Inter- and intramolecular Diels-Alder/retro-Diels-Alder reactions of 4-silylated oxazoles

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Dedicated to Professor Charles Rees F.R.S. on the occasion of his 75th birthday

Abstract
4-Silylated oxazoles have been shown to undergo inter- and intramolecular Diels-Alder/retro-Diels-Alder reactions with electron-poor alkynes to generate polysubstituted furans. The ease of synthesis of the requisite oxazoles by the rhodium-catalysed condensation of nitriles with silylated diazoacetate greatly increases the scope of this reaction.

Keywords: Silylated oxazoles, diazoacetate, furans, Diels-Alder, retro-Diels-Alder.

Introduction

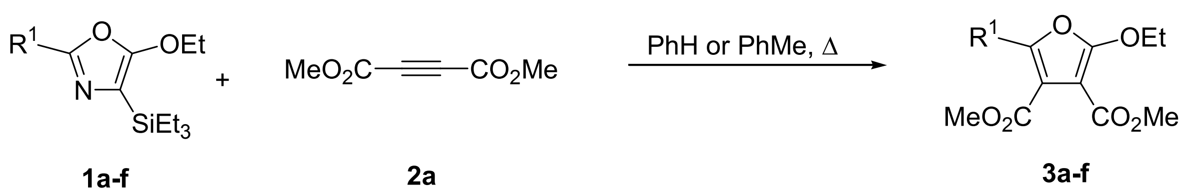
Oxazoles are well recognised for their ability to act as azadienes in Diels-Alder cycloaddition reactions with both alkenes and alkynes.[1] The adducts from the former class of reactions usually eliminate water to generate substituted pyridines, while the latter class gives substituted furans by retro-Diels-Alder elimination of nitriles. This has proven to be a powerful method for the synthesis of this important class of heterocycles and has been widely used in the context of complex natural product synthesis.[2]

One of the most convenient methods for the synthesis of oxazoles involves the condensation of diazocarbonyl compounds with nitriles, discovered by Huisgen in 1961.[3] Although the reaction can be carried out under a range of conditions (thermal, photochemical, Lewis-acid catalysed) the use of rhodium (II) carboxylate catalysts pioneered by Helquist[4] and Moody[5] offers particularly mild conditions which are compatible with highly functionalised substrates. One limitation of this method is that in general these reactions work best with doubly stabilised diazocarbonyl compounds such as diazomalonates, diazoketoesters and diazoketophosphonates so as to avoid competing carbene dimerisation.[6] This in turn limits the utility of this method as an approach to cycloaddition precursors, since the presence of electron-withdrawing groups on the oxazole deactivates the system toward cycloaddition and also oxazoles bearing carbonyl functions at the 4-position are susceptible to Cornforth rearrangement on thermolysis.[7] Indeed, to our knowledge there are no known successful examples of cycloadditions of oxazoles bearing a carbonyl group at the 4-position with alkynes, and only two reports of reactions with alkenes.[8]

We have recently shown that 4-silylated oxazoles can be readily prepared by the condensation of silyl diazoacetates with nitriles under rhodium catalysis.[9] The reluctance of silyl diazoacetates and their derived rhodium carbenoids to undergo dimerisation means that these reactions are operationally simple, requiring no precautions such as high dilution or slow addition of substrate. It therefore became apparent that were these substrates to undergo Diels-Alder reactions with alkynes, followed by subsequent retro-Diels-Alder elimination of silyl cyanide, then this would considerably broaden the scope of the overall furan synthesis. We report herein the successful Diels-Alder/retro-Diels-Alder reactions of silylated oxazoles with electron-poor alkynes in both inter- and intramolecular manifolds.

Results and Discussion

We elected first to study the intermolecular variant. The silylated oxazoles **1a**-**g** were prepared from the corresponding nitrile and ethyl (triethylsilyl)diazoacetate under rhodium (II) octanoate catalysis, according to our standard procedure.[9] Oxazoles **1a**-**f** were then thermolysed in turn with dimethyl acetylenedicarboxylate **2a** under the conditions shown (Scheme 1 and Table 1). Pleasingly, the desired Diels-Alder/retro-Diels-Alder sequence to yield the substituted furans **3** was observed in all but two cases. Where successful, the yields of the adducts were moderate to good except in the case of the simple methyl-substituted oxazole **1b**, which gave a very messy reaction from which only 18% of the clean furan could be isolated. Attempted reaction of the corresponding ethyl homologue also gave a messy reaction from which it was not possible to obtain completely pure furan, and it therefore appears that 2-alkyloxazoles are poor substrates for this reaction. As expected, the aryl- and heteroaryl-substituted oxazoles **1a**,**c** required higher temperatures to drive the reactions as a consequence of the loss of stabilising conjugation through the cycloaddition step.



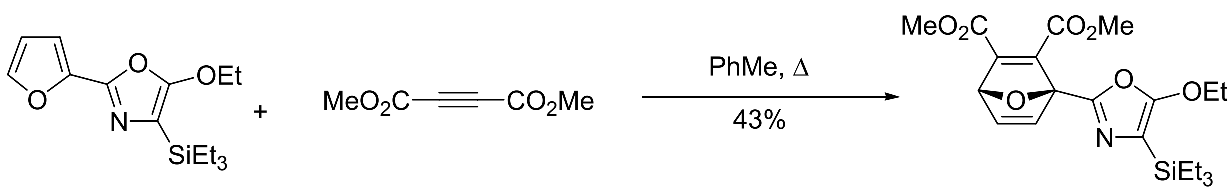
Scheme 1.

Table 1: Cycloaddition of oxazoles **1a-f** with dimethyl acetylenedicarboxylate **2a**

Entry	R^1	Temp.	Solvent	Yield
a	Ph	100	PhMe	65
b	Me	60	PhH	18
c	2-thiophenyl	120	PhMe	52
d	CO_2Me	120	PhMe	62
e	2-furanyl	110	PhMe	0[a]
f	NMe_2	60	PhH	0

[a] - 43% yield of **4** isolated (see **Scheme 2**)

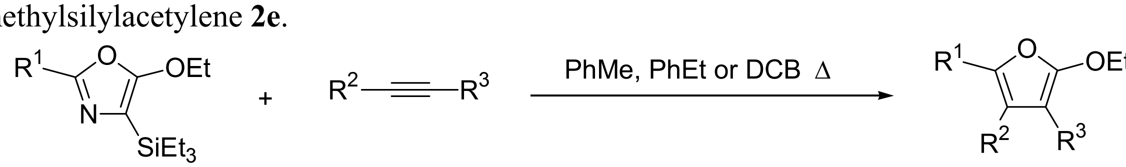
The reaction of 2-furanyl oxazole **1e** with **2a** gave an unoptimised 43% yield of a 1:1 cycloadduct **4** from addition across the more electron-rich furan ring rather than the oxazole (**Scheme 2**). The highly electron-rich dimethylamino-substituted oxazole **1f** underwent a rapid reaction to produce a new, more polar product as judged by TLC analysis, but despite significant effort this material could not be isolated following column chromatography.



1e **2a** **4**

Scheme 2.

We next investigated the intermolecular reactions of oxazoles **1a**/**g** with less activated dienophiles. Both oxazoles reacted in a completely regioselective manner with methyl propiolate **2b** to generate the furans **5a**/**g** in moderate yield (**Scheme 3** and **Table 2**). The regioselectivity mirrors that previously observed[8a,10] and as expected from the alignment of the electron-rich 2-position of the oxazole with the electron-deficient terminus of the alkyne. Notably, the presence of only a single activating group meant that higher temperatures were required than for the corresponding reactions with **2a**. In the light of this, it was felt that less-active dienophiles would be less likely still to undergo cycloaddition and indeed the oxazoles were recovered unchanged from attempted reaction with methyl 3-phenylpropiolate **2c**, diphenylacetylene **2d** and trimethylsilylacetylene **2e**.



