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A highly efficient and straightforward stereoselective synthesis of novel chiral α-acetylenic ketones

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Abstract

A very efficient and straightforward synthesis of novel chiral α-acetylenic ketones of type **3** has been developed. Starting from commercially available L-(−)-serine **4**, and through the Garner's aldehyde **5**, ethynyloxazolidine **2** was formed in good overall yield. Condensation of the corresponding lithium acetylide **7** with different aliphatic and aromatic aldehydes **5** and **8a**–**h** at low temperatures yielded the respective propargylic alcohols **9a**–**i**. Subsequent mild oxidation of **9a**–**i** with 10-I-4-iodinane oxide (IBX) **12** afforded chiral α-acetylenic ketones **3a**–**i** almost quantitatively.

1. Introduction

In recent years, as demonstrated mainly by the extensive and elegant work of Obrecht et al., α-acetylenic ketones of type **1** have been shown to be highly versatile building blocks, which are very useful in a number of synthetic transformations. Thus, these conjugated ynones have proven to be very suitable substrates for the synthesis of, for instance, (*E*)-3-acylpropenoic acids,[1] flavones, styrylchromones and 3-halofurans,[2] 2- and 5-substituted 3-bromothiophenes[3] and 3-halopyrroles,[4,5] 2,4-disubstituted quinolines,[6] 1,2,3-triazolylacylsilanes,[7] isoxazoles, isothiazoles and pyrazoles,[8,9] and for the synthesis of the natural product L-lathyrine and related analogues.[10] Furthermore, when properly functionalised, compounds of type **1** have also proven to be excellent substrates for the combinatorial and parallel synthesis on solid supports of highly molecularly diverse 2,4,6-trisubstituted pyrimidines.[11,12] In addition, these α-alkynyl ketones, formally analogues of β-dicarbonyl compounds although more reactive, can be produced readily, mainly by the reaction of alkynylzinc chlorides with acid halides,[13] or by the reaction of lithium or magnesium acetylides with aldehydes followed by subsequent oxidation with

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oxalyl chloride in DMSO (Swern oxidation),[14] MnO_2[2–4] or with *t*-butyl hydroperoxide.[15] Reactions of these metallated acetylides with carboxylic anhydrides, *N*,*N*-dialkylcarboxamides or Weinreb amides, followed by hydrolysis, have also been reported to afford compounds of type **1**.[2,13]

In view of the strong synthetic potential of these conjugated ynones, and in connection with our ongoing studies on the synthesis of non-proteinogenic aromatic and heteroaromatic α-amino acids in an optically active form,[16,17] we considered approaching the synthesis of a series of novel chiral α-alkynyl ketones of type **3** containing a masked α-amino acid moiety as suitable chiral precursors in our synthetic strategy. In this context, we focused our attention primarily on (*R*)-(−)-2,2-dimethyl-3-*t*-butoxycarbonyl-4-ethynyloxazolidine **2** as an appropriate starting material for the synthesis of these novel chiral conjugated ynones **3** (Fig. 1).

