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Ring opening of cyclic *N*,*O*-acetals with allyltrimethylsilane under Lewis acidic conditions

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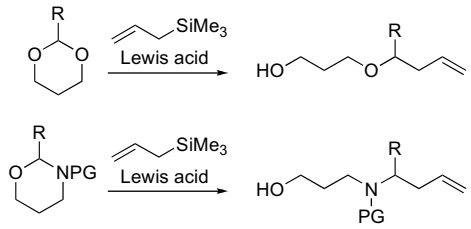
ABSTRACT

Five and six-membered cyclic *N*,*O*-acetals with *N*-carboxyalkyl and sulfonyl groups undergo clean and high yielding ring opening with allyltrimethylsilane in the presence of strong Lewis acids to give homoallylic amine derivatives.

1. Introduction

The reaction between cyclic *O*,*O*-acetals and silane reagents under Lewis acidic conditions is now well known and has been thoroughly studied.[1] The corresponding reactions of cyclic *N*,*O*-acetals, where the N bears an electron withdrawing group (PG), have not, to our knowledge, been systematically studied (Scheme 1). There have been several reports of the reactions of *N*,*O*-acetals of various types and applications in total synthesis.[2] In addition, the CNRS group has reported reactions of *N*,*O*-acetals lacking an electron withdrawing substituent.[3] The presumed intermediate in such reactions, in the cases where PG is a carbonyl function, would be an *N*-acyl iminium ion. These reactive intermediates have been shown to be valuable in organic synthesis.[4]

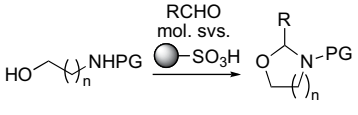


Scheme 1.

2. Results and discussion

We became interested in this area following difficulties in generating a homoallylic secondary amine, in which one or more of the alkyl substituents was secondary. Several methods, such as reductive amination and amide reduction, would not have been suitable for our purpose as problems of alkene reduction or migration could be anticipated. *N*,*O*-Acetal ring opening would directly deliver a homoallylic amine. We therefore made a systematic study of this reaction.

We found that *N*,*O*-acetals could be easily prepared in almost quantitative yield in many cases (Scheme 2). Stirring a mixture of the amino alcohol derivative, an aldehyde, amberlyst-15 and 4 Å molecular sieves in dichloromethane yielded the *N*,*O*-acetals in generally excellent yields (Table 1) after filtration and evaporation. The use of amberlyst-15 as the acid catalyst obviates the need for any extraction.



n = 1	PG = Ts	1
	PG = CO_2Me	2
n = 2	PG = Ts	3
	PG = CO_2Me	4
	PG = aloc	5
	PG = CBZ	6
	PG = Boc	7
	PG = PhCO	8

Scheme 2.

The reaction conditions for the synthesis of these *N*,*O*-acetals proved to be compatible with almost all *N*-protecting groups employed: tosyl, methoxycarbonyl, CBZ, Alloc and even *t*-Boc, with the exception of amides. It was only when an amide was employed, the *N*-benzoyl derivative, that a low yield of acetal was obtained (entry 16).

Acetalisation proved to be general for both aliphatic and aromatic aldehydes. Even paraformaldehyde lead to the formation of the corresponding methylene acetal (entry 8), albeit at slower rate due to the insolubility of the polymeric paraformaldehyde in the

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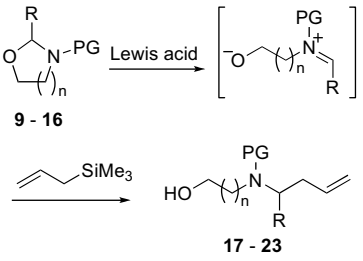
reaction medium. In contrast, when crotonaldehyde, an α,β-unsaturated aldehyde was used, no acetal could be isolated. Only a low yield of an unstable acetal could be obtained using acetone.

Table 1
Acetal formation and ring-opening reactions using $TiCl_4$

Entry	Amino alcohol derivative	*n*	R	PG	Acetal, yield (%)	Homoallylic amine derivative, yield (%)
1	**1**	1	Me	Ts	**9a**, 99	**17a**, 92
2	**1**	1	Et	Ts	**9b**, 81	**17b**, 88
3	**2**	1	Me	CO_2Me	**10a**, 73	**18a**, 80
4	**2**	1	Et	CO_2Me	**10b**, 87	**18b**, 92
5	**3**	2	Me	Ts	**11a**, 82	**19a**, 99
6	**3**	2	Et	Ts	**11b**, 99	**19b**, 99
7	**3**	2	Ph	Ts	**11c**, 91	**19c**, 32
8	**3**	2	H	Ts	**11d**, 94	**19d**, 99
9	**4**	2	Me	CO_2Me	**12a**, 85	**20a**, 99
10	**4**	2	Et	CO_2Me	**12b**, 87	**20b**, 99
11	**4**	2	Ph	CO_2Me	**12c**, 80	**20c**, 67
12	**4**	2	n-C_5H_{11}	CO_2Me	**12e**, 76	**20e**, 99
13	**5**	2	Et	Aloc	**13b**, 99	**21b**, 98
14	**6**	2	Et	CBZ	**14b**, 86	**22b**, 63
15	**7**	2	Et	*t*-Boc	**15b**, 86	**23b**, 66
16	**8**	2	Et	Bz	**16b**, 30	—

The ring-opening reaction (Scheme 3) using titanium tetrachloride at low temperature proved to be clean and efficient for all simple acetals derived from aliphatic substrates.



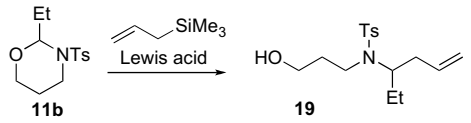
Scheme 3.

Titanium tetrachloride was effective as a Lewis acid at −78 °C. It was gratifying to find that the large excesses typically employed in the *O*,*O*-acetal chemistry[1] were unnecessary. As little as 1.2 equiv could be employed whilst still obtaining a good yield. The yields of ring opened products were excellent, especially for the six-membered ring acetals. The methylene acetal derived from paraformaldehyde also underwent efficient ring opening (entry 8). On the other hand, *N*,*O*-acetals derived from benzaldehyde gave lower yields (entries 7 and 11), accompanied by various by-products. These observations apply equally to the *N*-tosyl and *N*-methoxycarbonyl substrates. The Aloc group was found to be completely stable to the reaction conditions (entry 13). The yield of the ring-opening products derived from the CBZ and *t*-Boc protected acetals was lower, but still within a useful range (entries 14 and 15). It is particularly notable that the *t*-Boc group survives a sequence of two acidic steps.

The ring-opening reaction with allyltrimethylsilane was examined with a number of other Lewis acids using the six-membered ring *N*,*O*-acetal **11b** formed from propionaldehyde, with a tosyl *N*-protecting group, as the test substrate (Table 2; Scheme 4). The milder Lewis acids, titanium blend (Ti(Oi-Pr)$_4$/$TiCl_4$), Ti(Oi-Pr)$_4$, Yb(OTf)$_3$·*n*H_2O, In(OTf)$_3$ and titanocene triflate, a Lewis acid reported by Bosnich,[5] proved to be ineffective, while boron trifluoride etherate lead to a mixture of ring opening and acetal hydrolysis. Indium trichloride also resulted in destruction of the acetal functional group. The only Lewis acid that could show similar reactivity to titanium tetrachloride was tin(IV) chloride. It was possible to employ trimethylsilyl triflate as a Lewis acid catalyst, however, this required a longer reaction time and higher temperature, and gave a low yield.

Table 2
Use of alternative lewis acids

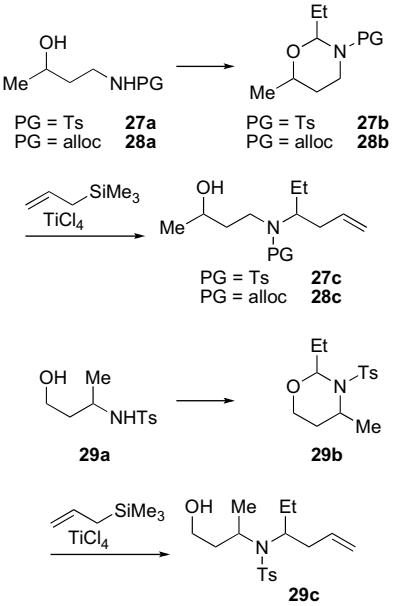
Entry	*n*	R	PG	Lewis Acid	Yield/%
1	2	Et	Ts	$BF_3·OEt_2$	33
2	2	Et	Ts	Me_3SiOTf	30
3	2	Et	Ts	$TiCl_4$	99
4	2	Et	Ts	$SnCl_4$	98



Scheme 4.