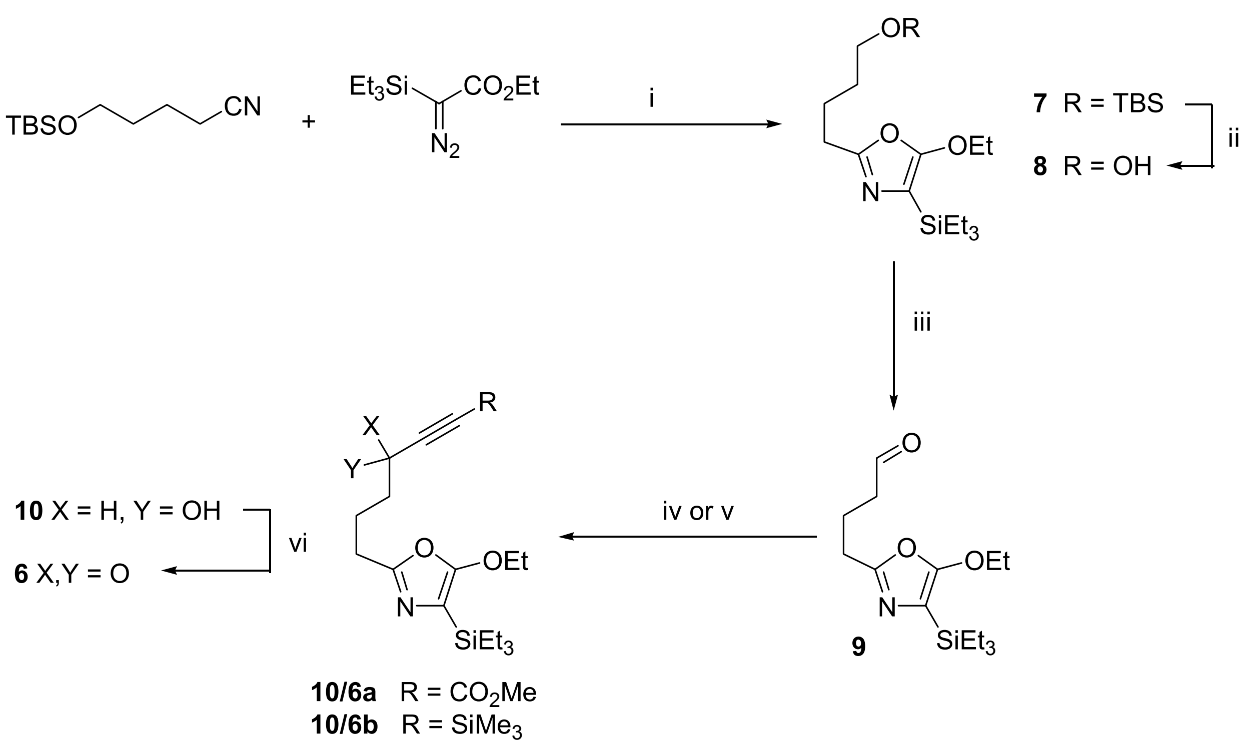
1a,g **2b-e** **5a,b**

Scheme 3.

Table 2: Attempted cycloaddition of oxazoles **1a**,**g** with dienophiles **2b-e**

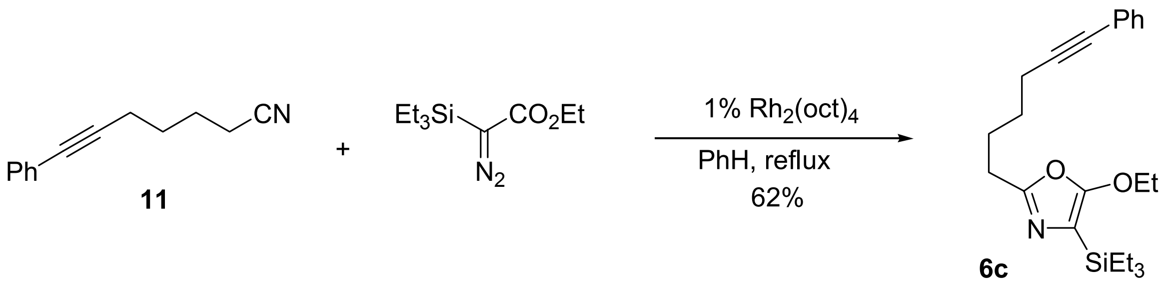
Entry	R[1]	R[2]	R[3]	Temp.	Solvent	Yield
a	Ph	H	CO_2Me	160	PhEt	43
b	Et	H	CO_2Me	110	PhMe	40
c	Ph	Ph	CO_2Me	160	PhEt	0
d	Et	Ph	CO_2Me	160	PhEt	0
e	Et	Ph	Ph	180	DCB	0
f	Et	H	$SiMe_3$	180	DCB	0

Finally, we turned our attention to intramolecular variants of the reaction. Three potential substrates were prepared, with varying degrees of activation in the dienophile part of the molecule. The diactivated and monoactivated oxazoles **6a**/**b** were prepared by the route shown in **Scheme 4**. Thus, condensation of 4-(*tert*-butyldimethylsilyloxy)pentanenitrile[11] with ethyl (triethylsilyl)diazoacetate under rhodium catalysis gave a 79% yield of the oxazole **7**. Deprotection with TBAF yielded alcohol **8** which was oxidised under Swern conditions to yield aldehyde **9**. Addition of lithiated methyl propiolate[12] or trimethylsilylacetylene to **9** gave the alcohols **10a**/**b**, which were oxidised with Dess-Martin periodinane to give **6a**/**b** in good yield.



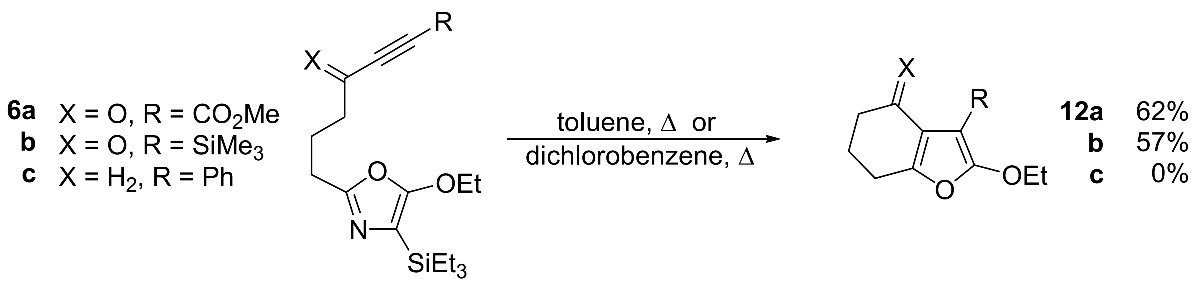
Scheme 4. (i). 1% $Rh_2(oct)_4$, benzene, 79%; (ii). TBAF, THF, r.t., 91%; (iii). $(COCl)_2$, DMSO, CH_2Cl_2, -78°C, then Et_3N, -78 °C to r.t., 73%; (iv). methyl propiolate, ^nBuLi, THF/Et_2O/pentane, -120°C, then add **9**, -120°C to -78 °C, 78%; (v). trimethylsilylacetylene, ^nBuLi, THF, -78°C, then add **9**, 90%; (vi). Dess-Martin periodinane, CH_2Cl_2, 77% (**6a**) and 80% (**6b**).

The non-activated alkyne **6c** was simply prepared by condensation of 7-phenylhept-6-ynylnitrile **11** with ethyl (triethylsilyl)diazoacetate to give **6c** in 62% yield (**Scheme 5**).



Scheme 5.