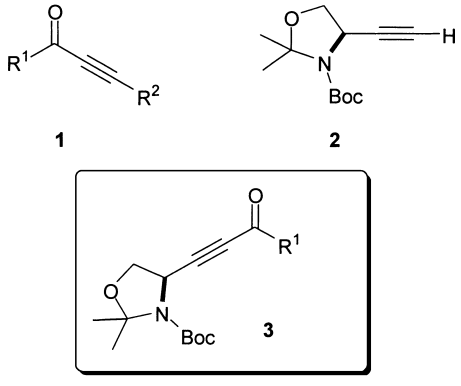


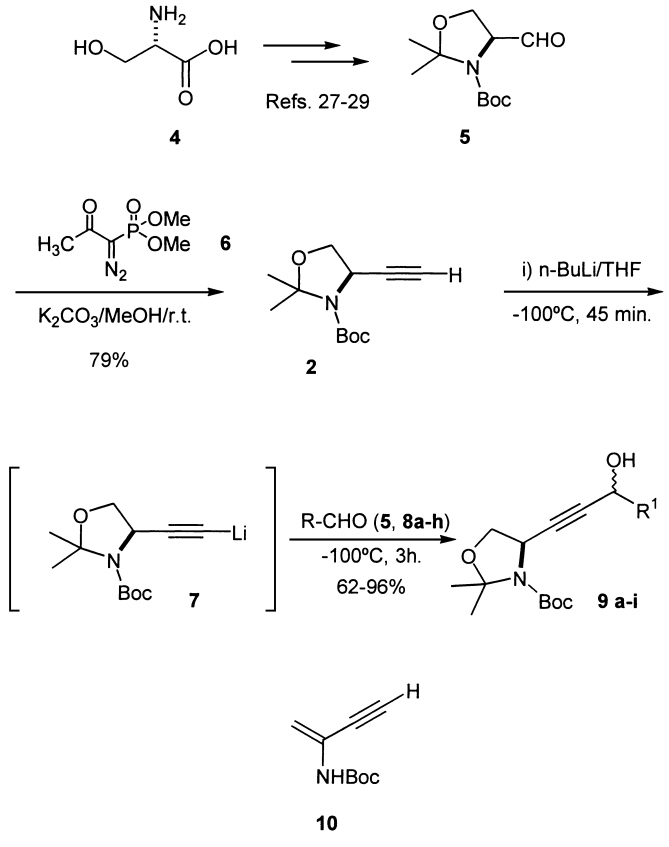
Figure 1.

2. Results and discussion

Recently, using naturally occurring serine **4** as the primary chiral source, the synthesis of compound **2** has been described,[18–21] either by using a procedure based on a modification of the well-known, two-step Corey–Fuchs[22,23] reaction, an aldehyde–alkyne homologation of the Garner aldehyde **5**, or via a Horner–Wadsworth–Emmons reaction between diazomethyl phosphonates and **5**.[24–26]

We proceeded by transforming L-(−)-serine **4** into the corresponding aldehyde **5** according to the procedure described by Garner.[27] The recently proposed alternative route based on a reduction–oxidation sequence[28,29] could also be followed and gave good yields of the desired aldehyde **5**. Next, we attempted the modified Corey–Fuchs procedure in order to obtain **2** from **5** as described by Reginato et al.,[19] and although compound **2** could be isolated in reasonable yields, it turned out that very careful control of the reaction conditions was necessary in order to avoid the formation of undesired by-products with a subsequent decrease in the yield. However, when dimethyl-1-diazo-2-oxopropylphosphonate **6**, readily available from tosyl azide and dimethyl-2-oxopropyl phosphonate,[30] was allowed to react in the presence of K_2CO_3 with aldehyde **5** in MeOH at rt, a very clean and efficient transformation to the enantiomerically pure alkyne **2** took place. Furthermore, this simple and one-step procedure is ideal for large-scale preparations. As expected, and due to the known configurational stability of **5** under strongly basic or nucleophilic conditions,[31] the alkyne **2** was isolated in enantiomerically pure form. Next, formation of the corresponding lithium acetylide **7** by reaction of **2** with *n*-BuLi in THF at −100°C and condensation with a number of different aromatic and aliphatic aldehydes, **5** and **8a**–**h**, afforded the corresponding pure propargyllic alcohol derivatives **9a**–**i** in 62–96% yield, generally as a 5:1 mixture of diastereoisomers.

No attempt was made to separate these mixtures (Scheme 1, Table 1). In marked contrast with previous reports about the condensation of lithium acetylide **7** with other electrophiles (alkyl halides, trialkyl silyl halides or acyl chlorides), under our reaction conditions, not even traces of enamine **10**, which is a degradation product of **2**, were ever detected.[18,21]

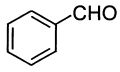
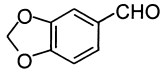
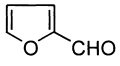
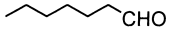
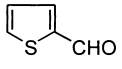
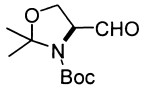
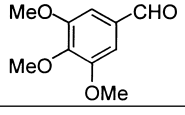


Scheme 1.

The oxidation of the prepared propargyllic alcohols **9a**–**i** to the corresponding α-acetylenic ketones **3a**–**i** deserved some optimisation because we found that, although the reaction of **9a**–**i** with 26 equiv. of MnO_2 in CH_2Cl_2 (Method A) proceeded smoothly at 0°C to give a very clean transformation with total disappearance of the starting material, only moderate yields of the final products could be isolated, even after extensive washing of the MnO_2 filtrate with large amounts of solvent. These findings showed that the final products **3a**–**i** were probably adsorbed on MnO_2 due to the fact that no other product was detected from the reaction mixture. Only in the reaction of **9h** with MnO_2 could another compound be identified in addition to the expected acetylenic ketone **3h**. This material was obtained in a 1:1 ratio with **3h** and was identified as the vinyl derivative **11**. Recently, MnO_2 has been reported to promote this type of dehydrogenation reaction in certain systems[32] (Scheme 2).

