 and 49.6 (C-1,7), 50.1 (C-10), 77.8 (C-2), 119.2 (2 × ArC), 120.1 (ArC), 129.6 (2 × ArC), 137.2 (ArC), 164.8 (C-1').

Similar reaction of crude 2-*exo*-hydroxy-*N*-(2-pyridinyl)bornane-10-sulfonamide (**7e**) afforded two products:

Fraction 1. 2-*exo*-Acryloyloxy-*N*-(2-pyridinyl)bornane-10-sulfonamide (9e) (37%), yellow solid contaminated with compound **11e**; δ_H (400 MHz; $CDCl_3$) 0.82 (3H, s, 9-Me), 0.85 (3H, s, 8-Me), 1.24-2.17 (7H, series of m, H_2-3,5,6, H-4), 3.06 and 3.57 (2H, AB system, *J* 14.4 Hz, H_2-10), 5.07 (1H, m, H-2), 5.73 (1H, d, J_{cis} 10.4 Hz, H_E-3'), 5.98 (1H, dd, *J* 10.4 and 17.6 Hz, H-2'), 6.26 (1H, d, J_{trans} 17.6 Hz, H_Z-3'), 6.55 (1H, br s, NH), 7.43-7.75 (4H, series of m, ArH).

Fraction 2. 2-*exo*-(3-Chloropropanoyloxy)-*N*-(2-pyridinyl)bornane-10-sulfonamide (11e) (63%), yellow solid contaminated with compound **9e**; δ_H (400 MHz; $CDCl_3$) 0.91 (3H, s, 9-Me), 1.01 (3H, s, 8-Me), 1.24-2.17 (7H, series of m, H_2-3,5,6, H-4), 3.04 and 3.57 (2H, AB system, *J* 14.4 Hz, H_2-10), 2.93 (2H, m, H_2-2'), 4.33 (2H, m, H_2-3'), 5.07 (1H, m, H-2), 6.48 (1H, br s, NH), 7.43-7.75 (4H, series of m, ArH).

Similar reaction of crude *N*-(1-adamantyl)-2-*exo*-hydroxybornane-10-sulfonamide **7f** afforded three products:

Fraction 1. The known 2-*exo*-acryloyloxy-*N*-(1-adamantyl)bornane-10-sulfonamide (**9f**)[6] as white crystals (60%).

Fraction 2. 2-*endo*-Acryloyloxy-*N*-(1-adamantyl)bornane-10-sulfonamide (**10f**) (contaminated with compound **11f**); δ_H (400 MHz; $CDCl_3$) 0.90 and 1.03 (6H, two s, 8,9-Me), 1.18-2.01 (6H, series of m, H_2-3,5,6), 1.60 and 1.92 (12H, two m, adamantyl CH_2), 1.79 (1H, m, H-4), 2.07 (3H, m, adamantyl CH), 2.91 and 3.56 (2H, AB system, *J* 14.0 Hz, H_2-10), 4.06 (1H, s, NH), 5.06 (1H, m, H-2), 5.79 (1H, d, J_{cis} 10.4 Hz, H_E-3'), 6.10 (1H, dd, *J* 10.4 and 17.2 Hz, H-2'), 6.35 (1H, d, J_{trans} 17.2 Hz, H_Z-3'); δ_C (100 MHz; $CDCl_3$) 20.0 and 20.4 (C-8,9), 27.1, 29.9, and 39.5 (C-3,5,6), 29.6 (adamantyl CH), 35.9 and 43.4 (adamantyl CH_2), 44.4 (C-4), 49.3 and 49.5 (C-1,7), 55.1 (C-10), 78.1 (C-2), 129.0 (C-2′), 130.0 (C-3′), 164.7 (C-1').

