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New routes to 5-substituted oxazoles

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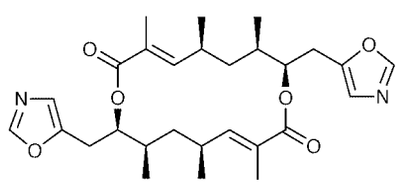
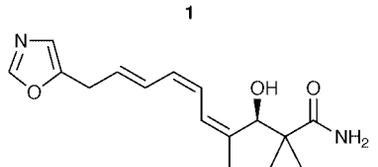
Ultrasound-promoted desulfonylation of 5-substituted 4-tosyloxazoles, prepared from tosylmethyl isocyanide and carboxylic acid chlorides or by dianion chemistry, leads to 5-monosubstituted oxazoles.

Recent years have seen the isolation of many biologically active oxazole-containing natural products from marine sources and nearly all contain the 2,4-disubstituted oxazole ring system.[1] However, a variety of *Streptomyces* strains have produced examples of 5-monosubstituted oxazoles with biological activity profiles ranging from herbicidal to antitumour. These include conglobatin[2] **1** and phthoxazolin A[3] **2**, a member of the oxazolomycin family.[4]



1

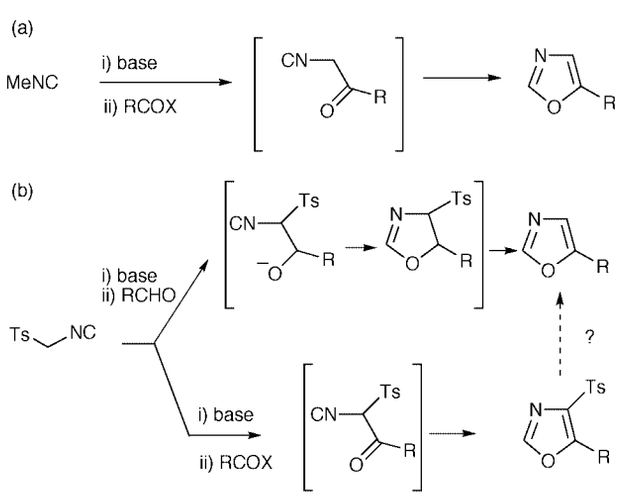


2

From a synthetic viewpoint, the most common entry to 5-monosubstituted oxazoles is *via* the Schöllkopf condensation of lithiated methyl isocyanide with carboxylic acid chlorides, esters and amides (Scheme 1a).[5] This involves the preparation and use of the highly toxic and volatile methyl isocyanide, although this methodology has been employed in the total syntheses of conglobatin[6] **1** and neooxazolomycin.[7]

The hazards associated with this alkyl isocyanide can be largely avoided by employing tosylmethyl isocyanide (TosMIC). The reaction of TosMIC with aldehydes under basic conditions affords 5-substituted oxazoles directly, as described by van Leusen *et al*.,[8] although this method is limited by the availability and/or stability of the requisite aldehyde. The reaction of the TosMIC anion with carboxylic acid chlorides[8], anhydrides[8] and esters[9] has also been carried out by van Leusen *et al*. but the resulting 5-substituted oxazoles now also possess a toluene-*p*-sulfonyl substituent in the 4-position (Scheme 1b).

To the best of our knowledge, there has been no disclosure of a method to remove this sulfonyl functionality from such systems. We felt that such a methodology would extend the usefulness of TosMIC in the preparation of 5-monosubstituted oxazoles and we report herein our results in this area.



Scheme 1

Results and discussion

a) Preparation of 5-substituted-4-tosyloxazoles 3a–d from acid chlorides

Based on the work of van Leusen *et al*.[8] 5-substituted-4-tosyloxazoles **3a**–**c** could be prepared from lithiated TosMIC and the appropriate carboxylic acid chloride in good yield. In the case of **3d**, the use of the more reactive TosMIC dianion[9] was found to be necessary to achieve a reasonable yield (Table 1).

b) Preparation of 5-substituted-4-tosyloxazoles 3a,e,f by dianion chemistry

Shafer and Molinski have recently reported the preparation of 5-substituted oxazoles by the selective C-5 lithiation of 2-(methylthio)oxazole followed by trapping with an electrophile and reductive desulfurisation.[10] Knight and co-workers have previously reported the regioselective lithiation of *N*,*N*-diethyl-2,5-dimethyloxazole-4-carboxamide at the 5-Me group.[11] Quenching with a range of electrophiles elaborated the substitution at the 5-position to give new trisubstituted oxazoles.