In view of these unsatisfactory results, we were prompted to seek another simple, mild and reliable oxidation method that could afford our desired targets efficiently. After some experimental work, we found that oxidation of propargyllic derivatives of type **9** to α-acetylenic ketones of type **3** could be

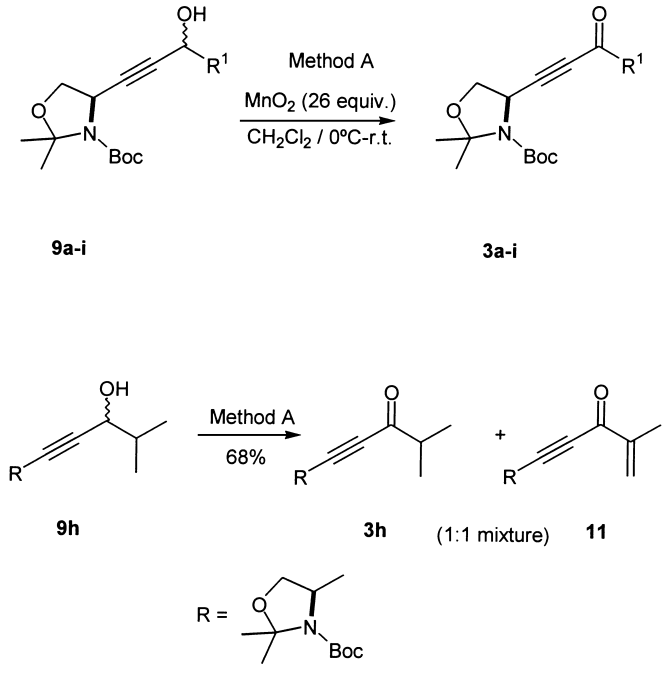
Table 1
Prepared propargyllic alcohol derivatives **9a–i**

Entry	R-CHO	Product	Yield (%)*
1		**9a**	95
2		**9b**	96
3		**9c**	93
4		**9d**	74
5		**9e**	83
6		**9f**	71
7		**9g**	62
8		**9h**	78
9		**9i**	96

* Isolated as a mixture of diastereoisomers (*ca.* 5:1)

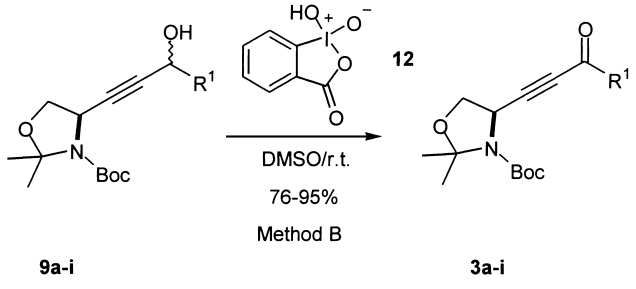
cleanly accomplished in near quantitative yields by employing 10-I-4-iodinane oxide **12** (caution)† at rt (Method B). This mild oxidising reagent offered several advantages: it is readily available from inexpensive starting materials in one synthetic step,[33] it provides operational simplicity and is easily handled, and no rigorous drying of solvent was necessary. To our knowledge, this is the first time that such

† Reagent **12** has been reported to cause explosion upon heavy impact and heating above 200°C.[33] In our hands, using **12** at temperatures between 20 and 70°C, no hazard has been experienced.



Scheme 2.

a reagent has been employed for the successful oxidation of propargyllic alcohols to the corresponding conjugated acetylenic ketones (Scheme 3, Table 2).



Scheme 3.