Fraction 3. 2-*exo*-[(3-Chloropropanoyl)oxy]-*N*-(adamantyl)bornane-10-sulfonamide (11f). White crystals (0.33 g, 34%), mp 146-148 °C; δ_H (400 MHz; $CDCl_3$) 0.90 and 1.03 (6H, 2 × s, 8- and 9-Me), 1.26 - 2.02 (6H, series of m, H_2-3,5,6), 1.67 and 1.95 (12H, two m, 12-, 14-, 16-, 17-, 19- and 20-CH_2), 1.79 (1H, m, 4-H), 2.11 (3H, m, 13-, 15- and 18-CH), 2.78 (2H, t, *J* 6.4 and 6.8 Hz, 2′-CH_2), 3.21 (2H, 2 × d, *J* 14.0 Hz, 10-CH_2), 3.75 (2H, m, 3′-CH_2), 4.02 (1H, s, NH) and 5.00 (1H, d, *J* 5.6 Hz, 2-CH); δ_C (100 MHz; $CDCl_3$) 20.0 and 20.4 (C-8 and C-9), 27.1, 30.1 and 39.5 (C-3, C-5 and C-6), 29.6 (C-13, C-15 and C-18), 36.0 (C-14, C-19 and C-20), 43.4 (C-12, C-16 and C-17), 38.0 (C-2′), 39.2 (C-3′), 44.5 (C-4), 49.4 and 49.5 (C-1 and C-7), 55.1 (C-11), 55.6 (C-10), 78.1 (C-2) and 168.8 (C=O).

Similar reaction of crude *N*-*t*-butyl-2-*exo*-hydroxybornane-10-sulfonamide **7h** afforded two fractions:

Fraction 1. 2-*exo*-Acryloyloxy-*N*-*t*-butylbornane-10-sulfonamide 9h. Colourless oil (0.86 g, 86%) (Found: MH^+, 344.1897. $C_{17}H_{30}NO_4S$ requires, M+H: 344.1896); δ_H (400 MHz; $CDCl_3$) 0.90 and 1.03 (6H, 2 × s, 8- and 9-Me), 1.34 [9H, s, $C(CH_3)_3$], 1.21-1.99 (7H, series of m, H_2-

3,5,6, H-4), 2.91 and 3.54 (2H, 2 × d, *J* 14.0 Hz, 10-CH_2), 4.12 (1H, s, NH), 5.05 (1H, d, *J* 7.2 Hz, 2-H), 5.79 (1H, d, *J* 10.4 Hz, 3′-H_E), 6.09 (1H, dd, *J* 10.4 and 17.2 Hz, 2′-H) and 6.34 (1H, d, *J* 17.2 Hz, 3′-H_Z); δ_C (100 MHz; $CDCl_3$) 20.0 and 20.4 (C-8 and C-9), 27.1, 29.9 and 39.5 (C-3, C-5 and C-6), 30.3 [C (*C*H_3)], 44.4 (C-4), 49.4 and 54.7 (C-7 and C-1), 54.8 [*C*$(CH_3)_3$] 58.9 (C-10), 78.0 (C-2), 129.0 (C-2′), 130.1 (C-3′) and 164.7 (C=O).

***Fraction 2*. 2-*endo*-Acryloyloxy-*N*-*t*-butylbornane-10-sulfonamide 10h.** Colourless oil (0.14 g, 14%) (Found: MH^+, 344.1892. $C_{17}H_{30}NO_4S$ requires, *M*+H: 344.1896); δ_H (400 MHz; $CDCl_3$) 0.94 and 0.98 (6H, 2 × s, 8- and 9-Me), 1.33 [9H, s, $C(CH_3)_3$], 1.07-1.78 (7H, series of m, H_2-3,5,6, H-4), 3.06 and 3.16 (2H, 2 × d, *J* 14.0 Hz, 10-CH_2), 4.01 (1H, s, NH), 5.05 (1H, d, *J* 9.6 Hz, 2-H), 5.86 (1H, d, *J* 10.8 Hz, 3′-H_E), 6.15 (1H, dd, *J* 10.8 and 17.2 Hz, 2′-H) and 6.47 (1H, d, *J* 17.2 Hz, 3′-H_Z); δ_C (100 MHz; $CDCl_3$) 19.7 and 19.9 (C-8 and C-9), 25.5, 28.0 and 29.7 (C-5, C-6 and C-3), 30.3 [C(*C*H_3)], 44.0 (C-4), 50.1 and 50.7 (C-7 and C-1), 54.5 [*C*$(CH_3)_3$] 58.9 (C-10), 78.0 (C-2), 128.9 (C-2′), 130.9 (C-3′) and 165.9 (C=O).