The Diels-Alder/retro-Diels-Alder reactions of **6a**/**b** proceeded smoothly to give the desired dihydrobenzofuranones **12a/b** in good yield (**Scheme 6**). Notably, in the intramolecular manifold it appears that one activating group (as in **6b**) is sufficient for effective reaction, though as expected the monoactivated system required higher temperatures (refluxing dichlorobenzene compared to toluene) to drive the reaction. It should also be noted that the silyl function in **12b** may potentially be utilised as a handle for the introduction of further functionality through *ipso*-electrophilic substitution reactions.[9] Finally, thermolysis of **6c** failed to give any cycloadduct even under forcing conditions (180°C in dichlorobenzene), with only starting material being recovered. This suggests that at least one activating group is required, although further experiments will be required to separate this effect from the entropic factors associated with exchange of the sp^2 carbonyl unit for a methylene unit in the linking chain.



Scheme 6.

In summary, we have shown that readily available 4-silyl oxazoles will participate in Diels-Alder/retro-Diels-Alder sequences, giving facile access to a range of polysubstituted furans in just two steps from nitriles.

Experimental Section

General procedure for the cycloaddition reactions: 2-ethoxy-3,4-di(methoxycarbonyl)-5-phenylfuran 3a. A solution of 5-ethoxy-2-phenyl-4-triethylsilyloxazole (0.121 g, 0.4 mmol) and dimethyl acetylenedicarboxylate (59 µl, 0.48 mmol) in toluene (0.5 ml) was heated to 100°C. The solution was cooled to room temperature, concentrated under reduced pressure and the residual oil purified by flash chromatography (60:40 petroleum ether:diethyl ether) to yield 2-ethoxy-3,4-di(methoxycarbonyl)-5-phenylfuran **3a** as a white solid (0.079 g, 65 %). m.p. 74-75°C; ν_{max} (KBr/film) 2987 w, 2952 w, 2904 w, 1724 s (C=O), 1602 s, 1573 w, 1492 w, 1459 m, 1446 m, 1417 w, 1390 w, 1346 m, 1222 m, 1097 s, 1051 m, 811 w, 781 w, 763 w, 692 w cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.48 (3 H, t, *J* = 7 Hz, $OCH_2\underline{CH_3}$), 3.78 (3 H, s, CO_2CH_3), 3.88 (3 H, s, CO_2CH_3), 4.51 (2 H, q, *J* = 7 Hz, $O\underline{CH_2}CH_3$), 7.30 - 7.38 (3 H, m, $H_{3',4'}$), 7.55 (2 H, m, $H_{2'}$); δ_C (75 MHz, $CDCl_3$) 14.9 $OCH_2\underline{CH_3}$, 51.5 $CO_2\underline{CH_3}$, 52.6 $CO_2\underline{CH_3}$, 68.5 $O\underline{CH_2}CH_3$, 93.1 C_3, 114.7 C_4, 125.2 $C_{3'}$, 128.4 $C_{4'}$, 128.5 $C_{1'}$, 128.6 $C_{2'}$, 141.8 C_5, 160.5 C_2, 162.3 $\underline{C}O_2CH_3$, 165.1 $\underline{C}O_2CH_3$; *m/z* (CI+, NH_3) 305 ($[M+H]^+$, 100), 105 (12); HRMS (CI+) Found $[M+H]^+$ 305.1034; $C_{16}H_{17}O_6$ requires 305.1025.

2-Ethoxy-3,4-di(methoxycarbonyl)-5-methylfuran 3b
The experiment was carried out by the general procedure with a solution of 5-ethoxy-2-methyl-4-triethylsilyloxazole (0.097 g, 0.4 mmol) and dimethyl acetylenedicarboxylate (51 µl, 0.42 mmol) in benzene (0.2 ml) heated to 60°C. The crude product was purified by flash chromatography (70:30 petroleum ether:diethyl ether) to yield 2-ethoxy-3,4-di(methoxycarbonyl)-5-methylfuran **3b** as a colourless liquid (0.017 g, 18 %). ν_{max} (KBr/film) 2955 s, 2921 s, 2881 s, 1722 s (C=O), 1611 s, 1512 w, 1447 s, 1331 s, 1216 s, 1088 s, 1024 s, 844 m, 811 m, 781 m, 746 m cm^{-1}; δ_H (270 MHz, $CDCl_3$) 1.40 (3 H, t, *J* = 7 Hz, $OCH_2\underline{CH_3}$), 2.36 (3 H, s, CH_3), 3.77 (3 H, s, CO_2CH_3), 3.81 (3 H, s, CO_2CH_3), 4.35 (2 H, q, *J* = 7 Hz, $O\underline{CH_2}CH_3$); δ_C (75 MHz, $CDCl_3$) 12.8 CH_3, 14.1 $OCH_2\underline{CH_3}$, 51.6 $CO_2\underline{CH_3}$, 51.8 $CO_2\underline{CH_3}$, 68.8 $O\underline{CH_2}CH_3$, 92.4 C_3, 113.8 C_4, 147.5 C_5, 159.7 $\underline{C}O_2CH_3$, 162.8 $\underline{C}O_2CH_3$, 163.9 C_2; *m/z* (CI+, NH_3) 243 ($[M+H]^+$, 100); HRMS (CI+) Found $[M+H]^+$ 243.0864; $C_{11}H_{15}O_6$ requires 243.0869.

2-Ethoxy-3,4-di(methoxycarbonyl)-5-(2-thiophenyl)furan 3c. The experiment was carried out by the general procedure with 5-ethoxy-2-(2-thiophenyl)-4-triethylsilyloxazole (0.115 g, 0.37 mmol) and dimethyl acetylenedicarboxylate (50 µl, 0.4 mmol) in toluene (0.4 ml) heated to 120°C. The crude product was purified by flash chromatography (50:50 petroleum ether:diethyl ether) to yield 2-ethoxy-3,4-di(methoxycarbonyl)-5-(2-thiophenyl)furan **3c** as a colourless oil (0.060 g, 52 %). ν_{max} (KBr/film) 2989 w, 2952 w, 1722 s (C=O), 1604 s, 1446 s, 1328 s, 1240 s, 1093 s, 707 w cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.46 (3 H, t, *J* = 7 Hz, $OCH_2\underline{CH_3}$), 3.78 (3 H, s, CO_2CH_3), 3.86 (3 H, s, CO_2CH_3), 4.48 (2 H, q, *J* = 7 Hz, $O\underline{CH_2}CH_3$), 7.02 (1H, dd, $J_{4'-3'}$ = 5 Hz, $J_{4'-5'}$ = 3.5 Hz, $H_{4'}$), 7.30 (1H, dd, $J_{3'-4'}$ = 5 Hz, $J_{3'-5'}$ = 1 Hz, $H_{3'}$), 7.43 (1H, dd, $J_{5'-4'}$ = 3.5 Hz, $J_{5'-3'}$ = 1 Hz, $H_{5'}$); δ_C (75 MHz, $CDCl_3$) 14.9 $OCH_2\underline{CH_3}$, 51.6 $CO_2\underline{CH_3}$, 52.3 $CO_2\underline{CH_3}$, 68.9

O<u>CH</u>$_2$CH$_3$, 93.3 C$_3$, 113.2 C$_4$, 126.3, 126.5 C$_{3',4'}$, 127.5 C$_{5'}$, 130.1 C$_{2'}$, 139.8 C$_5$, 159.9 C$_2$, 162.2 <u>C</u>O$_2$CH$_3$, 163.9 <u>C</u>O$_2$CH$_3$; *m/z* (CI+, NH$_3$) 311 ([M+H]+, 100), 111 (27); HRMS (CI+) Found $[M+H]^+$ 311.0583; $C_{14}H_{15}O_6S$ requires 311.0589.