Finally, the chiral ethynyl derivative **2** was obtained in an enantiomerically pure form, as deduced by comparing the specific rotation value with that reported in the literature.[19] Under our reaction conditions for the condensation of **7** with the aldehydes **5** and **8a**–**h**, followed by mild oxidation to the ketones **3a**–**i**, we did not expect that the integrity of the asymmetric centre in the oxazolidine ring could be affected. Therefore, no attempts to check enantiomeric excesses of compounds **3a**–**i** were made at this stage. However, in the case of **3a** we were able to grow crystals that were suitable for an X-ray crystal-structure determination, which showed that the crystals were enantiomerically pure. It was then assumed that they had the expected absolute configuration. This assumption was extended to the complete series of synthesised compounds, **3a**–**i** (Fig. 2).

In summary, we have developed an efficient procedure for the stereoselective synthesis of novel α-acetylenic ketones which contain a latent α-amino acid lateral chain. Key steps in this strategy were the transformation of Garner's aldehyde **5** into the enantiomerically pure ethynyl oxazolidine **2**, and the optimised reaction conditions for the condensation of the lithium acetylide **7** with the aldehydes **5** and

Table 2
Prepared chiral acetylenic ketones **3a–i**

Entry	Compound	Method A (%)	Method B (%)	m.p. (°C)	$[\alpha]_D^{20}$ in MeOH
1	**3a**	88	95	77-78	-141.6 (c = 1.11)
2	**3b**	78	94	99-100	-113.1 (c = 0.61)
3	**3c**	77	92	165-166	-191.7 (c = 0.42)
4	**3d**	72	92	Yellow oil	-63.8 (c = 1.17)
5	**3e**	68	93	Orange oil	-92.3 (c = 0.95)
6	**3f**	74	91	119-120	-155.2 (c = 0.96)
7	**3g**	52	76	Colourless oil	-165.1 (c = 0.45)
8	**3h**	68*	83	Colourless oil	-148.9 (c = 1.06)
9	**3i**	79	94	Yellowish oil	-126.5 (c = 0.83)

* Isolated together with **11** as *ca.* 1:1 mixture

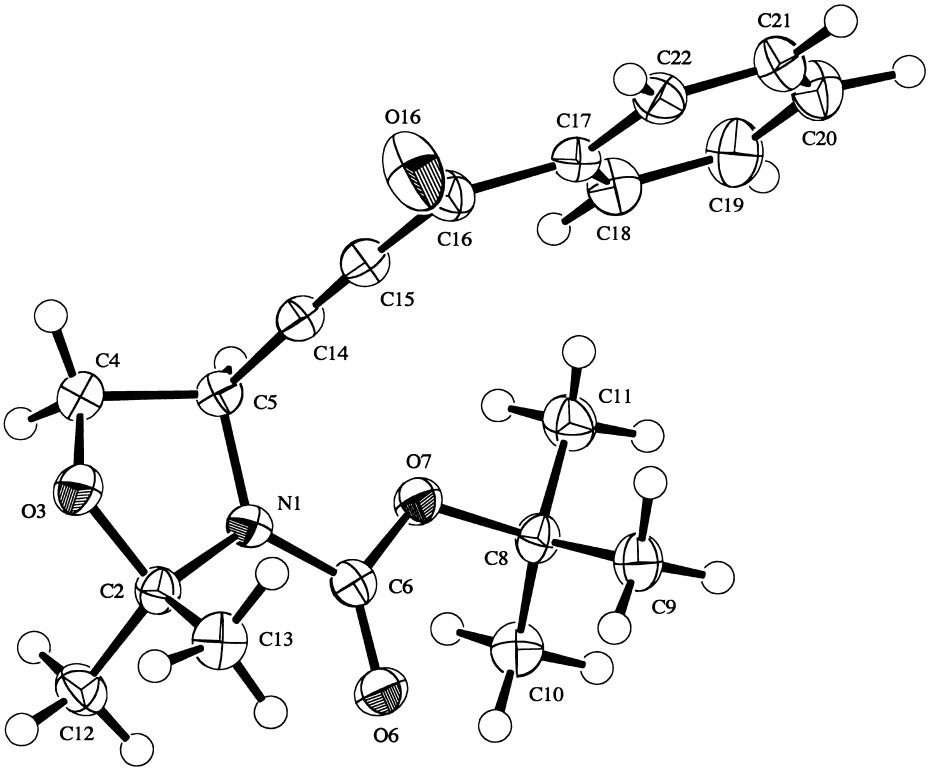


Figure 2. ORTEP plot[34] of the molecular structure of **3a** with 50% probability ellipsoids

8a–h to afford the propargyllic derivatives **9a–i**. The use for the first time of hypervalent iodine reagent **12** as a mild and effective oxidising agent for the transformation of propargyllic alcohols of type **9** into the corresponding ketones of type **3** in enantiomerically pure form proved to be an excellent alternative. The synthetic potential of these chiral building blocks for the preparation of elaborate non-proteinogenic aromatic and heteroaromatic α-amino acids is currently under investigation.