Similar reaction of crude *N*,*N*-dicyclohexyl-2-*exo*-hydroxybornane-10-sulfonamide (**7j**) afforded two products:

Fraction 1. 2-*exo*-Acryloyloxy-*N*,*N*-dicyclohexylbornane-10-sulfonamide (9j). (42%) white solid slightly contaminated with compound **11j**; δ_H (400 MHz; $CDCl_3$) 0.89 and 1.01 (6H, 2 × s, 8- and 9-Me), 1.05-3.22 (31H, series of m, 13 × CH_2 and 3 × CH), 5.09 (1H, d, *J* 7.6 Hz, 2-CH), 5.79 (1H, d, *J* 10.4 Hz, 3′-H_E), 6.10 (1H, dd, *J* 10.8 and 13.6 Hz, 2′-H) and 6.35 (1H, d, *J* 17.2 Hz, 3′-H_Z); δ_C (100 MHz; $CDCl_3$) 20.0 and 20.5 (C-8 and C-9), 44.6 (C-4), 57.4 (2 × CHN), 78.4 (C-2), 129.2 (C-2′), 129.8 (C-3′), 25.2, 26.4, 32.8 (cyclohexyl CH_2), 27.0, 29.9, 39.1 and 49.1 (camphor CH_2), 49.5 and 53.7 (C-1 and C-7) and 164.5 (C=O).

Fraction 2. 2-*exo*-[(3-Chloropropanoyl)oxy]-*N*,*N*-dicyclohexylbornane-10-sulfonamide (11j). (58%), white crystals slightly contaminated with compound **9j**; δ_H (400 MHz; $CDCl_3$) 0.88 and 0.99 (6H, 2 × s, 8- and 9-Me), 1.05-3.22 (31H, series of m, 13 × CH_2 and 3 × CH), 4.99 (1H, d, *J* 7.6 Hz, 2-CH), 2.77 (2H, t, *J* 7.0 Hz, 2′-CH_2) and 3.76 (2H, m, 3′-CH_2); δ_C (100 MHz; $CDCl_3$) 20.0 and 20.4 (C-8 and C-9), 57.4 (2 × CHN of cyclohexyl), 37.8 (C-2′), 39.1 (C-3′), 44.5 (C-4), 79.2 (C-2),25.1, 26.5 and 32.8 (cyclohexyl CH_2) , 27.0, 30.3, and 49.2 (camphor CH_2), 49.5 and 53.9 7 (C-1 and C-7) and 168.7 (C=O).

Exploratory MBH reactions. General procedure, exemplified by the preparation of the diastereomeric MBH products 12 and 13. To a solution of 2-*exo*-acryloyloxy-*N*-benzylbornane-10-sulfonamide (9a) (0.03 g, 0.07 mmol) in $CDCl_3$ (0.1 mL) was added pyridine-4-carbaldehyde (0.01 g, 0.07 mmol), and DABCO (0.001 g, 0.01 mmol). The solution was stirred at r.t. for 90 h and then concentrated *in vacuo*. The residue was purified by flash chromatography and HPLC [elution with hexane-EtOAc (8: 2)] to afford a mixture of the diastereomeric MBH products 12a as yellow crystals (0.03 g, 91%; 8% d.e.), m.p. 98-100 °C (Found: MH^+, 485.2111. $C_{26}H_{33}N_2O_5S$ requires *M*+H: 485.2110); ν_{max} (ATR)/cm^{-1} 3274 (OH); δ_H (400 MHz; $CDCl_3$) 0.67 (3H, s, 9-Me), 0.68 (3H, s, 8-Me), 0.92-1.87 (7H, series of m, H_2-3,5,6, H-4), 2.64 and 3.19 (2H, 2 × d, 14.0 Hz, 10-CH_2), 4.90 (2H, s, PhCH_2), 4.93 (2H, br s, 2-H and NH), 5.49 (1H, s, C*H*OH), 6.12 (1H, br s,

