Regiospecific Metallation of Furyl-4,5-dihydrooxazoles: Preparation of 2,5-Disubstituted and 2,3,5-Trisubstituted Furans

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Regiospecific metallation at C-5 of 2-(2-furyl)-4,4-dimethyl-4,5-dihydrooxazole **1** has been carried out using butyllithium in tetrahydrofuran (THF) and hexamethylphosphoramide (HMPA) as co-solvent. Reaction of the metallated species **1a** with various electrophiles allowed us to prepare the disubstituted furans **3–13**. The metallation of (5-alkyl- or 5-trialkylsilyl-2-furyl)-4,5-dihydrooxazoles **3, 4, 8, 9** or **10** with butyllithium in THF led to regiospecific metallation at C-3 and reaction with electrophiles provided the expected trisubstituted furans. C-3 Lithiation of (5-trialkylsilyl-2-furyl)-4,5-dihydrooxazoles **3** and **4** is a potential route to 2,3-disubstituted furans. All these reactions took place with generally good yields.

Furan derivatives are of importance both because of their occurrence as partial structure in natural products[1] and their versatility as intermediates for the preparation of highly functionalized cyclic and acyclic compounds.[1–3] Although numerous furans have been synthesized by ring-forming processes or electrophilic substitution on the aromatic ring,[4–6] there are few general methods for the preparation of trisubstituted furans.[7] We report here a synthesis of 2,3,5-trisubstituted furans by regioselective metallation of the furan moiety. 2-(2-Furyl)-4,4-dimethyl-4,5-dihydrooxazole was chosen as the starting material because of its availability from inexpensive furoic acid and the synthetic versatility of the 4,5-dihydrooxazole moiety.[8,9]

The regioselective metallation at C-3 adjacent to the directing group in 2-(2-furyl)-4,4-dimethyl-4,5-dihydrooxazole has been investigated by Chadwick and his co-workers.[10] Their best result in terms of regioselectivity was a 3:5 metallation ratio of 9.5:1 in dimethoxyethane (DME) (Scheme 1). This result

1
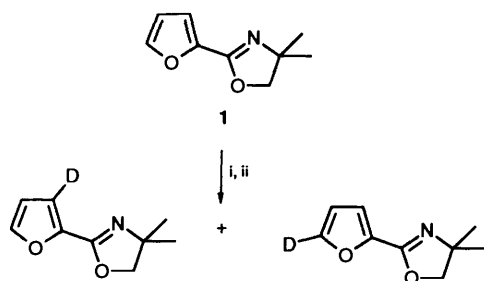
| solvent : | DME | (9.5 : 1) |
	THF	(1.5 : 1)
	Ether	(1 : 1)
	Hexane	(1 : 4.5)

Scheme 1 *Reagents and conditions:* i, BuLi, solvent, −78 °C, 0.25 h; ii, D₂O

prompted us, in order to prepare 2,3,5-trisubstituted furan derivatives in a regiospecific manner, to promote 5 metallation and thus obtain the pure 2,5-disubstituted species, which could be further metallated at the 3 position.

Results and Discussion

Metallation at the C-5 Position.—We have previously reported[11] that 4,4-dimethyl-2-(2-thienyl)-4,5-dihydrooxazole

undergoes regiospecific metallation at the 5 position with butyllithium as metallating agent in tetrahydrofuran (THF) at −78 °C in the presence of the polar co-solvent hexamethylphosphoramide (HMPA) (Scheme 2). Regioselective control of the
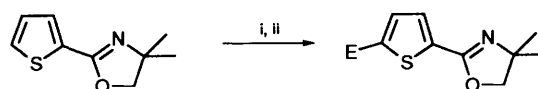
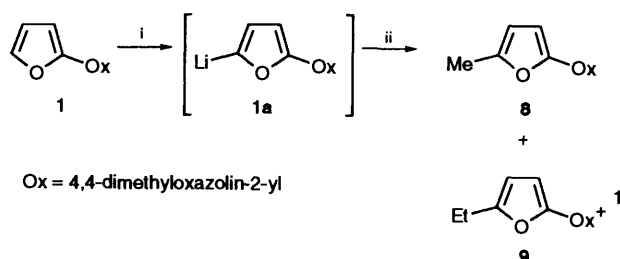**Scheme 2** *Reagents and conditions:* i, BuLi, THF–HMPA (4:1), −78 °C, 0.5 h; ii, electrophile

metallation of **1** may be achieved by using the same reaction conditions.

The dihydrooxazole **1**, prepared by a literature procedure[10] from 2-furoic acid, was lithiated with butyllithium (1.1 equiv.) in THF–HMPA (4:1) at −78 °C during 0.5 h. Deuterium exchange with MeOD showed that the metallation took place with high yield and total regioselectivity at the C-5 position. In Table 1 are listed the results of experiments on the reaction of various electrophiles with the lithiated species to provide 2,5-disubstituted furans (Scheme 3).