Three additional substrates examined possessed chirality in the amino alcohol chain (Scheme 5). 1-Aminobutan-3-ol **25** was prepared by reduction of the corresponding nitrile.[6] This nitrile could be prepared either by the reaction between lithioacetonitrile and acetaldehyde, or by ring opening of propylene glycol cyclic sulfate with cyanide. 3-Aminobutan-1-ol **26** was prepared by Bouveault–Blanc reduction of ethyl 3-aminocrotonate.[7] *N*,*O*-Acetals **27b** and **29b**, each with an *N*-tosyl group, were obtained as single diastereoisomers, which were crystalline solids. It is interesting to note that X-ray structure determination shows that for each acetal, the substituents adjacent to the *N*-Ts moiety prefer an axial orientation, even in acetal **29b**, which posses the methyl and ethyl groups in a 1,3-diaxial arrangement (Figs. 1 and 2).[8] *N*,*O*-Acetal **28c** with an alloc protecting group on the nitrogen atom was also prepared.

The ring-opening reaction was tested using these three related methyl substituted six-membered ring *N*,*O*-acetals (Table 3). While chemical yields were, as expected, good,[9] it was disappointing to find that the reaction proceeded with a modest de for all three substrates. It is notable that the highly selective opening of *O*,*O*-acetals employs derivatives of diols that possess two sterochemical centres, rather than the single chiral centre in this study.



Scheme 5.

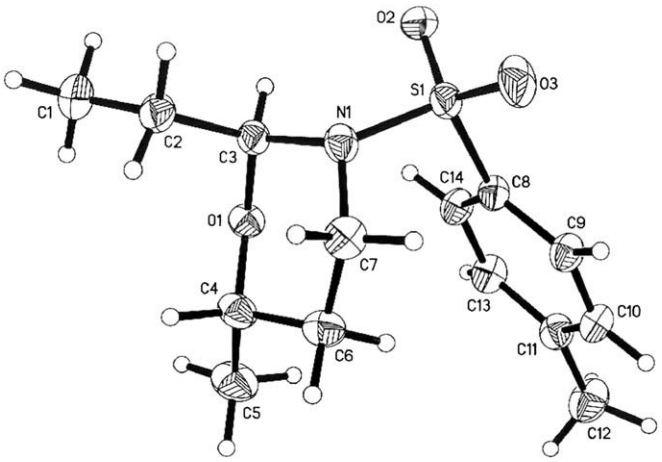


Figure 1. X-ray structure of acetal **27b**.

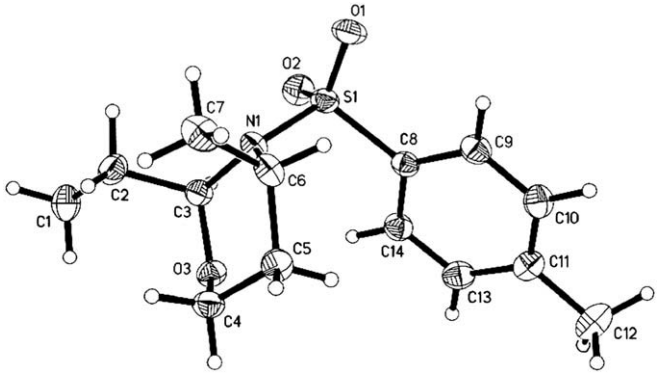


Figure 2. X-ray structure of acetal **29b**.

Table 3
Formation and ring opening of substituted *N*,*O*-acetals

Entry	Amino alcohol derivative	PG	*N*,*O*-Acetal, yield (%)	Homoallylic amine derivative, yield (%) (de %)
1	**27a**	Ts	**27b**, 97	**27c**, 87% (26)
2	**28a**	aloc	**28b**, 76[a]	**28c**, 74% (40)
3	**29a**	Ts	**29b**, 86	**29c**, 82% (29)

[a] 93:7 mixture of diastereoisomers.

3. Conclusions

In conclusion, cyclic *N*,*O*-acetals provide an efficient and convenient access to a wide range of protected homoallylic amines. Further investigation in this area is in hand, particularly using cyclic iminium ion intermediates.

4. Experimental

4.1. General procedures

All reactions were carried out under a dried nitrogen atmosphere using oven-dried glassware (120 °C), which was cooled under vacuum. All commercially obtained reagents were used as received. Amino alcohol derivatives **1**,[10] **2**,[11] **3**,[12] **4**,[13] **5**,[14] **6**,[15] **7**[16] and **8**[17] were prepared by standard procedures. Analytical TLC was carried out on precoated plates (silica gel 60, F_{254}). Column chromatography was performed with silica gel 60 (230–400 mesh). ^{1}H NMR spectra were recorded in $CDCl_3$ at 300 or 400 MHz in $CDCl_3$; chemical shift are expressed in parts per million relative to an internal standard. Peaks are assigned by consideration of chemical shift values and coupling patterns. Melting points are uncorrected. Infrared spectra were recorded using Nujol or neat.

4.2. General procedure for *n*-protected amino alcohols

Tosyl chloride (0.86 g, 4.50 mmol) was added slowly to a solution of 1-aminobutan-3-ol (0.38 g, 4.28 mmol) and triethylamine (0.52 g, 5.14 mmol) in CH_2Cl_2 (10 mL) at 0 °C. Then the reaction was allowed to warm to room temperature and further stirred for 6 h. Water was added and the mixture was extracted with dichloromethane×3. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo to give the sulfonamide (0.93 g, 90%) as a colourless solid, which was used without purification.

4.3. General procedure for the synthesis of cyclic *N*,*O*-acetals

Acetaldehyde (67 μL, 1.2 mmol) was added to a solution of *N*-(3-hydroxypropyl)-*p*-toluenesulfonamide (0.229 g, 1 mmol) in CH_2Cl_2 (10 mL) with trace of amberlyst-15 and 4 Å molecular sieves (pellets, ca. 500 mg) at room temperature. The mixture was stirred at room temperature for 2 h. It was filtered through Celite, and the filtrate was evaporated in vacuo to give **2a** (0.208 g, 82%) as a white solid, which was used in the next step without purification.

4.4. General procedure for the ring-opening reaction of cyclic *N*,*O*-acetals

A solution of the cyclic *N*,*O*-acetal (0.19 mmol) and allyltrimethylsilane (0.22 mmol) in anhydrous dichloromethane (5 mL) was cooled to −78 °C. $TiCl_4$ (0.22 mmol, 1 M in toluene) was added dropwise at this temperature. The reaction mixture was stirred at −78 °C for 0.5 h. After the reaction was complete, the solution was quenched with saturated aqueous $NaHCO_3$ solution and the mixture was extracted thrice with dichloromethane. The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to give the protected amino alcohol.

*4.4.1. 2-Methyl-3-tosyloxazolidine (**9a**)*

Yield 100%; colourless solid; mp 129–131 °C; ^{1}H NMR (300 MHz) δ 7.74 (2H, d, *J*=8.1 Hz, Ar), 7.34 (2H, d, *J*=8.1 Hz, Ar), 5.17 (1H, q, *J*=5.5 Hz, CH), 3.93–3.87 (1H, m, CH_2O), 3.47–3.42 (2H, m, CH_2N), 3.39–3.32 (1H, m, CH_2O), 2.44 (3H, s, $ArCH_3$), 1.48 (3H, d, *J*=5.5 Hz, CH_3–CH); ^{13}C NMR (100 MHz) δ 144.1, 134.2, 129.9, 127.8, 88.5, 65.2, 46.6, 22.1, 21.6; IR (Nujol) 1340, 1167, 673 cm^{-1}; MS (EI, *m*/*z*) 240 $(M-H)^+$, 226 (92%), 155 (82%), 91 (base peak). Anal. Calcd for $C_{11}H_{15}O_3NS$: C, 54.75; H, 6.27; N, 5.80. Found: C, 54.61; H, 6.22; N, 5.78.

*4.4.2. 2-Ethyl-3-tosyloxazolidine (**9b**)*

Yield 81%; colourless solid; mp 71–72 °C; ^{1}H NMR (300 MHz) δ 7.74 (2H, d, *J*=8.1 Hz, Ar), 7.33 (2H, d, *J*=8.1 Hz, Ar), 5.06 (1H, dd, *J*=4.5, 6.4 Hz, CH), 3.87–3.81 (1H, m, CH_2O), 3.24–3.55 (3H, m), 2.44 (3H, s, $ArCH_3$), 1.88–1.65 (2H, m, CH_3–CH_2), 0.97 (3H, t, *J*=7.4 Hz, CH_3–CH_2); ^{13}C NMR (75 MHz) δ 144.1, 134.2, 129.9, 127.7, 92.5, 65.1, 46.6, 28.5, 21.5, 8.5; IR (Nujol) 1342, 1165, 673 cm^{-1}; MS (EI, *m*/*z*) 254 $(M-H)^+$, 226 (base peak), 155 (92%), 91 (96%). Anal. Calcd for $C_{12}H_{17}O_3NS$: C, 56.45; H, 6.71; N, 5.49. Found: C, 56.41; H, 6.72; N, 5.49.