2-Ethoxy-3,4,5-tri(methoxycarbonyl)furan 3d. The experiment was carried out by the general procedure with 5-ethoxy-2-methoxycarbonyl-4-triethylsilyloxazole (0.144 g, 0.5 mmol) and dimethyl acetylenedicarboxylate (73 µl, 0.6 mmol) in toluene (0.5 ml) heated to 120°C. The crude product was purified by flash chromatography (30:70 petroleum ether:diethyl ether) to yield 2-ethoxy-3,4,5-tri(methoxycarbonyl)furan **3d** as a white solid (0.089 g, 62 %). m.p. 69-71 °C; ν_{max} (KBr/film) 2093 w, 2958 m, 1730 s (C=O), 1712 s (C=O), 1583 s, 1466 s, 1440 s, 1325 s, 1256 s, 1234 s, 1163 m, 1099 s, 1064 s, 809 w, 818 w, 785 m cm^{-1}; δ_H (300 MHz, CDCl$_3$) 1.45 (3 H, t, J = 7 Hz, OCH$_2$<u>CH</u>$_3$), 3.74 (3 H, s, CO$_2$CH$_3$), 3.79 (3 H, s, CO$_2$CH$_3$), 3.89 (3 H, s, CO$_2$CH$_3$), 4.55 (2 H, q, J = 7 Hz, O<u>CH</u>$_2$CH$_3$); δ_C (75 MHz, CDCl$_3$) 14.6 OCH$_2$<u>CH</u>$_3$, 51.7 CO$_2$<u>CH</u>$_3$, 52.1 CO$_2$<u>CH</u>$_3$, 52.9 CO$_2$<u>CH</u>$_3$, 68.9 O<u>CH</u>$_2$CH$_3$, 93.0 C$_3$, 127.9 C$_4$, 130.0 C$_5$, 157.2 C$_2$, 161.2 <u>C</u>O$_2$CH$_3$, 161.8 <u>C</u>O$_2$CH$_3$, 163.1 <u>C</u>O$_2$CH$_3$; *m/z* (CI+, NH$_3$) 287 ($[M+H]^+$, 15), 255 (98), 198 (100), 140 (29), 111 (28), 49 (52); HRMS (CI+) Found $[M+H]^+$ 287.0757; $C_{12}H_{15}O_8$ requires 287.0767.

2-(2,3-Di(methoxycarbonyl)-oxabicyclo[2.2.1]hepta-2,5-dienyl)-5-ethoxy-4-triethylsilyloxazole 4. The experiment was carried out by the general procedure with 5-ethoxy-2-(2-furanyl)-4-triethylsilyloxazole (0.034 g, 0.115 mmol) and dimethyl acetylenedicarboxylate (16 µl, 0.126 mmol) in toluene (0.2 ml) heated to 110°C. The crude product was purified by flash chromatography (70:30 petroleum ether:diethyl ether) to yield 2-(2,3-di(methoxycarbonyl)-oxabicyclo[2.2.1]hepta-2,5-dienyl)-5-ethoxy-4-triethylsilyloxazole **4** as a colourless oil (0.021 g, 43 %). ν_{max} (KBr/film) 2954 s, 2911 m, 2876 m, 1722 s (C=O), 1593 s, 1437 m, 1266 m, 1117 m, 1015 m, 945 w, 710 m cm^{-1}; δ_H (270 MHz, CDCl$_3$) 0.73 (6 H, q, J = 8 Hz, Si<u>CH</u>$_2$CH$_3$), 0.94 (9 H, t, J = 8 Hz, SiCH$_2$<u>CH</u>$_3$), 1.34 (3 H, t, J = 7 Hz, OCH$_2$<u>CH</u>$_3$), 3.73 (3 H, s, CO$_2$CH$_3$), 3.79 (3 H, s, CO$_2$CH$_3$), 4.19 (2 H, q, J = 7 Hz, O<u>CH</u>$_2$CH$_3$), 5.77 (1 H, d, $J_{4'-5'}$ = 2 Hz, H$_{4'}$), 7.29 (1 H, dd, $J_{5'-6'}$ = 5 Hz, $J_{5'-4'}$ = 2 Hz, H$_{5'}$), 7.46 (1 H, d, $J_{6'-5'}$ = 5 Hz, H$_{6'}$); δ_C (75 MHz, CDCl$_3$) 3.2 Si<u>CH</u>$_2$CH$_3$, 7.3 SiCH$_2$<u>CH</u>$_3$, 14.9 OCH$_2$<u>CH</u>$_3$, 52.3 CO$_2$<u>CH</u>$_3$, 52.4 CO$_2$<u>CH</u>$_3$, 69.3 O<u>CH</u>$_2$CH$_3$, 84.7 C$_{4'}$, 91.3 C$_{1'}$, 109.3 C$_4$, 142.7, 144.3 C$_{5',6'}$, 148.5 , 150.8 C$_{2',3'}$, 154.2 C$_2$, 162.4, 163.7, 165.4 C$_5$, <u>C</u>O$_2$CH$_3$; *m/z* (CI+, NH$_3$) 436 ($[M+H]^+$, 100); HRMS (CI+) Found $[M+H]^+$ 436.1794; $C_{21}H_{30}NO_7Si$ requires 436.1792.

2-Ethoxy-3-methoxycarbonyl-5-phenylfuran 5a. The experiment was carried out by the general procedure with 5-ethoxy-2-phenyl-4-triethylsilyloxazole (0.091 g, 0.3 mmol) and methyl propiolate (32 µl, 0.36 mmol) in DCB (0.3 ml) heated to 170°C. The crude product was purified by flash chromatography (80:20 petroleum ether:diethyl ether) to yield 2-ethoxy-3-methoxycarbonyl-5-phenylfuran **5a** as a white solid (0.032 g, 43 %). ν_{max} (KBr/film) 3108 w, 2910 w, 1705 s (C=O), 1597 s, 1567 m, 1463 s, 1378 s, 1250 s, 1030 m, 894 w, 754 w cm^{-1}; δ_H

(270 MHz, $CDCl_3$) 1.50 (3 H, t, *J* = 7 Hz, $OCH_2\underline{CH_3}$), 3.81 (3 H, s, CO_2CH_3), 4.54 (2 H, q, *J* = 7 Hz, $O\underline{CH_2}CH_3$), 6.83 (1 H, s, H_4), 7.21 (1 H, m, $H_{4'}$), 7.35 (2 H, m, $H_{3'}$), 7.51 (2 H, m, $H_{2'}$); δ_C (75 MHz, $CDCl_3$) 15.0 $OCH_2\underline{CH_3}$, 51.3 $CO_2\underline{CH_3}$, 68.0 $O\underline{CH_2}CH_3$, 93.7 C_3, 106.1 C_4, 122.8, 128.7 $C_{2',3'}$, 127.1 $C_{4'}$, 129.7 $C_{1'}$, 143.4 C_5, 161.3 C=O, 163.4 C_2; *m/z* (CI+, NH_3) 264 ($[M+NH_4]^+$, 47), 247 ($[M+H]^+$, 100); HRMS (CI+) Found $[M+H]^+$ 247.0973; $C_{14}H_{15}O_4$ requires 247.0970.