3. Experimental

3.1. General methods

All commercially available chemicals were used as purchased, except that THF was dried over Na/benzophenone prior to use. Reactions involving lithium acetylides were run under a dry N_2 atmosphere. Melting points (capillary tube) were measured with a Gallenkamp apparatus and are uncorrected. IR spectra were recorded on a Nicolet 205FT-IR. ^{1}H and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively, on a Bruker DPX200 Advance instrument with TMS as internal standard. MS spectra were recorded on a VG Quattro instrument in the positive ionisation FAB mode, using 3-NBA or 1-thioglycerol as the matrix, or on a HP 5989 A for spectra in the EI mode (70 eV) or in the CI mode (using NH_3 as carrier). Elemental analyses were performed on a Carlo Erba elemental analyser 1106. X-ray diffraction data were collected on a Rigaku AFC5R diffractometer using graphite-monochromated Mo Kα radiation (λ=0.71069 Å) and a 12 kW rotating anode generator. Optical rotation measurements were performed on a Perkin–Elmer 241 polarimeter. Analytical TLC was performed on precoated TLC plates, silica gel SIL G/UV_{254} from Macheray–Nagel. Flash-chromatography purifications were performed on SDS silica gel (230–400 mesh).

3.2. (R)-(−)-2,2-Dimethyl-3-t-butoxycarbonyl-4-ethynyloxazolidine **2**

A solution of **5** (12.12 g, 52.9 mmol) and dimethyl-1-diazo-2-oxopropylphosphonate (15.24 g, 79.4 mmol) **6** in MeOH (291 mL) was cooled at 0°C under Ar. With vigorous stirring, K_2CO_3 (14.6 g, 118.4 mmol) was added in one portion. The reaction mixture was stirred at 0°C for 1 h and then 12 h at rt. The reaction was quenched with a saturated solution of NH_4Cl (190 mL), filtered through a Celite® pad and the solvent concentrated under reduced pressure. The resulting aqueous solution was partitioned between AcOEt (240 mL) and H_2O (95 mL) and the layers separated. The aqueous layer was extracted with AcOEt (2×240 mL) and the combined organic layers washed with H_2O, dried over $MgSO_4$ and concentrated. Flash-chromatography (SiO_2, hexanes:AcOEt 9:1) afforded pure alkyne **2** (9.34 g, 79%) as a pale yellow oil. $[\alpha]_D^{20}$ 88.2 (C=1.05 $CHCl_3$); [lit.[19,21] −73.5, c=1.01 and −96.5, c=1.23]. IR (film, ν): 3293m, 3260m, 2982m, 2937m, 2880m, 1702s, 1478m, 1459m, 1381s, 1264m, 1247m, 1211m, 1174s, 1150m, 1097s, 1070m, 1054m, 855m, 770m, 676m cm^{-1}. ^{1}H NMR (DMSO-d_6, T=60°C), δ=4.65–4.6 (m, 1H, C*H*), 4.14 (dd, *J*=8.8 Hz, *J′*=6.0 Hz, 1H, CH_2O), 3.98 (dd, *J*=8.8 Hz, *J′*=2.4 Hz, 1H, CH_2O), 3.13 (d, *J*=2.2 Hz, 1H, ≡C*H*), 1.63 (s, 3H, C(CH_3)$_2$), 1.53 (s, 9H, C(CH_3)$_3$), 1.51 (s, 3H, C(CH_3)$_2$. ^{13}C NMR (DMSO, T=60°C), δ=150.6 (s, *C*O), 93.2 (s, *C*(CH$_3$)$_2$), 83.1 (s, *C*≡CH), 79.4 (s, *C*(CH$_3$)$_3$), 71.9 (d, C≡*C*H), 68.1 (t, *C*H$_2$), 47.7 (d, *C*H), 27.8 (q, C(*C*H$_3$)$_3$), 25.9 (q, C(*C*H$_3$)$_2$), 24.2 (q, C(*C*H$_3$)$_2$).