*4.4.3. 3-Methoxycarbonyl-2-methyloxazolidine (**10a**)*[18]

Yield 73%; colourless oil; ^{1}H NMR (300 MHz) δ 5.23 (1H, q, *J*=5.3 Hz, CH), 4.11–4.04 (1H, m, CH_2O), 3.87 (1H, dd, *J*=1.3, 7.3 Hz, CH_2O), 3.72 (3H, s, OCH_3), 3.73–3.58 (1H, m, CH_2N), 3.45–3.37 (1H, m, CH_2N), 1.41–1.40 (2H, m, CH_2–CH_2–CH_2); ^{13}C NMR (100 MHz) δ 154.0, 86.1, 65.4, 52.4, 44.5, 20.0; IR (neat) 1701, 1458, 1394, 771

cm^{-1}; MS (EI, *m*/*z*) 144 (M−H)$^+$, 130 (base peak); HRMS *m*/*z* calcd for $C_6H_{10}O_3N$ (M−H)$^+$ 144.0655, found 144.0654.

*4.4.4. 3-Methoxycarbonyl-2-ethyloxazolidine (**10b**)*

Yield 87%; colourless oil; ^{1}H NMR (400 MHz) δ 5.09 (1H, br dd, *J*=2.5, 6.3 Hz, CH), 4.90–4.83 (1H, m, CH_2O), 4.09–4.02 (1H, m, CH_2O), 3.72 (3H, s, OCH_3), 3.73–3.68 (1H, m, C*H*$_2$N), 3.40–3.32 (1H, m, C*H*$_2$N), 1.83–1.60 (2H, m, CH_2–C*H*$_2$–CH_2), 0.92 (3H, t, *J*=7.4 Hz, C*H*$_3$CH$_2$); ^{13}C NMR (100 MHz) δ 154.2, 90.0, 65.3, 52.3, 44.9, 26.5, 7.9; IR (neat) 1712, 1454, 1382, 769 cm^{-1}; MS (EI, *m*/*z*) 158 (M−H)$^+$, 130 (base peak); HRMS *m*/*z* calcd for $C_7H_{12}O_3N$ (M−H)$^+$ 158.0812, found 158.0813.

*4.4.5. 2-Methyl-3-tosyl-1,3-oxazinane (**11a**)*

Yield 82%; colourless solid; mp 92–93 °C; ^{1}H NMR (400 MHz) δ 7.78 (2H, d, *J*=8.2 Hz, Ar), 7.30 (2H, d, *J*=8.2 Hz, Ar), 5.62 (1H, q, *J*=6.3 Hz, CH), 3.89 (1H, dt, *J*=3.3, 11.4 Hz, CH_2O), 3.71–3.67 (1H, m, CH_2O), 3.59–3.51 (2H, m, C*H*$_2$N), 2.43 (3H, s, ArC*H*$_3$), 1.55 (3H, d, *J*=4.6 Hz, C*H*$_3$–CH), 1.40–1.24 (2H, m, CH_2–C*H*$_2$–CH_2); ^{13}C NMR (75 MHz) δ 143.3, 138.1, 129.7, 127.4, 80.8, 59.5, 39.4, 23.5, 21.5, 17.3; IR (Nujol) 1340, 1153, 858, 760, 665 cm^{-1}; MS (EI, *m*/*z*) 254 (M−H)$^+$, 240 (base peak), 155 (64%), 91 (68%). Anal. Calcd for $C_{12}H_{17}O_3NS$: C, 56.45; H, 6.71; N, 5.49. Found: C, 56.30; H, 6.66; N, 5.47.

*4.4.6. 2-Ethyl-3-tosyl-1,3-oxazinane (**11b**)*

Yield 100%; colourless solid; mp 53–54 °C; ^{1}H NMR (400 MHz) δ 7.79 (2H, d, *J*=8.1 Hz, Ar), 7.30 (2H, d, *J*=8.1 Hz, Ar), 5.38 (1H, t, *J*=7.2 Hz, CH), 3.84–3.72 (2H, m, CH_2O), 3.52–3.40 (2H, m, CH_2N), 2.42 (3H, s, ArC*H*$_3$), 2.03–1.88 (2H, m, CH_3–C*H*$_2$), 1.35–1.28 (1H, m, CH_2–C*H*$_2$–CH_2), 1.14 (1H, br d, *J*=13.4 Hz, CH_2–C*H*$_2$–CH_2), 0.95 (3H, t, *J*=7.4 Hz, C*H*$_3$–CH_2); ^{13}C NMR (75 MHz) δ 140.8, 135.8, 127.2, 125.0, 82.4, 56.4, 36.6, 20.5, 20.3, 19.1, 7.0; IR (Nujol) 1338, 1155, 964, 875, 663 cm^{-1}; MS (EI, *m*/*z*) 268 (M−H)$^+$, 240 (base peak), 155 (80%), 91 (88%). Anal. Calcd for $C_{13}H_{19}O_3NS$: C, 57.97; H, 7.11; N, 5.20. Found: C, 58.14; H, 7.32; N, 5.00.

*4.4.7. 2-Phenyl-3-tosyl-1,3-oxazinane (**11c**)*[19]

Yield 91%; colourless solid; ^{1}H NMR (300 MHz) δ 7.90 (2H, d, *J*=8.3 Hz, Ar), 7.51–7.34 (7H, m, Ar), 6.69 (1H, s, CH), 3.84 (1H, dd, *J*=4.2, 14.5 Hz, CH_2O), 3.72 (1H, td, *J*=2.8, 12.0 Hz, C*H*$_2$N), 3.59 (1H, dd, *J*=4.2, 11.6 Hz, CH_2O), 3.31 (1H, td, *J*=2.8, 14.1 Hz, CH_2N), 2.46 (3H, s, ArC*H*$_3$), 1.49–1.32 (2H, m, CH_2–C*H*$_2$–CH_2); ^{13}C NMR (75 MHz) δ 143.6, 138.1, 136.1, 129.8, 129.0, 128.2, 127.6, 127.2, 83.7, 60.0, 39.8, 23.1, 21.6.

*4.4.8. 3-Tosyl-1,3-oxazinane (**11d**)*[20]

Yield 94%; colourless solid; ^{1}H NMR (400 MHz) δ 7.78 (2H, d, *J*=8.1 Hz, Ar), 7.32 (2H, d, *J*=8.1 Hz, Ar), 4.94 (1H, s, CH_2), 3.71 (2H, t, *J*=5.3 Hz, CH_2O), 3.53 (2H, t, *J*=5.7 Hz, C*H*$_2$N), 2.44 (3H, s, $ArCH_3$), 1.35 (2H, tt, *J*=5.3, 5.7 Hz, CH_2–C*H*$_2$–CH_2); ^{13}C NMR (75 MHz) δ 143.4, 136.8, 129.5, 127.3, 78.1, 67.1, 44.1, 23.3, 21.2.

*4.4.9. 3-Methoxycarbonyl-2-methyl-1,3-oxazinane-3-carboxylate (**12a**)*

Yield 85%; colourless oil; ^{1}H NMR (400 MHz) δ 5.68 (1H, q, *J*=6.2 Hz, CH), 4.03–3.91 (2H, m, CH_2O), 3.71 (3H, s, OCH_3), 3.73–3.66 (1H, m, CH_2N), 3.23 (1H, dt, *J*=3.8, 12.6 Hz, CH_2N), 1.88–1.82 (1H, m, CH_2–C*H*$_2$–CH_2), 1.58–1.53 (1H, m, CH_2–C*H*$_2$–CH_2), 1.44 (3H, d, *J*=6.2 Hz, C*H*$_3$CH); ^{13}C NMR (100 MHz) δ 154.9, 79.1, 59.6, 52.6, 36.9, 25.3, 15.9; IR (neat) 1694, 1445, 1279, 770 cm^{-1}; MS (EI, *m*/*z*) 158 (M−H)$^+$, 144 (base peak), 88 (39%); HRMS *m*/*z* calcd for $C_7H_{12}O_3N$ (M−H)$^+$ 158.0812, found 158.0814.