1   **2-13**
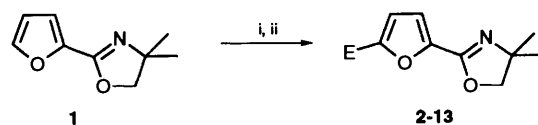
Scheme 3 *Reagents and conditions:* i, BuLi, THF–HMPA (4:1), −78 °C, 0.5 h; ii, electrophile

Addition of a solution of methyl iodide in THF to the reaction mixture containing the lithiated furyldihydrooxazole **1a** at −78 °C gave a mixture of 2-(5-methyl-2-furyl)-dihydrooxazoline **8**, the unexpected 2-(5-ethyl-2-furyl)oxazoline **9** and starting material **1** (Scheme 4). During addition of methyl


Ox = 4,4-dimethyloxazolin-2-yl

Scheme 4 *Reagents and conditions:* i, BuLi, THF–HMPA (4:1), −78 °C, 0.5 h; ii, MeI, −78 °C

Table 1 Preparation of 2-(5-substituted 2-furyl)-4,5-dihydrooxazoles 2–13

Entry	Electrophile	E	Product	Yield (%)[a]
1	MeOD	D	2	95[b]
2	TMSCl	TMS	3	91
3	TBDMSCl	TBDMS	4	87
4	PhCHO	PhCH(OH)	5	93
5	PrCHO	PrCH(OH)	6	72
6	Pr^{i}CHO	Pr^{i}CH(OH)	7	84
7	MeI	Me	8	85[c]
8	EtI	Et	9	78
9	Bu^{i}Br	Bu^i	10	33
10	DMF	CHO	11	52
11	I$_2$	I	12	77
12	ClSnMe$_3$	SnMe$_3$	13	74

[a] Yields are for isolated products. [b] Determined by ^{1}H NMR analysis. [c] The lithiated species was added to a solution of MeI in THF.

iodide, metallation of **8** by unchanged **1a** could account for the formation of the lithiated species **8a** and recovered **1**; **8a** could react with methyl iodide to form the ethyl compound **9** (Scheme 5).

Scheme 5
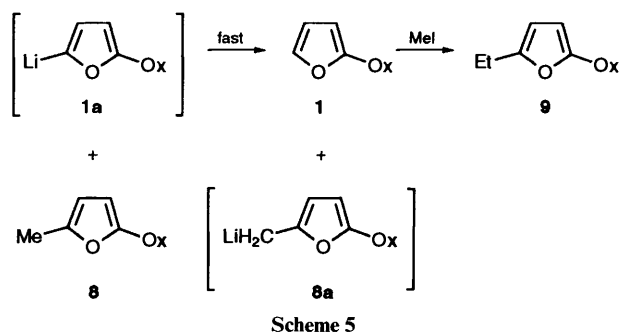
Fast addition of pure methyl iodide to the reaction vessel containing **1a** partially inhibits the metallation of **8** and results in a rise in the temperature of the reaction mixture. This problem was overcome by introducing a cold solution of **1a** to a vigorously stirred solution of methyl iodide in THF at −78 °C (entry 7). In this manner, compound **8** was synthesized in 85% yield, no compound **9** being detected (NMR). The low yield observed with isobutyl bromide as electrophile is probably the result of an elimination side reaction which leads to isobutene. Except for isobutyl bromide, reaction with electrophiles leads to the expected products with good to excellent yields.

Metallation at the C-3 Position.—In order to prepare 2,3,5-trisubstituted furans, a second metallation was carried out on (5-alkyl- and 5-trialkylsilyl-2-furyl)dihydrooxazoles. In the absence of a polar co-solvent, the dihydrooxazolyl group will act as an *ortho*-directing group permitting the metallation at C-3. Furyl dihydrooxazoles **8**, **9**, **10**, **3** and **4** have been metallated by butyllithium (1.1 equiv.) in THF at −78 °C during 0.5 h. Reaction of the lithiated species with electrophiles provided the expected trisubstituted furans (Scheme 6). The results are listed in Table 2.

3, 4, 8, 9 and 10 **14-24**

Scheme 6 *Reagents and conditions:* i, BuLi, THF, −78 °C, 0.5 h; ii, electrophile

Table 2 Preparation of the 2-(3,5-disubstituted-2-furyl)-4,5-dihydrooxazoles 14–24

Entry	R	Electrophile	E	Product	Yield (%)[a]
1	Me	MeI	Me	14	92
2	Me	PhCHO	PhCH(OH)	15	83
3	Et	MeI	Me	16	92
4	Et	PhCHO	PhCH(OH)	17	72
5	Bu^i	MeI	Me	18	77
6	TMS	MeI	Me	19	91
7	TMS	PhCHO	PhCH(OH)	20	44
8	TMS	EtCHO	EtCH(OH)	21	56
9	TMS	DMF	CHO	22	71
10	TBDMS	MeI	Me	23	80
11	TBDMS	PhCHO	PhCH(OH)	24	68

[a] Yields are for isolated products.