3.3. Synthesis of propargyllic alcohol derivatives **9a–i**. General procedure

To a cooled (−100°C) solution of **2** (2.25 g, 10 mmol) in dry THF (30 mL), *n*-BuLi (2 M solution in cyclohexane) (5.75 mL, 11.5 mmol) was added dropwise under Ar. The mixture was stirred at that temperature for 45 min. Then, a solution of the corresponding aldehyde **5** and **8a–h** (11 mmol, 1.1 equiv.) in dry THF (22 mL) was slowly added dropwise over a period of 15 min. The reaction mixture, under Ar, was stirred at −100°C for 3 h. Pre-cooled H_2O (5°C) (30 mL) was then added, and the reaction mixture slowly warmed to rt. The organic solvent was eliminated under reduced pressure, and the residue partitioned between AcOEt (30 mL) and H_2O (20 mL). The layers were separated, and the aqueous one extracted with AcOEt (3×30 mL). The combined organic layers were washed with sat. NaCl solution

(50 mL) and dried over $MgSO_4$, the solvent was evaporated and the resulting residue purified by flash-chromatography (hexanes:AcOEt).

3.4. tert-*Butyl (4*R*)-4-(3-hydroxy-3-phenyl-1-propynyl)-2,2-dimethyl-1,3-oxazolane-3-carboxylate* ***9a***

According to the general procedure described above, reaction between **2** and benzaldehyde **8a** afforded 3.14 g (95%) of **9a** as a yellowish oil. IR (film, ν): 3420br., 2980m, 2935m, 2878m, 1701s, 1685s, 1477m, 1455m, 1378s, 1367s, 1262m, 1246m, 1170m, 1123m, 1090m, 1056m, 1011m, 861m, 847m, 806d, 769m, 698m. ^{1}H NMR ($CDCl_3$), δ=7.6–7.3 (m, 5H, C*H* arom.), 5.5 (s, br., 1H, C*H*OH), 4.65–4.6 (m, 1H, C*H*), 4.1–4.05 (m, 2H, CH_2O), 2.8 (s, br., 1H, CHO*H*), 1.65 (s, 3H, C(CH_3)$_2$), 1.53, 1.42 (2s, 12H, [C(CH_3)$_3$+C(CH_3)$_2$]). ^{13}C NMR ($CDCl_3$), δ=151.5 (s, *C*O), 140.6 (s, *C* arom.), 128.4, 128.2, 126.6 (d, *C*H arom), 94.2 (s, *C*(CH$_3$)$_2$), 85.4 (s, *C*≡C), 81.9 (s, C≡*C*), 80.4(s, *C*(CH$_3$)$_3$), 68.6 (t, *C*H$_2$O), 64.4 (d, *C*HOH), 48.6 (d, *C*H), 28.3 (q, C(*C*H$_3$)$_3$), 25.9 (q, C(*C*H$_3$)$_2$), 24.4 (q, C(*C*H$_3$)$_2$). MS (EI) m/e: 314 ($M^{+\cdot}$−17, 17), 216 (16), 214 (32), 198 (14), 172 (25), 156 (33), 128 (27), 115 (49), 114 (52), 105 (22), 85 (36), 83 (57), 79 (28), 59 (29), 58 (57), 57 (100).

3.5. tert-*Butyl (4*R*)-4-(3-benzo[*d*][1,3]dioxol-5-yl-3-hydroxy-1-propynyl)-2,2-dimethyl-1,3-oxazolane-3-carboxylate* ***9b***