We prepared 5-methyl-4-tosyloxazole **4** from lithiated TosMIC and acetic anhydride in 87% yield[8] and decided to examine its lithiation chemistry as a possible entry to 5-substituted oxazoles. We anticipated that the 2-position of the oxazole ring would be the most acidic and it was hoped that a second equivalent of butyllithium would afford dianion **5** (Scheme 2).

Indeed, treatment of **4** with one equivalent of butyllithium in THF at −78 °C followed by the addition of D_2O resulted in the

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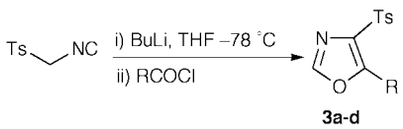
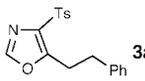
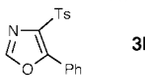
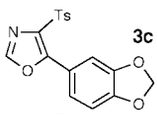
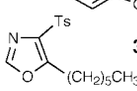
Table 1 Preparation of tosyloxazoles **3a–d**



3a-d

RCOCl	**3a–d** (Yield)
$PhCH_2CH_2COCl$	 **3a** (85%)
PhCOCl	 **3b** (64%)
Piperonoyl chloride	 **3c** (68%)
$CH_3(CH_2)_5COCl$	 **3d** (53%)[a]

[a] Obtained using dilithiated TosMIC (see Experimental section). Monolithiated TosMIC failed to give a clean, complete reaction.

loss of the singlet at δ 7.72 in the ^{1}H NMR spectrum, corresponding to the proton at the 2-position of the oxazole ring. It was pleasing to see that the use of two equivalents of butyllithium followed by the addition of D_2O resulted in the loss of the C-2 proton *and* a proton from the C-5 methyl group, giving rise to the characteristic two-proton signal at δ 2.69 corresponding to $-CH_2D$. This confirmed that the dianion **5** could be formed in solution, but would there be any regioselectivity in reactions with electrophiles?

The dianion **5** was formed in the usual manner and one equivalent of benzyl bromide was added to the reaction. This resulted in the formation of tosyloxazole **3a**, previously prepared by the alternative route, in 61% yield. It was found that benzaldehyde and allyl iodide also reacted regioselectively to give 5-substituted-4-tosyloxazoles **3e** and **3f**, respectively, and in good yield (Table 2).

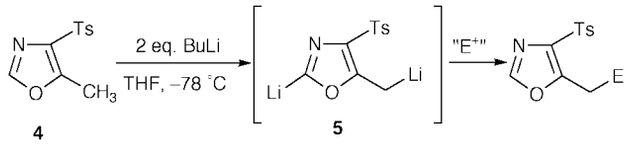
Unfortunately, dianion **5** did not give satisfactory results with all electrophiles. Attempts at acylation with ethyl chloroformate and benzoyl chloride failed to give the desired products, instead giving rise to intractable multicomponent reaction mixtures.

c) Desulfonylation of 5-substituted-4-tosyloxazoles 3a–f

Initial attempts to effect reductive desulfonylation of **3a** were unsuccessful. Many well-established techniques failed to give any observable reaction including use of samarium diiodide[12] in a range of solvents, magnesium in methanol[13,14] and aluminium amalgam.[15]

Some success was realised with sodium metal in ethanol–tetrahydrofuran (Table 3).[16] After considerable experimentation, however, the optimum conditions (8 eq. sodium, 12 eq. ethanol, THF, 0 °C, 2 h) afforded only a 27% yield of the desired 5-(2-phenylethyl)oxazole **6a**. The ^{1}H NMR spectrum showed no evidence of the tosyl functionality and the new oxazole proton at the 4-position was plainly visible at δ 6.75. No other products or remaining starting material could be isolated from the reaction as decomposition always accompanied the desired transformation.

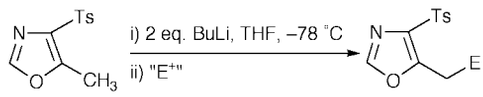
A similar result was encountered with 10% Na–Hg[17] and Na_2HPO_4 under the more forcing conditions of refluxing methanol over a period of 5 hours. This reaction turned out to be rather capricious, often with complete decomposition of the starting material being the only result. Attempts to employ milder conditions (*i.e.* running the reaction at room temperature or use of 5% Na–Hg) resulted in no reaction taking place.