Use of benzaldehyde as electrophile with the trimethylsilylated species **3** (entry 7), it has been shown by ^{1}H NMR analysis of the crude product that the low yield observed is a consequence of a disilylation side-reaction. This problem has been overcome by the use of a Bu^{i}Me$_2$Si instead of a Me$_2$Si group. These silylated compounds have potential as intermediates for the preparation of 2,3-disubstituted furans by subsequent fluoride-catalysed desilylation.[12]

Except in the case discussed above, the yields for these reactions are good, thus providing an efficient and regioselective synthesis of a wide variety of 2,3,5-trisubstituted furans.

Experimental

General.—All reactions involving organometallic compounds were carried out under argon. Tetrahydrofuran (THF) was distilled from sodiuim benzophenone ketyl. Ether refers to diethyl ether. Flash chromatography was performed on silica (0.063–0.200 mm) or neutral alumina (0.050–0.160 mm). Light petroleum for flash chromatography refers to the redistilled hydrocarbon fraction boiling in the range 40–60 °C. M.p.s were determined on a Kofler block and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AC 200 F (200 MHz) spectrometer using CDCl$_3$ as solvent with chemical shifts being reported as δ (ppm) from tetramethylsilane, and *J* values recorded in Hz. IR spectra were obtained on a Perkin–Elmer FTIR 1650 spectrometer. Mass spectra were recorded on a JEOL JMS-AX 500 instrument. Elemental analyses were performed on a Carlo Erba 1160 instrument.

2-(2-*Furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **1**.—Furoic acid (112 g, 1 mol) was added in portions to warm (50 °C), freshly distilled, thionyl chloride (120 cm^3, 1.67 mol) and the reaction mixture was heated to reflux for 3 h. Excess of thionyl chloride was distilled off and the residue was distilled *in vacuo* (77 °C, 15 mmHg) to give the acid chloride (124.4 g, 95%) as a colourless oil.

A solution of 2-amino-2-methylpropan-1-ol (170 g, 1.91 mol) in dichloromethane (250 cm^3) was added dropwise to an ice-cold solution of the acid chloride (124.4 g, 0.953 mol) in dichloromethane (500 cm^3), with the temperature at < 20 °C. The mixture was stirred for 2 h at room temperature, washed with water, dried (MgSO$_4$) and evaporated to afford *N*-(1-hydroxy-2,2-dimethylethyl)furan-2-carboxamide (156.1 g, 90%) as a white solid.

To an ice-cold suspension of the crude amide (155.5 g, 0.853 mol) in benzene (1 dm^3) was added dropwise, freshly distilled, thionyl chloride (245 cm^3, 3.41 mol) with the temperature at < 30 °C. Stirring was continued for 12 h at room temperature after which the benzene and excess of thionyl chloride were distilled off. The residue was taken up into water (400 cm^3), and

the solution basified (pH = 10) with sodium hydroxide and extracted with ether. The combined extracts were washed with brine, dried (MgSO$_4$) and evaporated to give the crude product which was distilled (104 °C, 15 mmHg) to leave the title compound 1 (111.3 g, 79%) as a colourless waxy solid, m.p. < 50 °C (Found: C, 64.5; H, 6.6; N, 8.4. C$_9$H$_{11}$NO$_2$ requires C, 65.4; H, 6.7; N, 8.5%); ν_{max}(KBr)/cm^{-1} 1672 (C=N); δ_H(200 MHz; CDCl$_3$) 1.35 (6 H, s, CH$_3$), 4.05 (2 H, s, oxazole CH$_2$), 6.45 (1 H, dd, J 3.4 and 1.7, furan 4-H), 6.90 (1 H, dd, J 3.4 and 0.7, furan 3-H) and 7.55 (1 H, dd, J 1.7 and 0.7, furan 5-H).