2-Ethoxy-5-ethyl-3-methoxycarbonylfuran 5b. The experiment was carried out by the general procedure with 5-ethoxy-2-ethyl-4-triethylsilyloxazole (0.102 g, 0.4 mmol) and methyl propiolate (43 µl, 0.48 mmol) in toluene (0.4 ml) heated to 110°C. The crude product was purified by flash chromatography (80:20 petroleum ether:diethyl ether) to yield 2-ethoxy-3-methoxy carbonyl-5-ethylfuran **5b** as colourless crystals (0.032 g, 40 %). m.p. 36-37°C; ν_{max} (KBr/film) 3125 w, 2976 s, 2955 s, 2879 m, 1719 s (C=O), 1604 s, 1458 m, 1416 w, 1388 w, 1363 w, 1248 m, 1197 m, 1138 m, 1087 s, 1020 m, 960 w, 890 w, 818 w, 776 m, 741 w cm^{-1}; δ_H (270 MHz, $CDCl_3$) 1.16 (3 H, t, *J* = 7.5 Hz, $\underline{CH_3}CH_2$), 1.42 (3 H, t, *J* = 7 Hz, $OCH_2\underline{CH_3}$), 2.50 (2 H, dq, *J* = 1 Hz, *J* = 7.5 Hz, $CH_3\underline{CH_2}$), 3.75 (3 H, s, CO_2CH_3), 4.39 (2 H, q, *J* = 7 Hz, $O\underline{CH_2}CH_3$), 6.14 (1 H, t, *J* = 1 Hz, H_4); δ_C (75 MHz, $CDCl_3$) 11.6 $\underline{CH_3}CH_2$, 15.0 $OCH_2\underline{CH_3}$, 20.9 $CH_3\underline{CH_2}$, 51.0 $CO_2\underline{CH_3}$, 67.1 $O\underline{CH_2}CH_3$, 92.1 C_3, 104.9 C_4, 147.3 C_5, 160.8 C_2, 163.7 $\underline{C}O_2CH_3$; *m/z* (CI+, NH_3) 216 ($[M+NH_4]^+$, 22), 199 ($[M+H]^+$, 46), 102 (34), 52 (100); HRMS (CI+) Found $[M+H]^+$ 199.0971; $C_{10}H_{15}O_4$ requires 199.0970.

2-(4-(*tert*-Butyldimethylsilyloxy)-butyl)-5-ethoxy-4-triethylsilyl oxazole 7. The experiment was carried out by the general procedure for the preparation of 4-silylated oxazoles with 5-(*tert*-butyldimethylsilyloxy)-pentanenitrile (2.77 g, 13 mmol), ethyl (triethylsilyl)diazoacetate (2.28 g, 10 mmol) and $Rh_2(octanoate)_4$ (78 mg, 0.1 mmol) in dry benzene (20 ml). The crude product was purified by flash chromatography (95:5 petroleum ether:diethyl ether) to yield 2-(4-(*tert*-butyldimethylsilyloxy)butyl)-5-ethoxy-4-triethylsilyloxazole **7** as a colourless liquid (3.30 g, 79 %). ν_{max} (KBr/film) 2953 s, 2934 s, 2874 s, 1605 s, 1577 w, 1462 w, 1389 w, 1255 m, 1105 m, 1019 m, 836 m, 775 w, 736 m, 734 m cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.02 (6 H, s, $SiCH_3$), 0.72 (6 H, q, *J* = 8 Hz, $Si\underline{CH_2}CH_3$), 0.86 (9 H, s, $SiC(\underline{CH_3})_3$), 0.94 (9 H, t, *J* = 8 Hz, $SiCH_2\underline{CH_3}$), 1.33 (3 H, t, *J* = 7 Hz, $OCH_2\underline{CH_3}$), 1.55 (2 H, p, *J* = 7 Hz, $H_{3'}$), 1.73 (2 H, p, *J* = 7 Hz, $H_{2'}$), 2.64 (2 H, t, $J_{1'-2'}$ = 7 Hz, $H_{1'}$), 3.60 (2 H, t, $J_{4'-3'}$ = 6.5 Hz, $H_{4'}$), 4.12 (2 H, q, *J* = 7 Hz, $O\underline{CH_2}CH_3$); δ_C (75 MHz, $CDCl_3$) -5.4 $SiCH_3$, 3.1 $Si\underline{CH_2}CH_3$, 7.3 $SiCH_2\underline{CH_3}$, 14.9 $OCH_2\underline{CH_3}$, 18.3 $Si\underline{C}(CH_3)_3$, 23.7 $C_{2'}$, 25.9 $SiC(\underline{C}H_3)_3$, 28.3 $C_{1'}$, 32.2 $C_{3'}$, 62.7 $C_{4'}$, 69.2 $O\underline{CH_2}CH_3$, 109.4 C_4, 157.1 C_2, 164.5 C_5; *m/z* (CI+, NH_3) 414 ($[M+H]^+$, 100), 356 (10), 208 (10), 132 ($[SiEt_3+NH_3]^+$, 5); HRMS (CI+) Found $[M+H]^+$ 414.2854; $C_{21}H_{44}NO_3Si_2$ requires 414.2860.

5-Ethoxy- 2-(4-hydroxybutyl)-4-triethylsilyloxazole 8. To a stirred solution of 2-(4-(*tert*-butyldimethylsilyloxy)butyl)-5-ethoxy-4-triethylsilyl oxazole **7** (3.20 g, 7.73 mmol) in THF (30 ml) was added TBAF (7.73 ml of a 1M solution in THF, 7.73 mmol). The mixture was stirred at rt and monitored by TLC. After complete consumption of the starting material, the reaction was quenched by the addition of sat. aq. NH_4Cl (30 ml). The aqueous layer was extracted with ether (3 x 30 ml) and the combined organics dried ($MgSO_4$), filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography (10:90 petroleum ether:diethyl ether) to yield 2-(4-hydroxybutyl)-5-ethoxy-4-triethylsilyloxazole **8** as a colourless oil (2.10 g, 91 %). ν_{max} (KBr/film) 3343 m (OH), 2954 s, 2933 s, 2872 s, 1606 m, 1512 w, 1465 w, 1377 w, 1246 m, 1067 m, 1017 m, 739 w cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.70 (6 H, q, J = 8 Hz, $Si\underline{CH_2}CH_3$), 0.92 (9 H, t, J = 8 Hz, $SiCH_2\underline{CH_3}$), 1.33 (3 H, t, J = 7 Hz, $OCH_2\underline{CH_3}$), 1.60 (2 H, p, J = 7 Hz, $H_{3'}$), 1.81 (2 H, p, $J_{2'-1'} = J_{2'-3'}$ = 7 Hz, $H_{2'}$), 2.66 (2 H, t, $J_{1'-2'}$ = 7 Hz, $H_{1'}$), 2.95 (1 H, br s, OH), 3.60 (2 H, t, $J_{4'-3'}$ = 6 Hz, $H_{4'}$), 4.12 (2 H, q, J = 7 Hz, $O\underline{CH_2}CH_3$) (O$\underline{H}$ not observed); δ_C (67.5 MHz, $CDCl_3$) 3.1 $Si\underline{CH_2}CH_3$, 7.3 $SiCH_2\underline{CH_3}$, 14.9 $OCH_2\underline{CH_3}$, 22.5 $C_{2'}$, 27.8 $C_{1'}$, 32.1 $C_{3'}$, 61.5 $C_{4'}$, 69.5 $O\underline{CH_2}CH_3$, 99.9 C_4, 157.4 C_2, 164.5 C_5; m/z (CI+, NH_3) 338 ($[M+2H+2NH_4]^+$, 14), 300 ($[M+H]^+$, 100); HRMS (CI+) Found $[M+H]^+$ 300.1992; $C_{15}H_{30}NO_3Si$ requires 300.1995.