4 **5**

Scheme 2

Table 2 Preparation of tosyloxazoles **3a,e,f**



4 **3a, e-f**

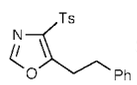
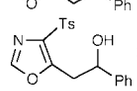
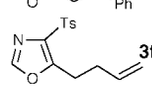
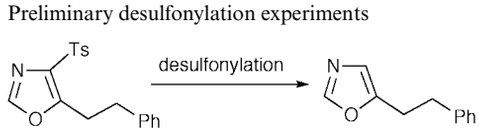
Electrophile	**3a,e,f** (Yield)
Benzyl bromide	 **3a** (61%)
Benzaldehyde	 **3e** (78%)
Allyl iodide	 **3f** (62%)

Table 3 Preliminary desulfonylation experiments



3a **6a**

Conditions	Time/h	Yield of **6a** (%)
8 eq. Na, 12 eq. EtOH, THF, 0 °C	2	27
20 eq. 10% Na–Hg[a,b] MeOH–THF (1:1),)))))	18	62
5 eq. 10% Na–Hg[a,c] ^{i}PrOH–THF (1:1),)))))	7	62
10 eq. 10% Na–Hg[a,b] EtOH–THF (1:1),)))))	4	72

[a] Reaction run in the presence of 4 eq. disodium hydrogen orthophosphate. [b] Added in two equal portions over the course of the reaction. [c] Added in one portion at the start of the reaction.

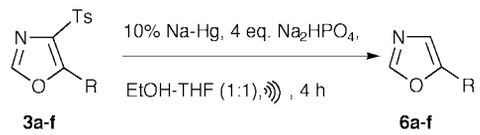
Intrigued by the use of ultrasound[18] to promote heterogeneous reactions we endeavoured to apply sonication to the sodium amalgam reaction. Initial reactions were extremely slow, but it was encouraging to see that the desired product **6a** was formed with sonication at room temperature. Most encouraging was that the starting material **3a** survived these conditions with little or no decomposition.

We were delighted to find that running the reactions in a 1:1 mixture of alcohol and THF afforded the required 5-monosubstituted oxazole **6a** in good yield (Table 3). After a basic aqueous work-up, it was found that the product of the reaction required no further purification.

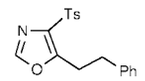
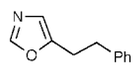
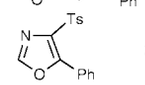
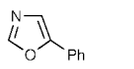
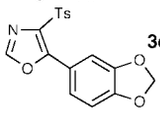
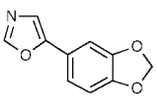
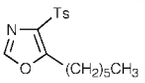
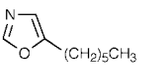
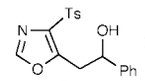
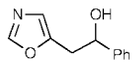
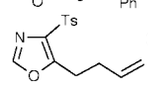
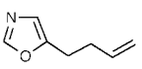
Using the optimum solvent mixture of EtOH–THF (1:1), the desulfonylation of oxazoles **3b–f** was investigated. It was gratifying to find that desulfonylation was effective in all cases (Table 4).

Where the 5-substituent was an aromatic ring, yields were quantitative. Alkyl 5-substituents gave lower, but still good, yields of desulfonylated products. Again, all reactions were very clean and products could be analysed without further purification. It was noted, however, that the 5-monosubstituted

Table 4 Desulfonylation of tosyloxazoles **3a–f**



3a-f **6a-f**

4-Tosyloxazole, **3a–f**	Product, **6a–f** (Yield)
 **3a**	 **6a** (72%)
 **3b**	 **6b** (100%)
 **3c**	 **6c** (98%)
 **3d**	 **6d** (64%)
 **3e**	 **6e** (51%)
 **3f**	 **6f** (65%)

oxazoles were not as stable as their 4-tosyl precursors, which could be stored for months under ambient conditions. The desulfonylated products **6a–f**, isolated as colourless oils or solids, began to decompose after a few days at ambient conditions.

In summary, the use of well-established routes, together with novel dianion procedures, to 5-substituted-4-tosyloxazoles, coupled with the ultrasound-promoted desulfonylation technology provides an efficient procedure for the synthesis of 5-monosubstituted oxazole systems.