Preparation of 4,4-*Dimethyl*-2-(5-*substituted* 2-*furyl*)-4,5-*dihydrooxazoles* **3–13.**—2-(2-Furyl)-4,4-dimethyloxazoline **1** (1.65 g, 10 mmol) was dissolved in THF–HMPA 4:1 (50 cm^3) under argon and the solution was cooled to −78 °C. Butyllithium in hexanes (4.4 cm^3, 11 mmol) was added dropwise to it with the temperature at < −65 °C to give a brown reaction mixture. After the mixture had been stirred for 0.5 h, the electrophile (12 mmol) was added to it and the whole stirred at −78 °C for a further 0.5 h. The mixture was then allowed to warm to 0 °C when it was diluted with water (10 cm^3) and ether (50 cm^3). The aqueous layer was separated and the organic layer was washed with water (4 × 20 cm^3) and brine (20 cm^3), dried (MgSO$_4$) and evaporated to leave the crude product.

4,4-*Dimethyl*-2-(5-*trimethylsilyl*-2-*furyl*)-4,5-*dihydrooxazole* **3.** Trimethylsilyl chloride was used as electrophile and recrystallization of the crude product from hexane afforded the *title compound* (91%), m.p. 74 °C (Found: C, 60.7; H, 8.2; N, 5.8. C$_{12}$H$_{19}$NO$_2$Si requires C, 60.7; H, 8.1; N, 5.9%); ν_{max}(KBr)/cm^{-1} 1672 (C=N); δ_H(200 MHz; CDCl$_3$) 0.30 (9 H, s, Si-CH$_3$), 1.39 (6 H, s, oxazole 4-Me), 4.07 (2 H, s, oxazole CH$_2$), 6.66 (1 H, d, J 3.4, furan 4-H) and 6.96 (1 H, d, J 3.4, furan 4-H).

2-(5-*tert*-*Butyldimethylsilyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazoline* **4.** *tert*-Butyldimethylsilyl chloride was used as electrophile and flash chromatography on silica of the crude product with hexane–ethyl acetate (4:1) as eluent afforded the *title compound* as a colourless oil (87%) (Found: C, 63.7; H, 9.1; N, 5.0. C$_{15}$H$_{25}$NO$_2$Si requires C, 64.5; H, 9.0; N, 5.0%); ν_{max}(film)/cm^{-1} 1672 (C=N); δ_H(200 MHz; CDCl$_3$) 0.27 (6 H, s, Si-CH$_3$), 0.94 (9 H, s, Bu^t-Si), 1.39 (6 H, s, oxazole 4-Me), 4.08 (2 H, s, oxazole CH$_2$), 6.69 (1 H, d, J 3.4, furan 4-H) and 6.99 (1 H, d, J 3.4, furan 3-H).

2-(5-*Hydroxybenzyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **5.** Benzaldehyde was used as electrophile and flash chromatography on silica of the crude product using hexane–ethyl acetate (1:3) as eluent afforded the *title compound* (93%), m.p. 124 °C (Found: C, 68.6; H, 6.0; N, 4.9. C$_{16}$H$_{17}$NO$_3$ requires C, 70.8; H, 6.3; N, 5.2%); ν_{max}(KBr)/cm^{-1} 3215 (OH) and 1672 (C=N); δ_H(200 MHz; CDCl$_3$) 1.27 (6 H, s, oxazole 4-Me), 4.03 (2 H, s, oxazole CH$_2$), 5.95 [1 H, s, CH(OH)], 6.10 (1 H, d, J 3.4, furan 4-H), 6.82 (1 H, d, J 3.4, furan 3-H) and 7.25–7.50 (5 H, m, phenyl H).

2-[5-(1-*Hydroxybutyl*)-2-*furyl*]-4,4-*dimethyl*-4,5-*dihydrooxazole* **6.** Butyraldehyde was used as electrophile and flash chromatography on silica of the crude product using hexane–ethyl acetate (3:1) as eluent afforded the *title compound* (72%), m.p. 109 °C (Found: C, 66.2; H, 8.1; N, 5.9. C$_{13}$H$_{19}$NO$_3$ requires C, 65.8; H, 8.1; N, 5.9%); ν_{max}(KBr)/cm^{-1} 3202 (OH) and 1655 (C=N); δ_H(200 MHz; CDCl$_3$) 0.93 (3 H, t, J 7.3, CH$_3$), 1.20–1.60 (2 H, m, CH$_2$), 1.36 (6 H, s, oxazole 4-Me), 1.83 (2 H, dt, CH$_2$), 3.40 (1 H, s, OH), 4.06 (2 H, s, oxazole CH$_2$), 4.76 [1 H, t, CH(OH)], 6.31 (1 H, d, J 3.4, furan 4-H) and 6.86 (1 H, d, J 3.4, furan 3-H).