*4.4.10. 3-Methoxycarbonyl-2-ethyl-1,3-oxazinane (**12b**)*

Yield 87%; colourless oil; ^{1}H NMR (300 MHz) δ 5.42 (1H, t, *J*=7.2 Hz, CH), 4.06 (1H, dd, *J*=5.2, 13.5 Hz, CH_2O), 3.89 (1H, dt, *J*=3.5, 11.6 Hz, NCH_2), 3.71 (3H, s, OCH_3), 3.69–3.66 (1H, m, CH_2O), 3.17 (1H, dt, *J*=3.6, 12.9 Hz, CH_2N), 2.04–1.87 (2H, m, CH_2–C*H*$_2$–CH_2), 1.85–1.37 (2H, m, CH_3CH_2), 0.91 (3H, t, *J*=7.4 Hz, C*H*$_3$CH); ^{13}C NMR (75 MHz) δ 155.3, 83.4, 59.4, 37.1, 25.3, 22.0, 9.1; IR (neat) 2966, 2876, 1701, 1450, 1279, 768 cm^{-1}; MS (EI, *m*/*z*) 174 (M+H)$^+$, 144 (base peak), 88 (24%); HRMS *m*/*z* calcd for $C_8H_{15}O_3N$ (M)$^+$ 173.1046, found 173.1045.

*4.4.11. 3-Methoxycarbonyl-2-phenyl-1,3-oxazinane (**12c**)*

Yield 80%; colourless oil; ^{1}H NMR (400 MHz) δ 7.43–7.31 (5H, m, Ar), 6.73 (1H, s, CH), 4.17 (1H, br d, *J*=11.0 Hz, CH_2O), 3.78 (3H, s, OCH_3), 3.76–3.68 (2H, m), 3.08 (1H, dt, *J*=3.1, 13.1 Hz, C*H*$_2$N), 2.39–1.96 (1H, m, CH_2–C*H*$_2$–CH_2), 1.38 (1H, d, *J*=13.2 Hz, CH_2–C*H*$_2$–CH_2); ^{13}C NMR (75 MHz) δ 156.1, 136.7, 128.9, 128.0, 126.9, 82.2, 60.4, 53.0, 38.3, 25.4; IR (neat) 1709, 1456, 1026, 721 cm^{-1}; MS (EI, *m*/*z*) 221 (M$^+$), 162 (76%), 105 (62%), 144 (base peak), 155 (64%), 91.27 (68%); HRMS *m*/*z* calcd for $C_{12}H_{15}O_3N$ (M)$^+$ 221.1046, found 221.1042.

*4.4.12. 3-Methoxycarbonyl-2-pentyl-1,3-oxazinane (**12e**)*

Yield 76%; colourless oil; ^{1}H NMR (400 MHz) δ 5.47 (1H, t, *J*=7.1 Hz, CH), 4.03 (1H, dd, *J*=4.5, 13.5 Hz, CH_2O), 3.87 (1H, dt, *J*=3.4, 23.1 Hz, NCH_2), 3.68 (3H, s, OCH_3), 3.70–3.61 (1H, m, CH_2O), 3.15 (1H, dt, *J*=3.6, 13.1 Hz, CH_2N), 1.92–1.81 (2H, m, CH–C*H*$_2$–CH_2); 1.74–1.68 (1H, m, OCH_2–C*H*$_2$–CH_2N), 1.49 (1H, td, *J*=2.5, 10.6 Hz, OCH_2–C*H*$_2$–CH_2N), 1.29–1.15 (6H, m), 0.87 (3H, t, *J*=3.7 Hz, CH_2CH_3); ^{13}C NMR (75 MHz) δ 155.2, 82.2, 59.4, 52.6, 37.1, 31.4, 28.8, 25.3, 24.4, 22.5, 13.9; IR (neat) 1703, 1449, 1410, 1277, 770 cm^{-1}; MS (EI, *m*/*z*) 216 (M+H)$^+$, 144 (base peak); HRMS *m*/*z* calcd for $C_{11}H_{22}O_3N$ (M+H)$^+$ 216.1594, found 216.1598.

*4.4.13. 3-Allyloxycarbonyl-2-ethyl-1,3-oxazinane (**13b**)*

Yield 100%; colourless oil; ^{1}H NMR (300 MHz) δ 6.00–5.87 (1H, m, C*H*=CH_2), 5.46 (1H, t, *J*=7.1 Hz, CH), 5.33–5.19 (2H, m, C*H*$_2$=CH), 4.61 (2H, dd, *J*=5.5, 1.4 Hz, C*H*$_2$–CH=CH_2), 4.08 (1H, dd, *J*=5.4, 13.6 Hz, OCH_2), 3.90 (1H, dt, *J*=3.5, 11.6 Hz, NCH_2), 3.74–3.69 (1H, m, OCH_2), 3.18 (1H, dt, *J*=3.6, 13.0 Hz, CH_2N), 2.00–1.76 (2H, m, C*H*$_2$CH$_3$), 1.59–1.56 (2H, m, CH_2C*H*$_2$CH$_2$), 0.92 (3H, t, *J*=4.4 Hz, CH_2C*H*$_3$); ^{13}C NMR (100 MHz) δ 154.5, 132.9, 117.4, 83.4, 66.0, 59.5, 37.1, 25.3, 22.1, 9.2; IR (neat) 1694, 1441, 1416, 1016, 766 cm^{-1}; MS (EI, *m*/*z*) 200 (M+H)$^+$, 170 (base peak), 126 (16%), 98 (36%), 70 (18%); HRMS calcd for $C_{10}H_{18}O_3N$ (M+H)$^+$ 200.1821, found 200.1273.

*4.4.14. 3-Benzyloxycarbonyl-2-ethyl-1,3-oxazinane (**14b**)*

Yield 86%; colourless oil; ^{1}H NMR (300 MHz) δ 7.36–7.33 (5H, m, Ar), 5.48 (1H, t, *J*=7.1 Hz, CH), 5.15 (2H, s, CH_2), 4.10 (1H, dd, *J*=5.1, 13.5 Hz, OCH_2), 3.89 (1H, dt, *J*=3.5, 11.6 Hz, NCH_2), 3.73–3.69 (1H, m, OCH_2), 3.19 (1H, dt, *J*=3.7, 13.0 Hz, NCH_2), 1.97–1.85 (2H, m, CH_3CH_2), 1.83–1.78 (1H, m, $CH_2CH_2CH_2$), 1.58–1.50 (1H, m, $CH_2CH_2CH_2$), 0.90 (3H, t, *J*=7.4 Hz, C*H*$_3$CH$_2$); ^{13}C NMR (100 MHz) δ 154.6, 136.6, 128.5, 128.0, 127.8, 83.5, 67.1, 59.5, 37.2, 25.3, 22.1, 9.2; IR (neat) 1697, 1454, 1418, 1016, 698 cm^{-1}; MS (EI, *m*/*z*) 250 (M+H)$^+$, 220 (46%), 176 (50%), 91 (base peak); HRMS calcd for $C_{14}H_{19}O_3N_1$ (M)$^+$ 249.1359, found 249.1358.

*4.4.15. 3-tert-Butoxycarbonyl 2-ethyl-1,3-oxazinane (**15b**)*

Yield 86%; colourless oil; ^{1}H NMR (300 MHz) δ 5.39 (1H, t, *J*=7.1 Hz, CH), 4.03 (1H, dd, *J*=5.1, 13.7 Hz, OCH_2), 3.87 (1H, dt, *J*=3.5, 11.6 Hz, NCH_2), 3.71–3.68 (2H, m, OCH_2), 3.09 (1H, dt, *J*=3.6, 13.2 Hz, NCH_2), 1.92–1.78 (2H, m, CH_3CH_2), 1.55–1.44 (2H, m, CH_2–C*H*$_2$CH$_2$), 1.46 (9H, s, $C(CH_3)_3$), 0.90 (3H, t, *J*=7.4 Hz, C*H*$_3$CH$_2$); ^{13}C NMR (75 MHz) δ 153.9, 83.3, 79.8, 59.4, 36.6, 28.3, 25.3, 22.0, 9.2; IR (neat) 1694, 1477, 1458, 1411, 1366, 1155 cm^{-1}; MS (EI, *m*/*z*) 216 (M+H)$^+$, 186 (24%), 130 (65%), 116 (50%), 86 (base peak); HRMS calcd for $C_{11}H_{21}O_3N$ (M)$^+$ 215.1516, found 215.1523.