Experimental

NMR spectra were recorded on a JEOL EX-270 instrument using tetramethylsilane as the internal standard. Coupling constants are given in Hz and ^{13}C spectra were verified using DEPT experiments. Melting points were recorded on an Electrothermal IA9100 digital melting point apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis FT-IR spectrometer using NaCl plates. Low resolution electron impact (EI) mass spectra were recorded on a Kratos MS 25 spectrometer. Chemical ionisation (CI) and high resolution mass spectra were recorded on a Micromass Autospec spectrometer. Elemental analyses were carried out at the University of Newcastle. Flash column chromatography was performed using Matrex silica gel 60 (70–200) and the eluent specified. THF is tetrahydrofuran, PE is the fraction of petroleum ether boiling in the range 40–60 °C, ether is diethyl ether, EtOAc is ethyl acetate, DCM is dichloromethane and EtOH is absolute ethanol. THF was distilled from sodium benzophenone ketyl immediately before use and EtOH was stored over 4 Å molecular sieves. Except where specified, all reagents were purchased from commercial sources and were used without further purification. TosMIC is [(4-methylphenyl)-sulfonyl]methyl isocyanide. All reactions were carried out in flame-dried apparatus under an atmosphere of oxygen-free nitrogen. Sonication was carried out using a Hilsonic FM100 (50/60 Hz) ultrasonic bath.

4-[(4-Methylphenyl)sulfonyl]-5-(2-phenylethyl)-1,3-oxazole 3a

Prepared according to the method of van Leusen *et al.*[8] To a stirred solution of TosMIC (1.464 g, 7.5 mmol) in THF (35 mL) at −78 °C was added *n*-butyllithium (1.6 M in hexanes, 5.2 mL, 8.25 mmol) dropwise. After 15 min, 3-phenylpropionyl chloride (0.74 mL, 5 mmol) was added dropwise and stirring continued at −78 °C for 1 h. The reaction mixture was then warmed to rt for 1.5 h before being poured into water (25 mL). After extraction with EtOAc (2 × 25 mL), the combined organic layers were washed with saturated $NaHCO_3$ solution (2 × 25 mL) and brine (25 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was purified by flash column chromatography (PE–EtOAc, 3:1) to give the *title compound* **3a** as a yellow solid (1.394 g, 85%), mp 94–95 °C; R_f 0.56 (ether–PE, 3:1); ν_{max} (Nujol®)/cm^{-1} 3141, 1718, 1587, 1510, 1377, 1329, 1240, 1147, 1101; δ_H (270 MHz; $CDCl_3$) 7.72–7.70 (3 H, m, 2 × tosyl-CH + H-2), 7.29–7.16 (7 H, m, 2 × tosyl-CH + Ph), 3.45 (2 H, t, *J* 7.5, CH_2), 3.04 (2 H, t, *J* 7.5, CH_2), 2.41 (3 H, s, tosyl-CH_3); δ_C (67.5 MHz; $CDCl_3$) 156.1 (C), 149.6 (CH, C-2), 144.7 (C), 139.6 (C), 137.0 (C), 135.8 (C), 129.8 (2 × CH), 128.6 (2 × CH), 128.4 (2 × CH), 128.0 (2 × CH), 126.5 (CH), 33.9 (CH_2), 27.3 (CH_2), 21.6 (CH_3); *m/z* (CI) 345 (MNH_4^+, 100%), 328 (MH^+, 75), 91 ($C_7H_7^+$, 26) [HRMS (CI): calcd. for $C_{18}H_{18}NO_3S$, 328.1007. Found: MH^+, 328.1006 (0.3 ppm error)].

4-[(4-Methylphenyl)sulfonyl]-5-phenyl-1,3-oxazole 3b

This reaction was carried out as described for the preparation of compound **3a** with TosMIC (0.703 g, 3.6 mmol), *n*-butyllithium (1.6 M in hexanes, 2.5 mL, 4 mmol) and benzoyl chloride (0.35 mL, 3 mmol). Purification by flash column chromatography (ether–PE, 1:1) afforded the *title compound* **3b** as a pale yellow solid (0.684 g, 64%), mp 143–144.5 °C (lit.[8] 142–143 °C); R_f 0.18 (ether–PE, 1:1); ν_{max} (Nujol®)/cm^{-1} 3143, 1510, 1313, 1269, 1143; δ_H (270 MHz; $CDCl_3$) 8.00–7.86 (5 H, m, 2 × tosyl-CH + 2 × phenyl-CH + H-2), 7.52–7.50 (3 H, m, 3 × phenyl-CH), 7.34–7.31 (2 H, m, 2 × tosyl-CH), 2.42 (3 H, s, tosyl-CH_3); δ_C (67.5 MHz; $CDCl_3$) 152.7 (C, C-5), 149.2 (CH, C-2), 145.0 (C), 137.1 (C), 135.6 (C), 130.9 (CH), 129.8 (2 × CH), 129.0 (2 × CH), 128.6 (2 × CH), 128.3 (2 × CH), 125.5 (C), 21.6 (CH_3); *m/z* (CI) 317 (MNH_4^+, 97%), 300 (MH^+, 100), 236 (20) [HRMS (CI): calcd. for $C_{16}H_{14}NO_3S$, 300.0694. Found: MH^+, 300.0688 (2.1 ppm error)].