2-[5-(1-*Hydroxy*-2-*methylpropyl*)-2-*furyl*]-4,4-*dimethyl*-4,5-*dihydrooxazole* **7.** 2-Methylpropanal was used as electrophile and recrystallization of the crude product from hexane–acetone

(4:1) afforded the *title compound* (84%), m.p. 149 °C (Found: C, 66.4; H, 8.6; N, 6.0. C$_{13}$H$_{19}$NO$_3$ requires C, 65.8; H, 8.1; N, 5.9%); ν_{max}(KBr)/cm^{-1} 3192 (OH) and 1655 (C=N); δ_H(200 MHz; CDCl$_3$) 0.95 (6 H, dd, J 6.7 and 16.2, Pr^{i}CH$_3$), 1.35 (6 H, s, oxazole 4-Me), 2.14 (1 H, m, Pr^{i}CH), 3.39 (1 H, s, OH), 4.05 (2 H, s, oxazole CH$_2$), 4.49 [1 H, d, J 6.2, CH(OH)], 6.32 (1 H, d, J 3.2, furan 4-H) and 6.87 (1 H, d, J 3.2, furan 3-H).

4,4-*Dimethyl*-2-(5-*methyl*-2-*furyl*)-4,5-dihydrooxazole **8.** The dihydrooxazole **1** (3.3 g, 20 mmol) was dissolved in THF–HMPA (4:1; 50 cm^3) under argon and the solution was cooled to −78 °C. Butyllithium in hexanes (8.8 cm^3, 22 mmol) was added dropwise to the solution with the temperature at < −65 °C to give a brown mixture. After being stirred for 0.5 h, the cold solution was transferred *via* a cannula to a flask containing a THF (10 cm^3) solution of methyl iodide (1.5 cm^3, 24 mmol) at −78 °C under argon. After being stirred for 0.25 h, the mixture was allowed to warm to 0 °C when it was treated with water (10 cm^3) to quench the reaction and then diluted with ether (50 cm^3). The aqueous layer was separated and the organic layer washed with water (4 × 20 cm^3) and brine (20 cm^3), dried (MgSO$_4$) and evaporated. Distillation (90 °C, 0.2 mmHg) of the residue afforded the title compound **8** (3.045 g, 85%) as a colourless oil (Found: C, 67.1; H, 7.6; N, 8.3. C$_{10}$H$_{13}$NO$_2$ requires C, 67.0; H, 7.3; N, 7.8%); ν_{max}(film)/cm^{-1} 1671 (C=N); δ_H(200 MHz; CDCl$_3$) 1.37 (6 H, s, oxazole 4-Me), 2.37 (3 H, s, furan 5-Me), 4.06 (2 H, s, oxazole CH$_2$), 6.07 (1 H, d, J 3.2 furan 4-H) and 6.81 (1 H, d, J 3.2, furan 3-H).

2-(5-*Ethyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **9.** Ethyl iodide was used as electrophile and distillation (110 °C, 0.2 mmHg) afforded the *title compound* as a colourless oil (78%) (Found: C, 67.7; H, 8.1; N, 7.5. C$_{11}$H$_{19}$NO$_2$ requires C, 68.4; H, 7.8; N, 7.3%); ν_{max}(film)/cm^{-1} 1671 (C=N); δ_H(200 MHz; CDCl$_3$) 1.25 (3 H, t, J 7.6, CH$_3$), 1.37 (6 H, s, oxazole 4-Me), 2.71 (2 H, q, J 7.6, CH$_2$), 4.05 (2 H, s, oxazole CH$_2$), 6.08 (1 H, d, J 3.4, furan 4-H) and 6.85 (1 H, d, J 3.4, furan 3-H).

2-(5-*Isobutyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **10.** Isobutyl bromide was used as electrophile and flash chromatography on silica of the crude product using hexane–ethyl acetate (3:1) as eluent afforded the *title compound* as a colourless oil (33%); ν_{max}(film)/cm^{-1} 1667 (C=N); δ_H(200 MHz; CDCl$_3$) 0.92 (6 H, d, J 7.6, CH$_3$), 1.37 (6 H, s, oxazole 4-Me), 2.03 (1 H, m, Bu^{i}CH), 2.54 (2 H, d, J 7.1, CH$_2$), 4.04 (2 H, s, oxazole CH$_2$), 6.08 (1 H, d, J 3.2, furan 4-H) and 6.84 (1 H, d, J 3.2, furan 3-H); m/z (EI) 221 (M$^+$, 17%) and 206 (100).

2-(5-*Formyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **11.** Dimethylformamide was used as electrophile and flash chromatography on silica of the crude product using hexane–ethyl acetate (1:1) as eluent afforded the *title compound* (52%); m.p. 80 °C (Found: C, 62.3; H, 6.0; N, 7.2. C$_{10}$H$_{11}$NO$_3$ requires C, 62.2; H, 5.7; N, 7.2%); ν_{max}(KBr)/cm^{-1} 1676 (C=O) and 1664 (C=N); δ_H(200 MHz; CDCl$_3$) 1.42 (6 H, s, oxazoline 4-Me), 4.16 (2 H, s, oxazole CH$_2$), 7.08 and 7.29 (each 1 H, d, J 3.7, furan 3-H and 4-H) and 9.81 (1 H, s, CHO).