5-Ethoxy-2-(4-oxobutyl)-4-triethylsilyloxazole 9. To a stirred solution of oxalyl chloride (0.95 g, 7.5 mmol) in dry DCM (30 ml) cooled to -78°C was added dropwise DMSO (1.06 ml, 15 mmol). The mixture was stirred for 5 min at -78°C and a solution of 2-(4-hydroxybutyl)-5-ethoxy-4-triethylsilyloxazole **8** (1.50 g, 5 mmol) in dry DCM (30 ml) was added in one portion. The reaction mixture was kept at -78°C for 30 min and was then treated with Et_3N (4.2 ml, 30 mmol). After an additional 10 min at -78°C the mixture was allowed to warm slowly to rt. H_2O (20 ml) was added and the organic phase was separated. The aqueous phase was washed with DCM (2 x 20 ml) and the combined organics were washed with saturated brine (20 ml), dried ($MgSO_4$), filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography (40:60 petroleum ether:diethyl ether) to yield 5-ethoxy-2-(4-oxobutyl)-4-triethylsilyloxazole **9** as a colourless oil (1.09 g, 73 %). ν_{max} (KBr/film) 2954 s, 2934 s, 2874 s, 1725 s (C=O), 1605 s, 1576 w, 1512 w, 1460 w, 1390 m, 1242 m, 1018 m, 737 m, 724 m cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.71 (6 H, q, J = 8 Hz, $Si\underline{CH_2}CH_3$), 0.93 (9 H, t, J = 8 Hz, $SiCH_2\underline{CH_3}$), 1.33 (3 H, t, J = 7 Hz, $OCH_2\underline{CH_3}$), 2.01 (2 H, p, $J_{2'-1'} = J_{2'-3'}$= 7 Hz, $H_{2'}$), 2.51 (2 H, dt, $J_{3'-4'}$ = 1 Hz, $J_{3'-2'}$ = 7 Hz, $H_{3'}$), 2.68 (2 H, t, $J_{1'-2'}$ = 7 Hz, $H_{1'}$), 4.13 (2 H, q, J = 7 Hz, $O\underline{CH_2}CH_3$), 9.74 (1 H, t, $J_{4'-3'}$ = 1 Hz, $H_{4'}$); δ_C (75 MHz, $CDCl_3$) 3.1 $Si\underline{CH_2}CH_3$, 7.3 $SiCH_2\underline{CH_3}$, 14.9 $OCH_2\underline{CH_3}$, 19.7 $C_{2'}$, 27.6 $C_{1'}$, 42.9 $C_{3'}$, 69.5 $O\underline{CH_2}CH_3$, 109.7 C_4, 156.0 C_2, 164.7 C_5, 201.5 C=O; m/z (CI+, NH_3) 298 ($[M+H]^+$, 100); HRMS (CI+) Found $[M+H]^+$ 298.1845; $C_{15}H_{28}NO_3Si$, requires 298.1838.

5-Ethoxy-2-(4-hydroxy-6-methoxycarbonyl-hex-5-ynyl)-4-triethylsilyloxazole 10a. A solution of methyl propiolate (0.29 ml, 3.26 mmol) in 4:1:1 dry THF/Et_2O/pentane (20 ml total) was cooled to -120°C (the cooling bath consisted of a 4:1:1 mixture of low boiling petroleum ether/acetone/isopropyl alcohol cooled with liquid nitrogen). *n*-BuLi (2.04 ml of a 1.6 M solution in THF, 3.26 mmol) was added dropwise, with vigorous stirring, over a period of 15 min while maintaining a temperature of -120°C. Stirring was continued for 15 min at -120°C to complete the formation of lithiated methyl propiolate. A solution of 5-ethoxy-2-(4-oxobutyl)-4-triethylsilyloxazole **9** (0.776 g, 2.6 mmol) in 4:1:1 dry THF/Et_2O/pentane (20 ml total) was then added dropwise with vigorous stirring. The mixture was stirred for 15 min at -120°C and the cooling bath was removed. After warming to -78°C, the reaction mixture was quenched with a 10 % aqueous solution of KH_2PO_4 (20 ml), washed with H_2O (20 ml) and extracted with Et_2O (3 x 20 ml). The combined organics were dried ($MgSO_4$), filtered and evaporated under reduced pressure to afford a yellow oil. The crude product was purified by flash chromatography (30:70 petroleum ether:diethyl ether) to yield 2-(4-hydroxy-6-methoxycarbonyl-hex-5-ynyl)-5-ethoxy-4-triethylsilyloxazole as a colourless oil (0.77 g, 78 %). ν_{max} (KBr/film) 3218 w (OH), 2954 m, 2912 w, 2235 w (C≡C), 1720 s (C=O), 1606 s, 1434 w, 1249 s, 1016 w, 738 w, 723 w cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.71 (6 H, q, *J* = 8 Hz, Si$\underline{CH_2}$$CH_3$) 0.93 (9 H, t, *J* = 8 Hz, Si$CH_2$$\underline{CH_3}$), 1.34 (3 H, t, *J* = 7 Hz, O$CH_2$$\underline{CH_3}$), 1.80-2.05 (4 H, m, $H_{2',3'}$), 2.60-2.82 (2 H, m, $H_{1'}$), 3.74 (3 H, s, CO_2CH_3), 4.13 (2 H, q, *J* = 7 Hz, O$\underline{CH_2}$$CH_3$), 4.50 (1 H, t, $J_{4'-3'}$ = 6 Hz, $H_{4'}$) (O$\underline{H}$ not observed); δ_C (75 MHz, $CDCl_3$) 3.1 Si$\underline{CH_2}$$CH_3$, 7.3 Si$CH_2$$\underline{CH_3}$, 15.0 O$CH_2$$\underline{CH_3}$, 21.0 $C_{2'}$, 27.4 $C_{1'}$, 36.1 $C_{3'}$, 52.7 $CO_2$$\underline{C}$$H_3$, 60.8 $C_{4'}$, 69.5 O$\underline{CH_2}$$CH_3$, 75.7 $C_{6'}$, 88.5 $C_{5'}$, 109.3 C_4, 153.8 C_2, 157.0 C_5, 164.6 C=O; *m/z* (CI+, NH_3) 382 ($[M+H]^+$, 100); HRMS (CI+) Found $[M+H]^+$ 382.2057; $C_{19}H_{32}NO_5Si$, requires 382.2050.

5-Ethoxy-2-(4-hydroxy-6-trimethylsilylhex-5-ynyl)-4-triethylsilyloxazole 10b. To a solution of (trimethylsilyl)acetylene (64 µl, 0.45 mmol) in THF (2 ml) cooled to -78°C was added dropwise *n*-BuLi (0.28 ml of a 1.6 M solution in THF, 0.45 mmol). Stirring was continued for 15 min at -78°C and a solution of 5-ethoxy-2-(4-oxobutyl)-4-triethylsilyloxazole **9** (0.089 g, 0.30 mmol) in THF (2 ml) was added in one portion. The reaction mixture was stirred for 15 min at -78°C and then was quenched with a 10 % aqueous solution of KH_2PO_4 (5 ml), washed with H_2O (5 ml) and extracted with Et_2O (3 x 5 ml). The combined organics were dried ($MgSO_4$), filtered and evaporated under reduced pressure to afford a yellow oil. The crude product was purified by flash chromatography (60:40 petroleum ether:diethyl ether) to yield 5-ethoxy-2-(4-hydroxy-6-trimethylsilylhex-5-ynyl)-4-triethylsilyloxazole as a colourless oil (0.107 g, 90 %). ν_{max} (KBr/film) 3275 s (OH), 2953 s, 2874 s, 2170 w (C≡C), 1727 m, 1606 s, 1574 m, 1458 m, 1414 m, 1391 m, 1249 s, 1132 m, 1076 m, 1017 s, 842 s, 737 s, 725 s cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.13 (9 H, s, $SiCH_3$), 0.72 (6 H, q, *J* = 8 Hz, Si$\underline{CH_2}$$CH_3$), 0.93 (9 H, t, *J* = 8 Hz, Si$CH_2$$\underline{CH_3}$), 1.34 (3 H, t, *J* = 7 Hz, O$CH_2$$\underline{CH_3}$), 1.71-1.80 (2 H, m, $H_{2'}$), 1.88 (2 H, appar q, *J* = 7 Hz, $H_{1'}$), 2.69 (2 H, app q, *J* = 7 Hz, $H_{3'}$), 3.06 (1 H, br s, OH), 4.13 (2 H, *J* = 7 Hz, q, O$\underline{CH_2}$$CH_3$), 4.37 (1 H, t, $J_{4'-3'}$ = 6.5 Hz, $H_{4'}$), δ_C (75 MHz, $CDCl_3$) -0.2 $SiCH_3$, 3.0 Si$\underline{CH_2}$$CH_3$, 7.2 Si$CH_2$$\underline{CH_3}$, 14.9 O$CH_2$$\underline{CH_3}$, 22.2 $C_{2'}$, 27.7 $C_{1'}$, 36.9 $C_{3'}$, 61.6 $C_{4'}$, 69.3 O$\underline{CH_2}$$CH_3$, 88.6 $C_{6'}$, 106.9 $C_{5'}$, 109.2 C_4, 157.1 C_2, 164.4 C_5; *m/z* (CI+, NH_3) 396 ($[M+H]^+$, 100), 298 (15); HRMS (CI+) Found $[M+H]^+$ 396.2398; $C_{20}H_{38}NO_3Si_2$, requires 396.2390.