5-(2*H*-1,3-Benzodioxol-5-yl)-4-[(4-methylphenyl)sulfonyl]-1,3-oxazole 3c

This reaction was carried out as described for the preparation of compound **3a** with TosMIC (0.703 g, 3.6 mmol), *n*-butyllithium (1.6 M in hexanes, 2.5 mL, 4 mmol) and piperonoyl chloride (0.554 g, 3 mmol) added to the reaction as a solution in THF (5 mL). The residue was taken up in DCM and passed through a plug of silica to afford the *title compound* **3c** as a pale yellow solid (0.699 g, 68%), mp 167–168 °C; R_f 0.26 (ether–PE, 1:1); ν_{max} (Nujol®)/cm^{-1} 3151, 1592, 1509, 1376, 1305, 1232, 1145, 1035; δ_H (270 MHz; $CDCl_3$) 7.91–7.88 (2 H, m, 2 × tosyl-CH), 7.80 (1 H, s, H-2), 7.55 (1 H, dd, *J* 8 and 2, H-6′), 7.46 (1 H, d, *J* 2, H-4′) 7.34–7.31 (2 H, m, 2 × tosyl-CH), 6.93 (1 H, d, *J* 8, H-7′), 6.06 (2 H, s, –OCH_2O–), 2.42 (3 H, s, tosyl-CH_3); δ_C (67.5 MHz; $CDCl_3$) 152.4 (C), 149.9 (C), 148.7 (CH, C-2), 147.9 (C), 144.9 (C), 137.2 (C), 134.5 (C), 129.8 (2 × CH), 128.2 (2 × CH), 124.2 (CH), 119.2 (C), 109.0 (CH), 108.5 (CH), 107.7 (CH_2), 21.6 (CH_3); *m/z* (CI) 361 (MNH_4^+, 100%), 344 (MH^+, 96), 280 (17), 190 (16) [Found: C, 59.71; H, 3.84; N, 4.09. $C_{17}H_{13}NO_5S$ requires C, 59.47; H, 3.82; N, 4.08%].

5-Hexyl-4-[(4-methylphenyl)sulfonyl]-1,3-oxazole 3d

This reaction was carried out as described for the preparation of compound **3a** with TosMIC (0.703 g, 3.6 mmol), *n*-butyllithium (1.6 M in hexanes, 5 mL, 8 mmol) and heptanoyl chloride (0.46 mL, 3 mmol). Purification by flash column

chromatography (PE–ether, 1 : 1) afforded the *title compound* **3d** as a viscous yellow oil which solidifies on standing (0.490 g, 53%), mp 34–35 °C; R_f 0.36 (ether–PE, 3 : 1); ν_{max} (Nujol®)/cm^{-1} 3134, 1718, 1593, 1517, 1331, 1240, 1149, 1085; δ_H (270 MHz; $CDCl_3$) 7.92–7.90 (2 H, m, 2 × tosyl-CH), 7.72 (1 H, s, H-2), 7.36–7.32 (2 H, m, 2 × tosyl-CH), 3.10 (2 H, t, *J* 7.5, $CH_3(CH_2)_4CH_2$-), 2.43 (3 H, s, tosyl-CH_3), 1.73–0.85 (11 H, m, 4 × CH_2 + CH_3); δ_C (67.5 MHz; $CDCl_3$) 157.3 (C), 149.4 (CH, C-2), 144.8 (C), 137.4 (C), 135.2 (C), 129.8 (2 × CH), 128.0 (2 × CH), 31.3 (CH_2), 28.7 (CH_2), 27.8 (CH_2), 25.3 (CH_2), 22.4 (CH_2), 21.6 (CH_3), 14.0 (CH_3); *m/z* (CI) 308 (MH^+, 100%) [Found: C, 62.37; H, 6.82; N, 4.39. $C_{16}H_{21}NO_3S$ requires C, 62.52; H, 6.89; N, 4.56%].