2-(5-*Iodo*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **12.** Iodine was used as electrophile and flash chromatography on silica of the crude product using hexane–ethyl acetate (9:1) as eluent afforded the *title compound* as a yellow solid (77%), m.p. 120 °C (Found: C, 37.6; H, 3.5; N, 4.9. C$_9$H$_{10}$INO$_2$ requires C, 37.1; H, 3.5; N, 4.8%); ν_{max}(KBr)/cm^{-1} 1664 (C=N); δ_H(200 MHz; CDCl$_3$) 1.36 (6 H, s, oxazole 4-Me), 4.05 (2 H, s, oxazole CH$_2$), 6.61 (1 H, d, J 3.4, furan 4-H) and 6.79 (1 H, d, J 3.4, furan 3-H).

4,4-*Dimethyl*-2-(5-*trimethylstannyl*-2-*furyl*)-4,5-*dihydrooxazole* **13.** Trimethylstannyl chloride was used as electrophile and distillation (150 °C, 0.2 mmHg) of the crude product afforded the *title compound* (74%), m.p. 64 °C (Found: C, 43.6; H, 6.1; N, 4.4. C$_{12}$H$_{19}$NO$_2$Sn requires C, 43.9; H, 5.8; N, 4.3%); ν_{max}(KBr)/cm^{-1} 1668 (C=N); δ_H(200 MHz; CDCl$_3$) 0.34 (9 H, s,

Sn-CH$_3$), 1.37 (6 H, s, oxazole 4-Me), 4.05 (2 H, s, oxazole CH$_2$), 6.62 (1 H, d, J 3.3, furan 4-H) and 6.94 (1 H, d, J 3.3, furan 3-H).

Preparation of 4,4-*Dimethyl*-2-(3,5-*disubstituted* 2-*furyl*)-4,5-*dihydrooxazoles* **14–24**.—To a THF (40 cm^3) solution of 4,4-dimethyl-2-(5-substituted 2-furyl)-4,5-dihydrooxazole **3, 4, 8, 9** or **10** (2 mmol) at −78 °C under argon was added dropwise butyllithium in hexanes (0.96 cm^3, 2.4 mmol), with the temperature at < −65 °C. The mixture was stirred for 0.5 h, electrophile (2.4 mmol) was added to it and stirring continued for a further 0.5 h at −78 °C. The mixture was then allowed to warm to 0 °C when water (5 cm^3) and ether (40 cm^3) were added to it and the aqueous layer was separated. The organic layer was washed with 20% aqueous ammonium chloride (10 cm^3) and brine (10 cm^3), dried (MgSO$_4$) and evaporated to leave the crude product.

2-(3,5-*Dimethyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **14**. 4,4-Dimethyl-2-(5-methyl-2-furyl)-4,5-dihydrooxazole **8** was used as substrate and methyl iodide as electrophile. Distillation (90 °C, 0.2 mmHg) of the crude product afforded the *title compound* as a colourless oil (92%) (Found: C, 67.3; H, 6.6; N, 8.8. C$_{11}$H$_{15}$NO$_2$ requires C, 68.4; H, 7.8; N, 7.3%); v_{max}(film)/cm^{-1} 1664 (C=N); δ_H(200 MHz; CDCl$_3$) 1.38 (6 H, s, oxazole 4-Me), 2.27 (3 H, s, furan 3-Me), 2.36 (3 H, s, furan 5-Me), 4.04 (2 H, s, oxazole CH$_2$) and 5.92 (1 H, s, furan 4-H).

2-(3-*Hydroxybenzyl*-5-*methyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **15**. 4,4-Dimethyl-2-(5-methyl-2-furyl)-4,5-dihydrooxazole **8** was used as substrate and benzaldehyde as electrophile. Flash chromatography on silica of the crude product using dichloromethane–ethyl acetate (9:1) as eluent afforded the *title compound* (83%), m.p. 95 °C (Found: C, 72.0; H, 6.9; N, 4.9. C$_{17}$H$_{19}$NO$_3$ requires C, 71.6; H, 6.7; N, 4.9%); v_{max}(KBr)/cm^{-1} 3220 (OH) and 1662 (C=N); δ_H(200 MHz; CDCl$_3$) 1.34 and 1.38 (each 3 H, s, oxazole 4-Me), 2.27 (3 H, s, furan 5-Me), 4.04 (2 H, s, oxazole CH$_2$), 5.79 and 5.85 (each 1 H, s, furan 4-H and carbinol CH) and 7.20–7.50 (5 H, m, phenyl H).