*4.4.16. 3-Benzoyl-2-ethyl-1,3-oxazinane (**16b**)*

Yield 30%; colourless oil; ^{1}H NMR (300 MHz) δ 7.40 (5H, m, Ar), 5.42 (1H, br, CH), 4.20 (1H, br, OCH_2), 3.96 (1H, dt, J=3.2, 11.8 Hz, NCH_2), 3.77 (1H, dd, J=5.3, 11.7 Hz, OCH_2), 3.25 (1H, dt, J=3.3, 13.2 Hz, NCH_2), 2.11–2.01 (2H, m, CH_3CH_2), 1.99–1.82 (1H, m, $CH_2CH_2CH_2$), 1.58–1.54 (1H, m, $CH_2CH_2CH_2$), 0.88 (3H, t, J=7.4 Hz, CH_3CH_2); ^{13}C NMR (75 MHz) δ 170.5, 135.9, 129.7, 128.5, 126.8, 59.5, 39.9, 38.0, 25.8, 21.9, 9.2; IR (neat) 2968, 2936, 2876, 1643, 1600, 1446, 1417, 1283, 880, 702 cm^{-1}; MS (EI, m/z) 220 (M+H)$^+$, 190 (68%), 105 (base peak); HRMS calcd for $C_{13}H_{17}O_2N$ (M)$^+$ 219.1254, found 219.1251.

*4.4.17. N-(2-Hydroxyethyl)-N-(pent-4-en-2-yl)-p-toluenesulfonamide (**17a**)*

Yield 92%; colourless oil; ^{1}H NMR (400 MHz) δ 7.63 (2H, d, J=8.1 Hz, Ar), 7.21 (2H, d, J=8.1 Hz, Ar), 5.60–5.50 (1H, m, CH_2=C*H*), 4.94 (1H, d, J=1.5 Hz, C*H*$_2$=CH), 4.91 (1H, s, C*H*$_2$=CH), 3.93–3.88 (1H, m, CHN), 3.73–3.70 (2H, br, OCH_2), 3.18–3.10 (2H, m, NCH_2), 2.70 (1H, br, OH), 2.33 (3H, s, $ArCH_3$), 2.33–1.98 (2H, m, C*H*$_2$CH=CH_2), 0.87 (3H, d, J=6.7 Hz, C*H*$_3$CH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 143.4, 137.0, 134.7, 129.6, 127.1, 117.4, 62.6, 53.9, 45.1, 39.8, 21.4, 18.0; IR (neat) 3524, 2976, 2930, 1597, 1456, 1337, 1153, 658 cm^{-1}; MS (EI, m/z) 284 (M+H)$^+$, 242 (base peak), 155 (42%), 91 (62%), 70 (98%); HRMS calcd for $C_{14}H_{20}O_3NS$ 282.1158 (M−H)$^+$, found 282.1144.

*4.4.18. N-(Hex-5-en-3-yl)-N-(2-hydroxyethyl)-p-toluenesulfonamide (**17b**)*

Yield 88%; colourless oil; ^{1}H NMR (300 MHz) δ 7.73 (2H, d, J=8.1 Hz, Ar), 7.30 (2H, d, J=8.1, Ar), 5.65–5.56 (1H, m, CH_2=C*H*), 4.99 (1H, d, J=6.6 Hz, C*H*$_2$=CH), 4.95 (1H, s, C*H*$_2$=CH), 3.84–3.37 (2H, m, OCH_2), 3.70–3.66 (1H, m, CHN), 3.24–3.19 (2H, m, NCH_2), 2.43 (3H, s, $ArCH_3$), 2.17–1.98 (2H, m, C*H*$_2$CH=CH_2), 1.57–1.48 (1H, m, CH_3CH_2), 1.33–1.23 (1H, m, CH_3CH_2), 0.83 (3H, t, J=7.4 Hz, C*H*$_3$CH$_2$); ^{13}C NMR (75 MHz; $CDCl_3$) δ 143.4, 137.3, 135.0, 123.0, 127.3, 117.4, 62.6, 60.5, 45.6, 37.8, 25.8, 21.5, 11.3; IR (neat) 3524, 2966, 2933, 2877, 1597, 1456, 1383, 1335, 1155, 658 cm^{-1}; MS (EI, m/z) 298 (M+H)$^+$, 256 (base peak), 155 (45%), 116 (44%), 91 (62%), 84 (85%); HRMS calcd for $C_{15}H_{22}O_3NS$ 296.1315 (M−H)$^+$, found 296.1320.

*4.4.19. Methyl 2-hydroxyethyl(pent-4-en-2-yl)carbamate (**18a**)*

Yield 80%; colourless oil; ^{1}H NMR (400 MHz) δ 5.69 (1H, br, CH_2=C*H*), 5.07–4.96 (2H, m, C*H*$_2$=CH), 4.11 (1H, br, $HOCH_2$), 3.69 (5H, br, O*CH*$_3$+*CH*$_2$OH+NH), 3.35–3.28 (2H, m, CH_2N), 2.27–2.18 (2H, m, C*H*$_2$CH=CH_2), 0.88 (3H, d, J=7.4 Hz, C*H*$_3$CH); ^{13}C NMR (75 MHz) δ 159.8, 135.0, 117.3, 63.5, 52.7, 52.3, 45.8, 39.3, 18.8; IR (neat) 3410, 1702, 1453 cm^{-1}; MS (EI, m/z) 188 (M+H)$^+$, 146 (base peak), 114 (28%), 70 (26%); HRMS calcd for $C_9H_{18}O_3N$ 188.1281 (M+H)$^+$, found 188.1273.

*4.4.20. Methyl hex-5-en-3-yl(2-hydroxyethyl)carbamate (**18b**)*

Yield 92%; colourless oil; ^{1}H NMR (300 MHz) δ 5.72–5.68 (1H, m, CH_2=C*H*), 5.06–5.01 (1H, m, C*H*$_2$=CH), 5.01 (1H, s, C*H*$_2$=CH), 3.87 (1H, br, CH_2OH), 3.69 (5H, br, O*CH*$_3$+*CH*$_2$OH+N*H*), 3.30–3.22 (1H, m, CH_2N), 2.20 (2H, m, C*H*$_2$CH=CH_2), 1.50–1.47 (2H, m, CH_3CH_2), 0.88 (3H, t, J=7.4 Hz, C*H*$_3$CH$_2$); ^{13}C NMR (75 MHz) δ 159.4, 135.0, 117.2, 63.2, 58.5, 52.8, 45.9, 37.8, 25.9, 11.0; IR (neat) 3437, 2965, 1712, 1469 cm^{-1}; MS (EI, m/z) 202 (M+H)$^+$, 160 (base peak), 128 (82%), 84 (24%); HRMS calcd for $C_{10}H_{19}O_3N_1$ 201.1359 (M)$^+$, found 201.1359.

*4.4.21. N-(3-Hydroxypropyl)-N-(pent-4-en-2-yl)-p-toluenesulfonamide (**19a**)*

Yield 100%; colourless oil; ^{1}H NMR (300 MHz) δ 7.70 (2H, d, J=8.3 Hz, Ar), 7.28 (2H, d, J=8.0 Hz, Ar), 5.68–5.54 (1H, m, CH_2=C*H*), 5.03 (1H, d, J=1.5 Hz, C*H*$_2$=CH), 5.00 (1H, s, C*H*$_2$=CH), 3.96–3.89 (1H, m, CHN), 3.75 (2H, t, J=6.8 Hz, OCH_2), 3.41–3.30 (2H, m, NCH_2), 2.41 (3H, s, $ArCH_3$), 2.27–2.06 (2H, m, C*H*$_2$CH=CH_2), 1.84 (2H, quint., J=6.3 Hz, $OCH_2CH_2CH_2$), 1.00 (3H, d, J=6.8 Hz, C*H*$_3$CH); ^{13}C NMR (75 MHz; $CDCl_3$) δ 143.2, 137.8, 134.8, 129.7, 127.0, 117.4, 59.2, 53.9, 40.2, 39.9, 34.0, 21.5, 18.4; IR (neat) 3524, 2972, 2930, 1599, 1456, 1337, 1153, 658 cm^{-1}; MS (EI, m/z) 256 (M−CH_2CH=CH_2), 212 (base peak), 155 (25%), 91 (28%); HRMS calcd for $C_{12}H_{18}O_3NS$ 256.1002 (M−CH_2CH=CH_2)$^+$, found 256.1005.