5-Methyl-4-[(4-methylphenyl)sulfonyl]-1,3-oxazole 4

Prepared according to the method of van Leusen *et al.*[8] To a stirred solution of TosMIC (0.976 g, 5 mmol) in THF (20 mL) at −78 °C was added *n*-butyllithium (1.6 M in hexanes, 3.4 mL, 5.5 mmol) dropwise. After 15 min, acetic anhydride (0.52 mL, 5.5 mmol) was added dropwise and stirring continued at −78 °C for 1 h. The reaction mixture was then warmed to rt for 2 h before being poured onto water (20 mL). After extraction with EtOAc (2 × 20 mL), the combined organic layers were dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was taken up in a small amount of DCM and passed through a very short column of silica (eluting with EtOAc) to give the *title compound* **4** as a yellow solid (1.027g, 87%), mp 134–135.5 °C (lit.[8] 136–137 °C); R_f 0.27 (ether–PE, 3 : 1); ν_{max} (Nujol®)/cm^{-1} 3141, 1592, 1376, 1326, 1294, 1241, 1149, 1100, 1066; δ_H (270 MHz; $CDCl_3$) 7.93–7.89 (2 H, m, 2 × tosyl-CH), 7.72 (1 H, s, H-2), 7.36–7.33 (2 H, m, 2 × tosyl-CH), 2.70 (3 H, s, oxazole-CH_3), 2.43 (3 H, s, tosyl-CH_3); δ_C (67.5 MHz; $CDCl_3$) 153.5 (C), 149.3 (CH, C-2), 144.8 (C), 137.3 (C), 135.6 (C), 129.8 (2 × CH), 127.9 (2 × CH), 21.6 (CH_3, tosyl-CH_3), 11.4 (CH_3, oxazole-CH_3); *m/z* (CI) 255 (MNH_4^+, 30%), 238 (MH^+, 100) [HRMS (CI): calcd. for $C_{11}H_{12}NO_3S$, 238.0538. Found: MH^+, 238.0538 (0.2 ppm error)].

General procedure for the reaction of 5 with electrophiles

To a stirred solution of **4** (0.237 g, 1 mmol) in THF (10 mL) at −78 °C was added *n*-butyllithium (1.6 M in hexanes, 1.4 mL, 2.2 mmol). After 30 min, the electrophile (1.05 mmol) was added and stirring continued at −78 °C for 1 h. The reaction was then warmed to rt for 1 h before being poured into water (20 mL) and extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with brine (20 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure.

4-[(4-Methylphenyl)sulfonyl]-5-(2-phenylethyl)-1,3-oxazole 3a. Using benzyl bromide (0.13 mL, 1.05 mmol). Purification by flash column chromatography (PE–ether, 1 : 1) afforded the *title compound* **3a** as a pale yellow solid (0.2 g, 61%). Analytical data was entirely consistent with that reported above.

2-{4-[(4-Methylphenyl)sulfonyl]-1,3-oxazol-5-yl}-1-phenylethanol 3e. Using benzaldehyde (0.11 mL, 1.05 mmol). Purification by flash column chromatography (ether–PE, 3 : 1) afforded the *title compound* **3e** as a colourless solid (0.267 g, 78%), mp 128.5–129.5 °C; R_f 0.13 (ether–PE, 3 : 1); ν_{max} (Nujol®)/cm^{-1} 3529, 3137, 1579, 1513, 1313, 1244, 1142, 1060; δ_H (270 MHz; $CDCl_3$) 7.86–7.83 (2 H, m, 2 × tosyl-CH), 7.72 (1 H, s, H-2), 7.43–7.29 (7 H, m, 5 × phenyl-CH + 2 × tosyl-CH), 5.16–5.12 (1 H, m, –CHOH), 3.62–3.46 (2 H, m, CH_2), 2.58 (1 H, d, *J* 4, –OH), 2.42 (3 H, s, tosyl-CH_3); δ_C (67.5 MHz; $CDCl_3$) 153.7 (C), 149.9 (CH, C-2), 145.0 (C), 142.7 (C), 136.9 (C), 136.8 (C), 129.8 (2 × CH), 128.7 (2 × CH), 128.1 (3 × CH), 125.6 (2 × CH), 72.7 (CH, –CHOH), 35.4 (CH_2), 21.6 (CH_3); *m/z* (CI) 361 (MNH_4^+, 99%), 345 (25), 326 (100), 255 (35), 190 (35) [Found: C, 63.04; H, 4.94; N, 3.98. $C_{18}H_{17}NO_4S$ requires C, 62.96; H, 4.99; N, 4.08%].