2-(5-*Ethyl*-3-*methyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **16**. 2-(5-Ethyl-2-furyl)-4,4-dimethyl-4,5-dihydrooxazole **9** was used as substrate and methyl iodide as electrophile. Flash chromatography on neutral alumina of the crude product using a hexane–ether (5:1) as eluent afforded the *title compound* (92%); v_{max}(film)/cm^{-1} 1664 (C=N); δ_H(200 MHz; CDCl$_3$) 1.15 (3 H, t, J 7.6, ethyl CH$_3$), 1.30 (6 H, s, oxazole 4-Me), 2.18 (3 H, s, furan 3-Me), 2.59 (2 H, q, J 7.6, ethyl CH$_2$), 3.97 (2 H, s, oxazole CH$_2$) and 5.87 (1 H, s, furan 4-H).

2-(5-*Ethyl*-3-*hydroxybenzyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **17**. 2-(5-Ethyl-2-furyl)-4,4-dimethyl-4,5-dihydrooxazole **9** was used as substrate and benzaldehyde as electrophile. Flash chromatography on neutral alumina of the crude product using hexane–dichloromethane (1:1) as eluent afforded the *title compound* as a colourless oil (72%) (Found: C, 69.4; H, 6.8; N, 4.5. C$_{18}$H$_{21}$NO$_3$ requires C, 72.5; H, 6.8; N, 4.7%); v_{max}(film)/cm^{-1} 3214 (OH) and 1643 (C=N); δ_H(200 MHz; CDCl$_3$) 1.19 (3 H, t, J 8, ethyl CH$_3$), 1.34 and 1.39 (each 3 H, s, oxazole 4-Me), 2.62 (2 H, q, J 8, ethyl CH$_2$), 4.14 (2 H, s, oxazole CH$_2$), 5.80 and 5.86 (each 1 H, s, furan 4-H and carbinol CH) and 7.22–7.46 (5 H, m, phenyl H).

2-(5-*Isobutyl*-3-*methyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **18**. 2-(5-Isobutyl-2-furyl)-4,4-dimethyl-4,5-dihydrooxazole **10** was used as substrate and methyl iodide as electrophile. Flash chromatography on silica of the crude product using hexane–ethyl acetate (4:1) as eluent followed by distillation (115 °C, 0.01 mmHg) afforded the *title compound* (78%); v_{max}(film)/cm^{-1} 1662 (C=N); δ_H(200 MHz; CDCl$_3$) 0.92 (6 H, d, J 7, isobutyl CH$_3$), 1.37 (6 H, s, oxazole 4-Me), 2.00 (1 H, m,

Bu^{i}CH), 2.25 (3 H, s, furan 3-Me), 2.48 (2 H, d, J 7, Bu^{i}CH$_2$), 4.04 (2 H, s, oxazole CH$_2$) and 5.94 (1 H, s, furan 4-H).

4,4-*Dimethyl*-2-(3-*methyl*-5-*trimethylsilyl*-2-*furyl*)-4,5-*dihydrooxazoline* **19**. 4,4-Dimethyl-2-(5-trimethylsilyl-2-furyl)-4,5-dihydrooxazole **3** was used as substrate and methyl iodide as electrophile. Flash chromatography on silica of the crude product using hexane–ethyl acetate (4:1) as eluent afforded the *title compound* (93%) (Found: C, 62.2; H, 8.7; N, 5.6. C$_{13}$H$_{21}$NO$_2$Si requires C, 62.2; H, 8.4; N, 5.6%); v_{max}(film)/cm^{-1} 1665 (C=N); δ_H(200 MHz; CDCl$_3$) 0.25 (9 H, s, Si-CH$_3$), 1.35 (6 H, s, oxazole 4-Me), 2.25 (3 H, s, furan 3-Me), 4.01 (2 H, s, oxazole CH$_2$) and 6.48 (1 H, s, furan 4-H).

2-(3-*Hydroxybenzyl*-5-*trimethylsilyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **20**. 4,4-Dimethyl-2-(5-trimethylsilyl-2-furyl)-4,5-dihydrooxazole **3** was used as substrate and benzaldehyde as electrophile. Flash chromatography on silica of the crude product using hexane–ethyl acetate (4:1) as eluent afforded the *title compound* (44%) (Found: C, 66.1; H, 7.1; N, 4.1. C$_{19}$H$_{25}$NO$_3$Si requires C, 66.4; H, 7.3; N, 4.1%); v_{max}(film)/cm^{-1} 3225 (OH) and 1642 (C=N); δ_H(200 MHz; CDCl$_3$) 0.30 (9 H, s, Si-CH$_3$), 1.37 and 1.43 (each 3 H, s, oxazole 4-Me), 4.18 (2 H, s, oxazole CH$_2$), 5.95 (1 H, s, furan 4-H), 6.40 (1 H, s, carbinol CH) and 7.33–7.51 (5 H, m, phenyl H).