*4.4.22. N-(Hex-5-en-3-yl)-N-(3-hydroxypropyl)-p-toluenesulfonamide (**19b**)*

Yield 100%; colourless oil; ^{1}H NMR (300 MHz) δ 7.71 (2H, d, J=8.3 Hz, Ar), 7.28 (2H, d, J=8.3 Hz, Ar), 5.58–5.53 (1H, m, CH_2=C*H*), 4.97 (1H, d, J=4.1 Hz, C*H*$_2$=CH), 4.92 (1H, br, C*H*$_2$=CH), 3.75 (2H, br, OCH_2), 3.64–3.60 (1H, m, CHN), 3.28–3.22 (2H, m, NCH_2), 2.42 (3H, s, $ArCH_3$), 2.22–2.01 (2H, m, C*H*$_2$CH=CH_2), 1.87–1.79 (2H, m, $OCH_2CH_2CH_2$), 1.57–1.50 (1H, m, CH_3CH_2), 1.38–1.25 (1H, m, CH_3CH_2), 0.79 (3H, t, J=7.3 Hz, C*H*$_3$CH$_2$); ^{13}C NMR (75 MHz; $CDCl_3$) δ 143.1, 137.9, 135.1, 129.5, 127.1, 117.2, 60.3, 59.5, 40.4, 38.1, 34.0, 25.8, 21.5, 11.4; IR (neat) 3524, 2966, 2936, 2877, 1599, 1456, 1383, 1334, 1153, 658 cm^{-1}; MS (EI, m/z) 270 (M−CH_2CH=CH_2)$^+$, 226 (45%), 155 (38%), 91 (60%); HRMS calcd for $C_{13}H_{20}O_3NS$ 270.1158 (M−CH_2CH=CH_2)$^+$, found 270.1158.

*4.4.23. N-(3-Hydroxypropyl)-N-(1-phenylbut-3-enyl)-p-toluenesulfonamide (**19c**)*

Yield 32%; colourless oil; ^{1}H NMR (300 MHz; $CDCl_3$) δ 7.71 (2H, d, J=8.3 Hz, Ar), 7.31–7.24 (7H, m, Ar), 5.63–5.49 (1H, m, C*H*=CH_2), 5.06–5.01 (1H, m, PhCH), 4.96–4.91 (2H, m, CH=C*H*$_2$), 3.53–3.46 (2H, m, CH_2O), 3.24–3.18 (2H, m, CH_2N), 2.88–2.78 (1H, m, C*H*$_2$CH=CH_2), 2.41 (3H, s, Ar), 2.40–2.33 (1H, m, C*H*$_2$CH=CH_2), 2.03 (1H, br, OH), 1.47–1.36 (2H, m, $CH_2CH_2CH_2$); ^{13}C NMR (100 MHz) δ 143.3, 137.8, 134.2, 129.7, 128.5, 128.4, 128.0, 127.2, 117.7, 60.2, 59.0, 40.8, 35.2, 32.9, 21.5; IR (neat) 3524, 3065, 2947, 2878, 1599, 1454, 1335, 1157, 662 cm^{-1}; MS (EI, m/z) 318 (M−CH_2CH=CH_2)$^+$, 91 (base peak); HRMS calcd for $C_{17}H_{20}O_3NS$ 318.1158 (M−CH_2CH=CH_2)$^+$, found 318.1159.

*4.4.24. N-(But-3-enyl)-N-(3-hydroxypropyl)-p-toluenesulfonamide (**19d**)*

Yield 100%; colourless oil; ^{1}H NMR (300 MHz) δ 7.67 (2H, d, J=8.1 Hz, Ar), 7.28 (2H, d, J=8.1 Hz, Ar), 5.68–5.55 (1H, m, CH_2=C*H*), 5.00–4.93 (2H, m, C*H*$_2$=CH), 3.66 (2H, t, J=5.7 Hz, OCH_2), 3.21–3.09 (4H, m, N$CH_2CH_2CH_2$CH, N$CH_2(CH_2)_3$), 2.35 (3H, s, $ArCH_3$), 2.25–2.17 (2H, m, C*H*$_2$CH=CH_2), 1.70–1.67 (2H, m, $OCH_2CH_2CH_2N$); ^{13}C NMR (75 MHz; $CDCl_3$) δ 143.3, 136.4, 134.5, 129.7, 127.0, 117.1, 58.7, 48.3, 45.1, 33.2, 31.2, 21.4; IR (neat) 3437, 2930, 2876, 1641, 1599, 1458, 1155, 918 cm^{-1}; MS (EI, m/z) 284 (M+H)$^+$, 242 (M−CH_2CH=CH_2)$^+$, 198 (base peak), 155 (20%), 91 (22%); HRMS calcd for $C_{11}H_{16}O_3NS$ 242.0845 (M−CH_2CH=CH_2)$^+$, found 242.0838.

*4.4.25. Methyl 3-hydroxypropyl(pent-4-en-2-yl)carbamate (**20a**)*

Yield 100%; colourless oil; ^{1}H NMR (300 MHz) δ 5.73–5.63 (1H, m, CH_2=C*H*), 5.06–4.98 (2H, m, C*H*$_2$=CH), 3.67 (3H, s, OCH_3), 3.62–3.47 (1H, br, CH_2O), 3.31 (2H, br, CH_2N), 2.32–2.19 (2H, m, C*H*$_2$CH=CH_2), 1.68 (2H, br, $CH_2CH_2CH_2$), 1.16 (3H, d, J=6.9 Hz, C*H*$_3$CH); ^{13}C NMR (75 MHz; $CDCl_3$) δ 158.3, 135.1, 117.1, 59.0, 58.8, 52.5, 40.3, 39.4, 32.6, 18.9; IR (neat) 3435, 2955, 2930, 2874, 1694, 1057 cm^{-1}; MS (EI, m/z) 202 (M+H)$^+$, 160 (M−*CH*$_2$CH=CH_2, 58%), 116 (base peak), 84 (24%); HRMS calcd for $C_{10}H_{19}O_3N$ 201.1359 (M)$^+$, found 201.1359.

*4.4.26. Methyl hex-5-en-3-yl(3-hydroxypropyl)carbamate (**20b**)*

Yield 100%; colourless oil; ^{1}H NMR (300 MHz) δ 5.77–5.65 (1H, m, CH_2=C*H*), 5.05 (1H, d, J=7.9 Hz, C*H*$_2$=CH), 5.01 (1H, s, C*H*$_2$=CH), 3.92 (1H, br, NCH), 3.71 (3H, s, OCH_3), 3.72–3.60 (2H, m, CH_2O), 3.36–3.17 (1H, m, CH_2N), 2.30–2.26 (2H, m, C*H*$_2$CH=CH_2), 1.72–1.58 (1H, m, $CH_2CH_2CH_2$), 1.56–1.50 (2H, m, CH_3CH_2), 0.88 (3H, t, J=7.4 Hz, C*H*$_3$CH$_2$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 158.8, 135.2, 117.1, 60.2,

59.0, 52.7, 40.6, 38.0, 32.4, 26.0, 11.2; IR (neat) 3439, 3076, 2961, 2875, 1693, 1060, 916, 773 cm^{-1}; MS (EI, *m*/*z*) 216 $(M+H)^+$, 174 (67%), 142 (32%), 130 (base peak); HRMS calcd for $C_{11}H_{20}O_3N_1$ 214.1438 $(M-H)^+$, found 214.1440.

*4.4.27. Methyl 3-hydroxypropyl(1-phenylbut-3-enyl)-carbamate (**20c**)*

Yield 67%; colourless oil; ^1H NMR (300 MHz) δ 7.28–7.33 (5H, m, Ar), 5.84–5.71 (1H, m, CH_2=C*H*), 5.29 (1H, br, NCH), 5.29–5.06 (2H, m, C*H*$_2$=CH), 3.71 (3H, s, OCH_3), 3.41 (2H, t, *J*=5.7 Hz, CH_2O), 3.27–3.20 (2H, m, CH_2N), 2.78–2.72 (2H, m, C*H*$_2$CH=CH_2), 1.59 (1H, br, $CH_2CH_2CH_2$), 1.40 (1H, br, $CH_2CH_2CH_2$); ^{13}C NMR (75 MHz; $CDCl_3$) δ 158.0, 139.5, 134.7, 128.5, 128.0, 127.8, 117.6, 59.0, 58.6, 52.9, 40.1, 35.3, 32.1; IR (neat) 3443, 2954, 1672, 1469, 1447, 1404, 1057, 702 cm^{-1}; MS (EI, *m*/*z*) 264 $(M+H)^+$, 222 (74%), 118 (72%), 121 (52%), 91 (base peak); HRMS calcd for $C_{15}H_{21}O_3N$ 263.1516 $(M-H)^+$, found 263.1507.