5-(But-3-enyl)-4-[(4-methylphenyl)sulfonyl]-1,3-oxazole 3f. Using **4** (0.300 g, 1.27 mmol), *n*-butyllithium (1.6 M in hexanes, 1.75 mL, 2.8 mmol) and allyl iodide (0.12 mL, 1.33 mmol). Purification by flash column chromatography (PE–ether, 1 : 1) afforded the *title compound* **3f** as a yellow oil which solidifies on standing (0.219 g, 62%), mp 52–55 °C; R_f 0.26 (ether–PE, 1 : 1); ν_{max} (Nujol®)/cm^{-1} 3124, 3047, 1579, 1515, 1376, 1319, 1253, 1151, 1085; δ_H (270 MHz; $CDCl_3$) 7.93–7.90 (2 H, m, 2 × tosyl-CH), 7.73 (1 H, s, H-2), 7.35–7.33 (2 H, m, 2 × tosyl-CH), 5.89–5.74 (1 H, m, vinyl-CH), 5.09–4.98 (2 H, m, vinyl-CH_2), 3.23 (2 H, t, *J* 7, allyl-CH_2), 2.52–2.43 (5 H, m, CH_2 + tosyl-CH_3); δ_C (67.5 MHz; $CDCl_3$) 156.2 (C), 149.5 (CH), 144.7 (C), 137.2 (C), 135.7 (CH), 135.5 (C), 129.7 (2 × CH), 127.9 (2 × CH), 116.4 (CH_2), 31.6 (CH_2), 24.7 (CH_2), 21.5 (CH_3); *m/z* (CI) 295 (MNH_4^+, 10%), 278 (MH^+, 100), 238 (6), 139 (8), 122 (18) [HRMS (CI): calcd. for $C_{14}H_{16}NO_3S$, 278.0851. Found: MH^+, 278.0856 (1.7 ppm error)] [Found: C, 60.18; H, 5.41; N, 4.94. $C_{14}H_{15}NO_3S$ requires C, 60.63; H, 5.45; N, 5.05%].

General procedure for desulfonylation of tosyloxazoles 3a–f

To a solution of the tosyloxazole **3a**–**f** (0.5 mmol) in THF–EtOH (1 : 1, 10 mL) was added Na_2HPO_4 (0.283 g, 2 mmol). Sonication was begun and 10% Na–Hg (0.575 g, 2.5 mmol Na) was quickly added. After 2 h, another portion of 10% Na–Hg (0.575 g, 2.5 mmol Na) was added and sonication continued for a further 2 h. After the sonication had been stopped, EtOAc (20 mL) was added to the reaction and the whole mixture was decanted into water (20 mL). The layers were separated and the aqueous layer was further extracted with EtOAc (20 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (2 × 20 mL) and brine (20 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The compounds so afforded did not require further purification.

5-(2-Phenylethyl)-1,3-oxazole 6a. Pale yellow oil (0.062 g, 72%); R_f 0.33 (ether–PE, 1 : 1); ν_{max} (neat)/cm^{-1} 3127, 3085, 3028, 2929, 2862, 1670, 1602, 1510, 1454, 1101; δ_H (270 MHz; $CDCl_3$) 7.87 (1 H, s, H-2), 7.33–7.15 (5 H, m, 5 × phenyl-CH), 6.75 (1 H, s, H-4), 3.00–2.97 (4 H, br m, 2 × CH_2); δ_C (67.5 MHz; $CDCl_3$) 152.1 (C, C-5), 150.0 (CH, C-2), 140.3 (C, phenyl), 128.4 (2 × CH, phenyl), 128.2 (2 × CH, phenyl), 126.3 (CH, phenyl), 122.2 (CH, C-4), 33.7 (CH_2), 27.2 (CH_2); *m/z* (CI) 174 (MH^+, 100%), 91 ($C_7H_7^+$, 10) [HRMS (CI): calcd. for $C_{11}H_{12}NO$, 174.0919. Found: MH^+, 174.0916 (1.4 ppm error)].