2-[3-(1-*Hydroxypropyl*)-5-*trimethylsilyl*-2-*furyl*]-4,4-*dimethyl*-4,5-*dihydrooxazole* **21**. 4,4-Dimethyl-2-(5-trimethylsilyl-2-furyl)-4,5-dihydrooxazole **3** was used as substrate and propanal as electrophile. Flash chromatography on silica of the crude product using hexane–ethyl acetate (4:1) as eluent afforded the *title compound* (56%) (Found: C, 59.4; H, 8.7; N, 5.5. C$_{15}$H$_{25}$NO$_3$Si requires C, 61.0; H, 8.5; N, 4.7%); v_{max}(film)/cm^{-1} 3282 (OH) and 1640 (C=N); δ_H(200 MHz; CDCl$_3$) 0.27 (9 H, s, Si-CH$_3$), 0.98 (3 H, t, J 7.4, CH$_3$), 1.36 (6 H, s, oxazole 4-Me), 1.81 (2 H, dq, J 6.6 and 7.4, CH$_2$), 4.14 (2 H, s, oxazole CH$_2$), 4.62 (1 H, t, J 6.6, carbinol CH) and 6.55 (1 H, s, furan 4-H).

2-(3-*Formyl*-5-*trimethylsilyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **22**. 4,4-Dimethyl-2-(5-trimethylsilyl-2-furyl)-4,5-dihydrooxazole **3** was used as substrate and dimethylformamide as electrophile. Flash chromatography on silica of the crude product using hexane–ethyl acetate (4:1) as eluent afforded the *title compound* (71%), m.p. 120 °C (Found: C, 58.7; H, 7.3; N, 5.1. C$_{13}$H$_{19}$NO$_3$Si requires C, 58.9; H, 7.2; N, 5.3%); v_{max}(KBr)/cm^{-1} 1686 (C=O) and 1645 (C=N); δ_H(200 MHz; CDCl$_3$) 0.32 (9 H, s, Si-CH$_3$), 1.43 (6 H, s, oxazole 4-Me), 4.17 (2 H, s, oxazole CH$_2$), 7.06 (1 H, s, furan 4-H) and 10.48 (1 H, s, CHO).

4,4-*Dimethyl*-2-(3-*methyl*-5-tert-*butyldimethylsilyl*-2-*furyl*)-4,5-*dihydrooxazole* **23**. 2-(*tert*-Butyldimethylsilyl-2-furyl)-4,4-dimethyl-4,5-dihydrooxazole **4** was used as substrate and methyl iodide as electrophile. Flash chromatography on silica of the crude product using light petroleum–ethyl acetate (9:1) as eluent afforded the *title compound* (80%) (Found: C, 64.3; H, 9.2; N, 4.7. C$_{16}$H$_{27}$NO$_2$Si requires C, 65.5; H, 9.3; N, 4.8%); v_{max}(film)/cm^{-1} 1649 (C=N); δ_H(200 MHz; CDCl$_3$) 0.25 (6 H, s, Si-CH$_3$), 0.93 (9 H, s, Bu^t), 1.37 (6 H, s, oxazole 4-Me), 2.30 (3 H, s, furan 3-Me), 4.03 (2 H, s, oxazole CH$_2$) and 6.53 (1 H, s, furan 4-H).

2-(3-*Hydroxybenzyl*-5-tert-*butyldimethylsilyl*-2-*furyl*)-4,4-*dimethyl*-4,5-*dihydrooxazole* **24**. 2-(5-*tert*-Butyldimethylsilyl-2-furyl)-4,4-dimethyl-4,5-dihydrooxazole **4** was used as substrate and benzaldehyde as electrophile. Flash chromatography on neutral alumina of the crude product using hexane–ethyl acetate (9:1) as eluent afforded the *title compound* (68%), m.p. 111 °C (Found: C, 69.2; H, 8.2; N, 3.6. C$_{22}$H$_{31}$NO$_3$Si requires C, 68.5; H, 8.1; N, 3.6%); v_{max}(film)/cm^{-1} 3202 (OH) and 1635 (C=N); δ_H(200 MHz; CDCl$_3$) 0.22 (6 H, s, Si-CH$_3$), 0.93 (9 H, s, Bu^t), 1.33 and 1.40 (each 3 H, s, oxazole 4-Me), 4.16 (2 H, s,

oxazole CH$_2$), 5.87 (1 H, s, furan 4-H), 6.35 (1 H, s, carbinol CH) and 7.31–7.46 (5 H, m, phenyl H).

Acknowledgements

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