5-Ethoxy-2-(4-oxo-6-methoxycarbonylhex-5-ynyl)-4-triethylsilyloxazole 6a. To a solution of 5-ethoxy-2-(4-hydroxy-6-methoxycarbonyl-hex-5-ynyl)-4-triethylsilyloxazole **10a** (0.496 g, 1.3

mmol) in DCM (8 ml) at rt was added Dess-Martin periodinane (0.652 g, 1.56 mmol). After the reaction was complete as indicated by TLC analysis, the reaction mixture was quenched by the addition of sat. aq. $NaHCO_3$ (10 ml). The mixture was partitioned between DCM and sat. aq. $NaHCO_3$. The combined organics were dried ($MgSO_4$), filtered and evaporated under reduced pressure to afford a pale yellow oil. The crude product was purified by flash chromatography (50:50 petroleum ether:diethyl ether) to yield 5-ethoxy-2-(4-oxo-6-methoxycarbonylhex-5-ynyl)-4-triethylsilyloxazole **6a** as a colourless oil (0.379 g, 77 %) which was used directly in the next step. ν_{max} (KBr/film) 2954 s, 2911 m, 2876 m, 2214 w (C≡C), 1726 s (CO_2Me), 1691 s (C=O), 1606 s, 1435 w, 1254 s, 1115 w, 1010 m, 890 w, 737 m, 725 m cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.66 (6 H, q, *J* = 8 Hz, Si<u>CH$_2$</u>CH$_3$), 0.88 (9 H, t, *J* = 8 Hz, SiCH$_2$<u>CH$_3$</u>), 1.28 (3 H, t, *J* = 7 Hz, OCH$_2$<u>CH$_3$</u>), 2.00 (2 H, p, *J* = 7 Hz, $H_{2'}$), 2.64 (4 H, appar p, *J* = 7 Hz, $H_{1',3'}$), 3.76 (3 H, s, CO_2Me), 4.08 (2 H, q, *J* = 7 Hz, O<u>CH$_2$</u>CH$_3$); δ_C (75 MHz, $CDCl_3$) 3.1 Si<u>CH$_2$</u>CH$_3$, 7.3 SiCH$_2$<u>CH$_3$</u>, 14.9 OCH$_2$<u>CH$_3$</u>, 20.7 $C_{2'}$, 27.2 $C_{1'}$, 44.1 $C_{3'}$, 53.3 CO$_2$<u>C</u>H$_3$, 69.4 O<u>CH$_2$</u>CH$_3$, 77.8 $C_{6'}$, 80.6 $C_{5'}$, 109.7 C_4, 152.5 C_2, 155.5 C_5, 164.6 <u>C</u>O$_2$Me, 184.8 $C_{4'}$; *m/z* (CI+, NH_3) 398 ($[M+NH_4]^+$, 22), 380 ($[M+H]^+$, 73), 239 (100); HRMS (CI+) Found $[M+H]^+$ 380.1899; $C_{19}H_{30}NO_5Si$, requires 380.1893.

5-Ethoxy-2-(4-oxo-6-trimethylsilylhex-5-ynyl)-4-triethylsilyloxazole 6b. The experiment was carried out by the procedure used for the preparation of **6a** with 2-(4-hydroxy-6-trimethylsilylhex-5-ynyl)-5-ethoxy-4-triethylsilyloxazole (0.112 g, 0.283 mmol) and Dess-Martin periodinane (0.142 g, 0.34 mmol) in dry DCM (2 ml). The crude product was purified by flash chromatography (60:40 petroleum ether:diethyl ether) to yield 5-ethoxy-2-(4-oxo-6-trimethylsilylhex-5-ynyl)-4-triethylsilyloxazole **6b** as a colourless liquid (0.089 g, 80 %). ν_{max} (KBr/film) 2954 s, 2911 s, 2874 s, 2150 w (C≡C), 1679 s (C=O), 1605 s, 1252 s, 1110 s, 1019 m, 847 s, 737 s, 724 s cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.20 (9 H, s, $SiCH_3$), 0.71 (6 H, q, *J* = 8 Hz, Si<u>CH$_2$</u>CH$_3$), 0.93 (9 H, t, *J* = 8 Hz, SiCH$_2$<u>CH$_3$</u>), 1.33 (3 H, t, *J* = 7 Hz, OCH$_2$<u>CH$_3$</u>), 2.02 (2 H, p, *J* = 7 Hz, $H_{2'}$), 2.62 (2 H, t, *J* = 7 Hz, $H_{1'}$), 2.65 (2 H, t, *J* = 7 Hz, $H_{3'}$), 4.12 (2 H, q, *J* = 7 Hz, O<u>CH$_2$</u>CH$_3$); δ_C (75 MHz, $CDCl_3$) -0.8 $SiCH_3$, 3.1 Si<u>CH$_2$</u>CH$_3$, 7.3, SiCH$_2$<u>CH$_3$</u>, 14.9 OCH$_2$<u>CH$_3$</u>, 21.2 $C_{2'}$, 27.5 $C_{1'}$, 44.2 $C_{3'}$, 69.4 O<u>CH$_2$</u>CH$_3$, 98.0 $C_{6'}$, 101.8 $C_{5'}$, 109.6 C_4, 156.0 C_2, 164.6 C_5, 186.7 $C_{4'}$; *m/z* (CI+, NH_3) 394 ($[M+H]^+$, 100), 132 ($[SiEt_3+NH_3]^+$, 26), 90 (37); HRMS (CI+) Found $[M+H]^+$ 394.2246; $C_{20}H_{36}NO_3Si$, requires 394.2234.

Preparation of 7-phenyl-hept-6-ynenitrile 11. A solution of 6-bromo-1-phenylhex-1-yne[13] (1.34 g, 5.65 mmol) and KCN (1.47 g, 22.6 mmol) in acetone (4 ml) and water (4 ml) was heated to 65 °C for 35 h. The reaction mixture was diluted with water (20 ml) and extracted with ether (3 x 30 ml). The combined organics were washed with brine (2 x 20 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residual oil was purified by flash chromatography (70:30 petroleum ether:diethyl ether) to yield 7-phenyl-hept-6-ynenitrile **11** as a colourless liquid (0.636 g, 62 %). ν_{max} (KBr/film) 3057 w, 2934 s, 2867 m, 2245 w (CN), 1597 w, 1489 s, 1441 m, 1249 w, 1070 w, 757 s, 693 s cm^{-1}, δ_H (270 MHz, $CDCl_3$) 1.66-1.88 (4 H, m, $H_{3,4}$), 2.37 (2 H, t, H_5, $J_{5\text{-}4}$ = 6.5 Hz), 2.45 (2 H, t, H_2, $J_{2\text{-}3}$ = 6.5 Hz), 7.23-7.32 (3 H, m, $H_{3',4'}$), 7.34-7.40 (2 H, m, $H_{2'}$), δ_C (67.5 MHz, $CDCl_3$) 16.6 C_5, 18.5 C_2, 24.4, 27.3 $C_{3,4}$, 81.4 C_7, 88.5 C_6, 119.4 C_1, 123.4 $C_{1'}$, 127.6 $C_{4'}$, 128.1 $C_{3'}$, 131.4 $C_{2'}$; *m/z* (CI+, NH_3) 201 ($[M+NH_4]^+$, 100); HRMS (CI+) Found $[M+NH_4]^+$ 201.1390 $C_{13}H_{17}N_2$ requires 201.1392