*4.4.28. Methyl 3-hydroxypropyl(non-1-en-4-yl)carbamate (**20e**)*

Yield 100%; colourless oil; ^1H NMR (400 MHz) δ 5.71–5.64 (1H, m, CH_2=C*H*), 5.00–5.04 (2H, m, C*H*$_2$=CH), 4.01–3.83 (1H, m, CHN), 3.69 (3H, s, OCH_3), 3.69–3.57 (2H, m, CH_2O), 3.37–3.14 (2H, m, NCH_2), 2.29–2.19 (2H, m, C*H*$_2$CH=CH_2), 1.67–1.69 (2H, m, $OCH_2CH_2CH_2N$), 1.48–1.46 (2H, br, CH_2CH_2CH), 1.27–1.25 (6H, br, C*H*$_2$C*H*$_2$C*H*$_2$), 0.86 (3H, t, *J*=6.6 Hz, C*H*$_3$CH$_2$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 158.8, 135.2, 117.1, 59.0, 57.2, 52.7, 40.0, 38.2, 33.1, 32.5, 31.6, 26.2, 22.6, 14.0; IR (neat) 3418, 2954, 2928, 2858, 1694, 1061, 914, 773 cm^{-1}; MS (EI, *m*/*z*) 258 $(M+H)^+$, 216 (76%), 184 (44%), 172 (48%), 102 (base peak); HRMS calcd for $C_{14}H_{27}O_3N$ 257.1985 $(M)^+$, found 257.1982.

*4.4.29. Allyl hex-5-en-3-yl(3-hydroxypropyl)carbamate (**21b**)*

Yield 98%; colourless oil; ^1H NMR (300 MHz) δ 5.94–5.85 (1H, m, OCH_2CH_2=C*H*), 5.76–5.63 (1H, m, $CHCH_2CH_2$=C*H*), 5.30–5.16 (2H, m, OCH_2CH_2=CH), 5.04–4.98 (2H, m, $CHCH_2CH_2$=CH), 4.58 (2H, d, *J*=3.7 Hz, OCH_2CH_2=CH), 4.56 (2H, br, CH_2OH), 3.91–3.75 (1H, br, CHN), 3.56 (2H, br, CH_2OH), 3.31–3.13 (2H, m, CH_2N), 2.30–2.21 (2H, m, $CHCH_2CH$=CH_2), 1.77–1.66 (2H, m, $OCH_2CH_2CH_2N$), 1.59–1.48 (2H, m, CH_3CH_2), 0.85 (3H, t, *J*=7.4 Hz, CH_3CH_2); ^{13}C NMR (75 MHz) δ 157.8, 135.2, 132.9, 117.4, 117.1, 66.1, 60.2, 59.0, 40.7, 38.0, 32.4, 26.1, 11.2; IR (neat) 3435, 2965, 2932, 2875, 1672, 1059, 916, 733 cm^{-1}; MS (EI, *m*/*z*) 242 $(M+H)^+$, 200 (M−CH_2CH=CH_2, base peak), 156 (68), 142 (48%), 112 (48%), 72 (42%); HRMS calcd for $C_{13}H_{22}O_3N$ 240.1594 $(M-H)^+$, found 240.1588.

*4.4.30. Benzyl hex-5-en-3-yl(3-hydroxypropyl)carbamate (**22b**)*

Yield 63%; colourless oil; ^1H NMR (400 MHz) δ 7.36 (5H, m, Ar), 5.69–5.62 (1H, m, CH_2=C*H*), 5.15 (2H, s, CH_2Ph), 5.00 (1H, d, *J*=7.9 Hz, C*H*$_2$=CH), 4.97 (1H, s, C*H*$_2$=CH), 3.94–3.81 (1H, m, NCH), 3.61 (2H, t, *J*=5.7 Hz, CH_2O), 3.36–3.19 (2H, m, CH_2N), 2.29–2.24 (2H, m, C*H*$_2$CH=CH_2), 1.76–1.69 (1H, m, $OCH_2CH_2CH_2N$), 1.59–1.50 (2H, m, CH_3CH_2), 0.85 (3H, t, *J*=7.4 Hz, CH_3CH_2); ^{13}C NMR (75 MHz) δ 158.1, 136.6, 135.2, 128.5, 128.1, 128.0, 127.8, 117.2, 67.4, 60.4, 59.0, 40.7, 38.0, 32.4, 26.1, 11.2; IR (neat) 3428, 2965, 2934, 2876, 1693, 1643, 1454, 1418, 1344, 1057, 698 cm^{-1}; MS (EI, *m*/*z*) 292 $(M+1)^+$, 250 (M−CH_2CH=CH_2, 26%), 206 (40%), 91 (base peak); HRMS for $C_{18}H_{20}O_3N$ 250.1438 $(M-CH_2CH=CH_2)^+$, found 250.1436.

*4.4.31. tert-Butyl hex-5-en-3-yl(3-hydroxypropyl)carbamate (**23b**)*

Yield 66%; colourless oil; ^1H NMR (300 MHz) δ 5.76–5.67 (1H, m, CH_2=C*H*), 5.06–5.00 (2H, m, C*H*$_2$=CH), 4.02–3.91 (1H, br, CH), 3.57 (2H, br, CH_2O), 3.31–3.15 (2H, br, CH_2N), 2.28–2.21 (2H, m, C*H*$_2$CH=CH_2), 1.78–1.66 (2H, m, $CH_2CH_2CH_2$), 1.65–1.55 (2H, m, CH_3CH_2), 1.45 (9H, s, $C(CH_3)_3$), 0.87 (3H, t, *J*=7.4 Hz, CH_3CH_2); ^{13}C NMR (100 MHz) δ 157.6, 135.5, 116.9, 80.1, 59.6, 58.8, 40.6, 38.1, 32.4, 28.4, 26.3, 11.3; IR (neat) 3429, 2968, 2932, 2876, 1694, 1366, 1165 cm^{-1}; MS (EI, *m*/*z*) 258 $(M+H)^+$, 216 (M−CH_2CH=CH_2, 6%), 116 (base peak), 72 (58%); HRMS calcd for $C_{11}H_{22}O_3N$ 216.1594 $(M-CH_2CH=CH_2)^+$, found 216.1590.

*4.4.32. N-(3-Hydroxybutyl)-p-toluenesulfonamide (**27a**)*

Yield 90%; colourless solid; ^1H NMR (400 MHz) δ 7.75 (2H, d, *J*=8.1 Hz, Ar), 7.31 (2H, d, *J*=8.1 Hz, Ar), 5.08 (1H, br, NH), 3.94–3.91 (1H, m, CH), 3.19–3.15 (1H, m, CH_2N), 3.03–3.00 (1H, m, CH_2N), 2.43 (3H, s, Ar–CH_3), 1.68–1.52 (2H, m, NCH_2–C*H*$_2$–CHO), 1.17 (3H, d, *J*=6.2 Hz, C*H*$_3$–CH); ^{13}C NMR (75 MHz) δ 143.1, 136.5, 129.5, 126.8, 65.8, 40.4, 37.5, 23.2, 21.3; IR (Nujol) 3282, 1598, 1157, 816, 663 cm^{-1}; MS (EI, *m*/*z*) 244 $(M+H)^+$, 184 (39%), 155 (base peak), 91 (98%); HRMS *m*/*z* calcd for $C_{11}H_{17}O_3NS$ $(M)^+$ 243.0924, found 243.0929.

*4.4.33. trans-2-Ethyl-6-methyl-3-tosyl-1,3-oxazinane (**27b**)*

Yield 81%; colourless solid; mp 80–82 °C; ^1H NMR (400 MHz) δ 7.80 (2H, d, *J*=8.1 Hz, Ar), 7.30 (2H, d, *J*=8.1 Hz, Ar), 5.49 (1H, t, *J*=7.4 Hz, OCHN), 3.86–3.81 (1H, m, CH_2N), 3.79–3.74 (1H, m, C*H*–CH_3), 3.45–3.41 (1H, m, CH_2N), 2.43 (3H, s, ArC*H*$_3$), 2.03–1.84 (2H, m, CH–C*H*$_2$–CH_3), 1.14 (1H, br d, *J*=13.4 Hz, CH–C*H*$_2$–CH_2); 0.96 (3H, t, *J*=7.4 Hz, C*H*$_3$–CH_2), 0.89 (3H, d, *J*=6.0 Hz, C*H*$_3$–CH); ^{13}C NMR (100 MHz) δ 143.2, 138.1, 129.4, 127.6, 84.8, 63.6, 38.9, 29.8, 23.0, 21.6, 21.4, 9.56; IR (Nujol) 1335, 1157, 675 cm^{-1}; MS (EI, *m*/*z*) 282 $(M-H)^+$, 254 (base peak), 155 (51%), 91 (45%). Anal. Calcd for $C_{14}H_{21}O_3NS$: C, 59.34; H, 7.47; N, 4.94. Found: C, 59.33; H, 7.53; N, 4.83.