5-Phenyl-1,3-oxazole 6b. Pale brown solid (0.073 g, 100%), mp 36–37 °C (lit.[8] 36–38 °C); R_f 0.35 (PE–ether, 1 : 1); δ_H (270 MHz; $CDCl_3$) 7.92 (1 H, s, H-2), 7.68–7.26 (6 H, m, 5 × phenyl + H-4). ^{13}C NMR data consistent with published values.[19]

5-(2*H*-1,3-Benzodioxol-5-yl)-1,3-oxazole 6c. Colourless solid (0.093 g, 98%), mp 83–85 °C; R_f 0.27 (PE–ether, 1 : 1); ν_{max} (Nujol®)/cm^{-1} 3141, 1506, 1482, 1376, 1365, 1259, 1232, 1099, 1037; δ_H (270 MHz; $CDCl_3$) 7.86 (1 H, s, H-2), 7.27–6.85 (4 H, m, 3 × phenyl-CH + H-4), 6.00 (2 H, s, –OCH_2O–); δ_C (67.5 MHz; $CDCl_3$) 151.4 (C), 149.9 (CH, C-2), 148.2 (C), 148.0 (C), 121.9 (C), 120.4 (CH), 118.5 (CH), 108.8 (CH), 105.0 (CH), 101.4 (CH_2); *m/z* (CI) 190 (MH^+, 100%) [HRMS (CI): calcd. for $C_{10}H_8NO_3$, 190.0504. Found: MH^+, 190.0504 (0.3 ppm error)].

5-Hexyl-1,3-oxazole 6d. Yellow oil (0.049 g, 64%); R_f 0.39 (ether–PE, 1 : 1); ν_{max} (neat)/cm^{-1} 2929, 2856, 1724, 1662, 1464, 1379; δ_H (270 MHz; $CDCl_3$) 7.76 (1 H, s, H-2), 6.75 (1 H, s, H-4), 2.65 (2 H, t, *J* 7, –$CH_2(CH_2)_4CH_3$), 1.67–0.86 (11 H, m, alkyl); δ_C (67.5 MHz; $CDCl_3$) 153.3 (C), 149.9 (CH), 121.6

(CH), 31.4 (CH_2), 28.6 (CH_2), 27.4 (CH_2), 25.3 (CH_2), 22.4 (CH_2), 14.0 (CH_3); *m/z* (CI) 154 (MH^+, 100%) [HRMS (CI): calcd. for $C_9H_{16}NO$, 154.1232. Found: MH^+, 154.1236 (2.6 ppm error)].

2-(1,3-Oxazol-5-yl)-1-phenylethanol 6e. Colourless oil (0.097 g, 51%); R_f 0.13 (ether–PE, 3:1); ν_{max} (neat)/cm^{-1} 3332 (br), 2923, 1683, 1602, 1512, 1454, 1199, 1120, 1087, 1054; δ_H (270 MHz; $CDCl_3$) 7.64 (1 H, s, H-2), 7.33–7.26 (5 H, m, phenyl), 6.69 (1 H, s, H-4), 4.94 (1 H, dd, *J* 7 and 5, –CHOH), 3.44 (1 H, br s, –OH), 3.14–2.94 (2 H, m, $–CH_2–$); δ_C (67.5 MHz; $CDCl_3$) 150.3 (CH, C-2), 149.7 (C), 143.2 (C), 128.4 (2 × CH), 127.8 (CH) 125.6 (2 × CH), 123.5 (CH), 64.9 (CH, –CHOH), 35.3 (CH_2); *m/z* (CI) 190 (MH^+, 100%) [HRMS (CI): calcd. for $C_{11}H_{12}NO_2$, 190.0868. Found: MH^+, 190.0867 (0.8 ppm error)].

5-(But-3-enyl)-1,3-oxazole 6f. Colourless oil (0.04 g, 65%); R_f 0.29 (ether–PE, 1:1); ν_{max} (neat)/cm^{-1} 3126, 3080, 2929, 1664, 1641, 1512, 1448, 1374, 1321, 1101; δ_H (270 MHz; $CDCl_3$) 7.77 (1 H, s, H-2), 6.78 (1 H, s, H-4), 5.90–5.75 (1 H, m, vinyl-CH), 5.11–5.00 (2 H, m, vinyl-CH_2), 2.77 (2 H, t, *J* 7, CH_2), 2.45–2.04 (2 H, m, allyl-CH_2); δ_C (67.5 MHz; $CDCl_3$) 152.4 (C), 150.0 (CH), 136.6 (CH), 122.0 (CH), 115.8 (CH_2), 31.5 (CH_2), 24.9 (CH_2); *m/z* (CI) 124 (MH^+, 100%), 113 (6) [HRMS (CI): calcd. for $C_7H_{10}NO$, 124.0760. Found: MH^+, 124.0762 (1.8 ppm error)].

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