OH), 5.72 and 6.17 (2H, 2 × s, 9′-CH_2), 7.40 (2H, d, *J* 4.5 Hz, ArH), 8.38 (5H, overlapping signals, ArH) and 8.56 (2H, d, *J* 4.5 Hz, ArH).

Similar reactions afforded the following MBH products as diastereomeric mixtures.

MBH products 13a. **B**rown oil (0.03 g, 100%; 33% d.e.) (Found: MH^+, 499.2252. $C_{27}H_{35}N_2O_5S$ requires, *M*+H: 499.2267); ν_{max} (ATR)/cm^{-1} 3266 (OH); δ_H (400 MHz; $CDCl_3$) 0.78 (3H, s, 9-Me), 0.93 (3H, s, 8-Me), 1.14-1.97 (6H, series of m, H_2-3,5,6), 2.17 (1H, s, 4-H), 2.65 and 3.27 (2H, 2 × d, 14.0 Hz, 10-CH_2), 4.18 (2H, d, *J* 5.6 Hz, PhCH_2), 4.27 (1H, t, 4.8 Hz, NH), 5.00 (1H, d, *J* 5.6 Hz, 2-H), 5.46 (1H, s, OH), 5.64 (1H, s, C*H*OH), 5.95 and 6.29 (2H, 2 × s, 9′-CH_2), 7.14 (2H, m, ArH), 7.33 (5H, overlapping signals, ArH) and 7.70 (1H, m, ArH).

MBH products 12b. **Y**ellow oil (0.03 g, 92%; 7% d.e.) (Found: MH^+, 505.1542. $C_{25}H_{30}ClN_2O_5S$ requires, *M*+H: 505.1564); ν_{max} (ATR)/cm^{-1} 3374 (OH); δ_H (400 MHz; $CDCl_3$) 0.76 (3H, s, 9-Me), 0.81 (3H, s, 8-Me), 0.97-1.90 (7H, series of m, H_2-3,5,6, H-4), 3.05 and 3.44 (2H, 2 × d,*J* 14.4 Hz, 10-CH_2), 5.00 (2H, m, 2-H and NH), .93 (2H, br s, 2-H and NH), 5.53 (1H, s, C*H*OH), 5.67 and 6.16 (2H, 2 × s, 9′-CH_2), 6.43 (1H, br s, OH) and 6.99-7.31 (8H, overlapping signals, ArH).

MBH products 13b. Yellow oil (0.03 g, 98%; 21% d.e.) (Found: MH^+, 520.3279. $C_{25}H_{30}ClN_2O_5S$ requires, *M*+H: 519.1720); ν_{max} (ATR)/cm^{-1} 3510 (OH); δ_H (400 MHz; $CDCl_3$) 0.69 (3H, s, 9-Me), 0.82 (3H, s, 8-Me), 0.99-1.95 (7H, series of m, H_2-3,5,6, H-4), 2.63 (3H, s, ArCH_3), 2.91 and 3.30 (2H, 2 × d, 14.4 Hz, 10-CH_2), 5.05 (2H, m, 2-H and NH), 5.52 (1H, s, C*H*OH), 5.64 and 6.15 (2H, 2 × s, 9′-CH_2), 5.71 (1H, br s, OH) and 6.97-7.75 (7H, overlapping signals, ArH).

The known MBH products **12f**[6] as yellow crystals (0.03 g, 93%; 8% d.e.).

The known MBH products **13f**[6] as **a** brown oil (0.03 g, 96%; 15% d.e.).

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