*4.4.34. N-(Hex-5-en-3-yl)-N-(3-hydroxybutyl)-p-toluene sulfonamide (**27c**) (mixture of isomers)*

Yield 87%; colourless oil; ^1H NMR (400 MHz) δ 7.69 (4H, d, *J*=8.3 Hz, Ar), 7.27 (4H, d, *J*=8.3 Hz, Ar), 5.54–5.60 (0.58H, m, CH_2=C*H*), 5.42–5.34 (1H, m, CH_2=C*H*), 4.99–4.87 (3H, m, C*H*$_2$=CH), 3.95–3.93 (2H, m), 3.60–3.58 (2H, m), 3.36–3.29 (2H, m), 3.15–3.09 (2H, m), 2.42 (6H, s, $ArCH_3$), 2.17–2.08 (2H, m), 1.92–1.77 (2H, m), 1.64–1.35 (8H, m), 1.26–1.19 (6H, m), 0.86 (3H, t, *J*=7.3 Hz, CH_3CH_2), 0.69 (1.8H, t, *J*=7.3 Hz, CH_3CH_2).

*4.4.35. Allyl 3-hydroxybutylcarbamate (**28a**)*

Yield 71%; colourless oil; ^1H NMR (400 MHz) δ 5.98–5.85 (1H, m, C*H*=CH_2), 5.30 (1H, dd, *J*=2.0, 22.9 Hz, C*H*$_2$=CH), 5.21 (1H, dd, *J*=1.7, 13.9 Hz, C*H*$_2$=CH), 5.08 (1H, br, NH), 4.56 (2H, d, *J*=7.4 Hz, C*H*$_2$–CH=CH_2), 3.90–3.84 (1H, m, CH), 3.52–3.47 (1H, m, NCH_2), 3.22–3.15 (1H, m, CH_2N), 1.69–1.51 (2H, m, $CHCH_2CH_3$), 1.21 (3H, d, *J*=6.6 Hz, $CHCH_3$); ^{13}C NMR (75 MHz) δ 157.0, 132.7, 117.3, 65.3, 65.1, 38.6, 37.8, 23.1; IR (neat) 3420, 2965, 2932, 2874, 1694 cm^{-1}; MS (EI, *m*/*z*) 174 $(M+H)^+$, 156 (24%), 114 (36%), 88 (52%), 58 (base peak); HRMS *m*/*z* calcd for $C_8H_{15}O_3N$ $(M)^+$ 173.1046, found 173.1042.

*4.4.36. trans-3-Allyloxycarbonyl-2-ethyl-6-methyl-1,3-oxazinane (**28b**)*

Yield 76%; colourless oil; ^1H NMR (400 MHz) δ 5.96–5.90 (1H, m, CH_2=C*H*), 5.56 (1H, br, OCHN), 5.31–5.18 (2H, m, C*H*$_2$=CH), 4.59 (2H, d, *J*=4.2 Hz, C*H*$_2$CH=CH_2), 4.14–4.08 (1H, m, CH_2O), 3.96–3.91 (1H, m, CH_3–C*H*), 3.13–3.15 (1H, m, CH_2O), 1.98–1.94 (1H, m, C*H*$_2$–CH_3), 1.79 (1H, br, C*H*$_2$–CH_3), 1.52–1.46 (2H, m, CH–C*H*$_2$–CH_2), 1.16 (3H, d, *J*=4.9 Hz, C*H*$_3$CH), 0.90 (3H, t, *J*=5.9 Hz, C*H*$_3$–CH_2); ^{13}C NMR (125 MHz) δ 154.4, 133.0, 117.3, 83.1, 66.0, 64.3, 37.2, 32.6, 22.0, 21.8, 9.4; IR (neat) 2972, 2936, 2878, 1697, 766 cm^{-1}; MS (EI, *m*/*z*) 214 $(M+H)^+$, 184 (base peak), 98 (48%), 70 (28%); HRMS *m*/*z* calcd for $C_{11}H_{20}O_3N$ $(M+H)^+$ 214.1438, found 214.1446.

*4.4.37. Allyl hex-5-en-3-yl(3-hydroxybutyl)carbamate (**28c**) (mixture of isomers)*

Yield 74%; colourless oil; ^1H NMR (400 MHz) δ 5.94–5.88 (1H, m, OCH_2CH_2=C*H*), 5.76–5.63 (1H, m, $CHCH_2CH_2$=C*H*), 5.31–5.19 (2H, m, OCH_2CH_2=CH), 5.05–4.99 (2H, m, $CHCH_2CH_2$=CH), 4.58 (2H, br d, *J*=4.9 Hz, OCH_2CH_2=CH), 4.92–3.56 (3H, m), 3.19–3.00 (1H, m),

2.30–2.23 (2H, m, $CHCH_2CH{=}CH_2$), 1.70–1.43 (2H, m), 0.91–0.83 (3H, m, CH_3CH_2).

*4.4.38. N-(4-Hydroxybutan-2-yl)-p-toluenesulfonamide (**29a**)*

Yield 68%; colourless solid; mp 58–59 °C; ^{1}H NMR (300 MHz) δ 7.77 (2H, d, J=8.1 Hz, Ar), 7.29 (2H, d, J=8.1 Hz, Ar), 4.74 (1H, d, J=8.2 Hz, NH), 3.89–3.81 (1H, m, CH), 3.66–3.49 (2H, m, CH_2O), 2.43 (3H, s, $ArCH_3$), 2.18 (1H, t, J=5.2 Hz, OH), 1.76–1.65 (1H, m, $NCH–CH_2–CH_2O$), 1.51–1.42 (1H, m, $NCH–CH_2–CH_2O$), 1.00 (3H, d, J=6.6 Hz, $CH_3–CH$); ^{13}C NMR (125 MHz) δ 143.4, 137.8, 129.7, 127.0, 59.1, 47.5, 39.4, 21.7, 21.5; IR (Nujol) 3171, 1317, 918, 665 cm^{-1}; MS (EI, m/z) 244 $(M+H)^+$, 198 (base peak), 155 (74%), 91 (59%); HRMS m/z calcd for $C_{11}H_{17}O_3NS$ $(M)^+$ 243.0924, found 243.0925.

*4.4.39. cis-2-Ethyl-4-methyl-3-tosyl-1,3-oxazinane (**29b**)*

Yield 86%; colourless solid; mp 115–116 °C; ^{1}H NMR (400 MHz) δ 7.76 (2H, d, J=8.1 Hz, Ar), 7.29 (2H, d, J=8.1 Hz, Ar), 5.36 (1H, t, J=7.2 Hz, OCHN), 4.02–3.96 (1H, m, CH_2O), 3.86 (1H, dt, J=3.1, 11.4 Hz, CH_2O), 3.79–3.74 (1H, m, $CH–CH_3$), 3.45–3.41 (1H, m, CH_2N), 2.41 (3H, s, $ArCH_3$), 2.04–1.90 (2H, m, $CH_2–CH_3$), 1.52–1.40 (1H, m, $CH–CH_2–CH_2$), 1.43 (3H, d, J=7.1 Hz, $CH_3–CH$), 1.18 (1H, dd, J=2.8, 13.6 Hz, $CH–CH_2–CH_2$), 0.99 (3H, d, J=7.4 Hz, $CH_3–CH_2$); ^{13}C NMR (100 MHz) δ 143.2, 137.6, 129.6, 127.2, 84.9, 55.6, 46.5, 28.0, 27.9, 22.8, 21.5, 10.2; IR (Nujol) 1331, 1155, 814, 667 cm^{-1}; MS (EI, m/z) 284 $(M+H)^+$, 254 (base peak), 173 (26%), 155 (43%), 91 (41%); HRMS m/z calcd for $C_{14}H_{20}O_3NS$ $(M+H)^+$ 282.1158, found 282.1155.

*4.4.40. N-(Hex-5-en-3-yl)-N-(1-methyl-3-hydroxypropyl)-p-toluenesulfonamide (**29c**) (mixture of isomers)*

Yield 82%; colourless oil; ^{1}H NMR (400 MHz) δ 7.76–7.74 (4H, m, Ar), 7.29–7.27 (4H, m, Ar), 5.75–5.66 (1H, m, $CH_2{=}CH$), 5.60–5.53 (1H, m, $CH_2{=}CH$), 5.09–4.95 (3H, m, $CH_2{=}CH$), 3.89–3.87 (1H, m), 3.85–3.77 (2H, m), 3.60–3.54 (1.5H, m), 3.12–3.09 (1.5H, m), 2.53–2.49 (2H, m), 2.42 (6H, s, $ArCH_3$), 2.34–2.30 (1H, m), 1.86–1.60 (6H, m), 1.18–1.13 (4.5H, m), 0.89 (1.6H, t, J=7.4 Hz, CH_3CH_2), 0.77 (3H, t, J=7.4 Hz, CH_3CH_2).

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