5-Ethoxy-2-(6-phenylhex-5-ynyl)-4-triethylsilyloxazole 6c. 7-Phenyl-hept-6-ynenitrile **11** (0.137 g, 0.75 mmol), ethyl (triethylsilyl)diazoacetate (0.114 g, 0.5 mmol) and $Rh_2(octanoate)_4$ (4 mg, 0.005 mmol) were dissolved in dry benzene (2 ml) and heated to reflux. On consumption of the silyldiazoester by TLC, the reaction was cooled to room temperature and concentrated under reduced pressure. The crude product was purified by flash chromatography (90:10 petroleum ether:diethyl ether) to yield 5-ethoxy-2-(6-phenylhex-5-ynyl)-4-triethylsilyloxazole **6c** as a colourless liquid (0.119 g, 62 %). ν_{max} (KBr/film) 2950 s, 2874 s, 2231 w (C≡C), 1605 s, 1574 w, 1461 w, 1244 m, 1018 m, 755 m, 737 m, 724 m, 692 m cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.72 (6 H, q, *J* = 8 Hz, $Si\underline{CH_2}CH_3$), 0.94 (9 H, t, *J* = 8 Hz, $SiCH_2\underline{CH_3}$), 1.32 (3 H, t, *J* = 7 Hz, $OCH_2\underline{CH_3}$), 1.59-1.68 (2 H, m, $H_{3'}$), 1.81-1.91 (2 H, m, $H_{2'}$), 2.42 (2 H, t, $J_{4'\text{-}3'}$ = 7 Hz, $H_{4'}$), 2.69 (2 H, t, $J_{1'\text{-}2'}$ = 7.5 Hz, $H_{1'}$), 4.12 (2 H, q, *J* = 7 Hz, $O\underline{CH_2}CH_3$), 7.22-7.27 (3 H, m, $H_{9',10'}$), 7.33-7.38 (2 H, m, $H_{8'}$); δ_C (75 MHz, $CDCl_3$) 3.1 $Si\underline{CH_2}CH_3$, 7.3 $SiCH_2\underline{CH_3}$, 14.9 $OCH_2\underline{CH_3}$, 19.0 $C_{4'}$, 26.5, 28.1 (2 peaks) $C_{1',2',3'}$, 69.4 $O\underline{CH_2}CH_3$, 80.9 $C_{6'}$, 89.7 $C_{5'}$, 109.5 C_4, 123.9 $C_{7'}$, 127.5 $C_{10'}$, 128.1 $C_{9'}$, 131.5 $C_{8'}$, 156.9 C_2, 164.5 C_5; *m/z* (CI+, NH_3) 384 ($[M+H]^+$, 40), 354 (65), 326 (57), 310 (20), 282 ($[M-C_6H_5C{\equiv}C]^+$, 19), 224 (14), 115 (56), 103 (33), 87 (40), 75 (42), 49 (100); HRMS (CI+) Found $[M+H]^+$ 384.2361; $C_{23}H_{34}NO_2Si$ requires 384.2359.

2-Ethoxy-3-methoxycarbonyl-6,7-dihydro-*5H*-benzofuran-4-one 12a. A solution of 5-ethoxy-2-(4-oxo-6-methoxycarbonylhex-5-ynyl)-4-triethylsilyloxazole **6a** (0.24 g, 0.632 mmol) in toluene (2 ml) was heated to 120°C and monitored by TLC for complete consumption of the alkyne. The solution was cooled to room temperature, concentrated under reduced pressure and the residual oil purified by flash chromatography (10:90 petroleum ether:diethyl ether) to yield 2-ethoxy-3-methoxy carbonyl-4-oxo-4,5,6,7-tetrahydrobenzofuran **12a** as a white solid (0.093 g, 62 %). m.p. 67-68 °C; ν_{max} (KBr/film) 2973 w, 2945 w, 2903 w, 1681 s (C=O), 1608 s (C=O), 1593 m, 1451 w, 1263 m, 1224 m, 1108 w, 1085 m, 1010 w cm^{-1}; δ_H (270 MHz, $CDCl_3$) 1.39 (3 H, t, *J* = 7 Hz, $OCH_2\underline{CH_3}$), 2.09 (2 H, p, *J* = 6.5 Hz, H_6), 2.45 (2 H, t, $J_{7\text{-}6}$= 6.5 Hz, H_7), 2.73 (2 H, t, $J_{5\text{-}6}$ = 6.5 Hz, H_5), 3.77 (3 H, s, CO_2Me), 4.36 (2 H, q, *J* = 7 Hz, $O\underline{CH_2}CH_3$); δ_C (67.5 MHz, $CDCl_3$) 14.8 $OCH_2\underline{CH_3}$, 21.9, 22.8 $C_{6,7}$, 38.3 C_5, 51.5 $CO_2\underline{C}H_3$, 69.1 $O\underline{CH_2}CH_3$, 90.3 C_3, 119.6 C_{3a}, 157.8 C_{7a}, 161.7 $\underline{C}O_2CH_3$, 162.7 C_2, 191.8 C=O; *m/z* (CI+, NH_3) 239 ($[M+H]^+$, 100); HRMS (CI+) Found $[M+H]^+$ 239.0923; $C_{12}H_{15}O_5$ requires 239.0920.

2-Ethoxy-3-trimethylsilyl-6,7-dihydro-5*H*-benzofuran-4-one 12b. A solution of 2-(4-oxo-6-trimethylsilylhex-5-ynyl)-5-ethoxy-4-triethylsilyloxazole **6b** (0.088 g, 0.223 mmol) in DCB (0.5 ml) was heated to 180 °C and monitored by TLC for complete consumption of the alkyne. The solution was cooled to room temperature, concentrated under reduced pressure and the residual oil purified by flash chromatography (70:30 petroleum ether:diethyl ether) to yield 2-ethoxy-3-trimethyl silyl-6,7-dihydro-5*H*-benzofuran-4-one **12b** as a colourless liquid (0.032 g, 57 %). ν_{max} (KBr/film) 2954 s, 2898 m, 1677 s (C=O), 1587 s, 1406 m, 1273 m, 1242 s, 1060 w, 1005 s, 844 s, 762 w cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.22 (9 H, s, $SiMe_3$), 1.34 (3 H, t, J = 7 Hz, $OCH_2\underline{CH_3}$), 2.11 (2 H, p, J = 6.5 Hz, H_6), 2.42 (2 H, t, $J_{7\text{-}6}$ = 6.5 Hz, H_7), 2.74 (2 H, t, $J_{5\text{-}6}$ = 6.5 Hz, H_5), 4.14 (2 H, q, J = 7 Hz, $O\underline{CH_2}CH_3$); δ_C (75 MHz, $CDCl_3$) -0.3 $SiMe_3$, 14.9 $OCH_2\underline{CH_3}$, 22.4, 22.9 $C_{6,7}$, 37.8 C_5, 69.1 $O\underline{CH_2}CH_3$, 89.7 C_3, 125.2 C_{3a}, 159.9 C_{7a}, 163.1 C_2, 194.6 C=O; *m/z* (CI+, NH_3) 253 ($[M+H]^+$, 100), 237 (40), 181 ($[M\text{-}SiMe_3+H]^+$, 10); HRMS (CI+) Found $[M+H]^+$ 253.1259; $C_{13}H_{21}O_3Si$ requires 253.1260.

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