According to the general procedure described above, reaction between **2** and piperonal **8b** afforded 3.6 g (96%) of **9b** as a yellow oil. IR (film, ν): 3400br., 2981m, 2934m, 2884m, 1698s, 1504m, 1487m, 1443m, 1392s, 1378s, 1367s, 1247s, 1246m, 1169m, 1094m, 1040m, 1011d, 938m, 863m, 846m, 810d, 770m. ^{1}H NMR ($CDCl_3$), δ=7.05–6.75 (m, 3H, C*H* arom.), 5.96 (s, 2H, OCH_2O), 5.38 (s, br., 1H, C*H*OH), 4.65 (s, br., 1H, C*H*), 4.10 (m, 2H, CH_2O), 3.46 (br., 0.5H, CHO*H*), 2.88 (br., 0.5H, CHO*H*), 1.64 (s, 3H, C(CH_3)$_2$), 1.51, 1.48 (2s, 12H, [C(CH_3)$_3$+C(CH_3)$_2$]). ^{13}C NMR ($CDCl_3$), δ=151.4 (s, *C*O), 147.8, 147.5 (s, *C* arom.), 134.8, 134.2 (s, *C* arom), 120.3, 120.2 (d, *C*H arom), 108.1, 107.9 (d, *C*H arom), 107.4 (d, *C*H arom), 101.15, 101.06 (t, OCH$_2$O), 94.0 (s, *C*(CH$_3$)$_2$), 85.3 (s, *C*≡C), 82.8, 80.4 (s, C≡*C*+*C*(CH$_3$)$_3$), 68.5 (t, *C*H$_2$O), 64.2, 64.1 (d, *C*HOH), 48.6 (d, *C*H), 28.3, 28.2 (q, C(*C*H$_3$)$_3$), 26.3 (q, C(*C*H$_3$)$_2$), 24.7 (q, C(*C*H$_3$)$_2$). MS (EI) m/e: 375 (M^+, 7), 319 (10), 242 (20), 200 (36), 149 (10), 57 (100).

3.6. tert-*Butyl (4*R*)-4-[3-(2-furyl)-3-hydroxy-1-propynyl]-2,2-dimethyl-1,3-oxazolane-3-carboxylate* ***9c***

According to the general procedure described above, reaction between **2** and furfural **8c** afforded 2.98 g (93%) of **9c** as a brown solid. IR (KBr, ν): 3420br., 2981m, 2934m, 2882m, 1700s, 1671s, 1503w, 1477m, 1458m, 1403s, 1388s, 1367s, 1264m, 1246m, 1156m, 1125m, 1087m, 1053m, 1011m, 846m, 806d, 759m, 736m, 672m. ^{1}H NMR ($CDCl_3$), δ=7.36 (m, 1H, C*H* arom.), 6.46 (s, br., 1H, C*H* arom.), 6.36 (s, br., 1H, C*H* arom.), 5.48 (s, br., 1H, C*H*OH), 4.66 (s, br., 1H, C*H*), 4.08 (m, 2H, CH_2O), 2.75 (s, br., 1H, CHO*H*), 1.65 (s, 3H, C(CH_3)$_2$), 1.53, 1.42 (2s, 12H, [C(CH_3)$_3$+C(CH_3)$_2$]). ^{13}C NMR ($CDCl_3$), δ=153.0 (s, *C* arom), 151.5 (s, *C*O), 142.8, 110.3, 107.7 (d, *C*H arom.), 94.3 (s, *C*(CH$_3$)$_2$), 84.5 (s, *C*≡C), 80.5+79.6 (s, C≡*C*+*C*(CH$_3$)$_3$), 68.5 (t, *C*H$_2$O), 58.0 (d, *C*HOH), 48.6 (d, *C*H), 28.3 (q, C(*C*H$_3$)$_3$), 26.0 (q, C(*C*H$_3$)$_2$), 24.4 (q, C(*C*H$_3$)$_2$). MS (EI) m/e: 306 (M^+−15, 18), 250 (10), 206 (10), 188 (10), 146 (26), 118 (10), 57 (100).

3.7. tert-*Butyl (4*R*)-4-(3-hydroxy-1-pentynyl)-2,2-dimethyl-1,3-oxazolane-3-carboxylate* ***9d***

According to the general procedure described above, reaction between **2** and propanal **8d** afforded 2.09 g (74%) of **9d** as a yellow oil. IR (film, ν): 3400br., 2977m, 2936m, 2878m, 1704s, 1477m, 1457m, 1391s, 1379s, 1246m, 1210m, 1172m, 1134m, 1096m, 1056m, 1031m, 970m, 861m, 844m, 807d, 770m, 672d. ^{1}H NMR ($CDCl_3$), δ=4.60 (m, 1H, C*H*), 4.34 (t, *J*=8.7, 1H, C*H*OH), 4.02 (m, 2H, CH_2O), 2.39 (s, br., 1H, CHO*H*), 1.75 (m, 2H, CH_2CH$_3$), 1.63 (s, 3H, C(CH_3)$_2$), 1.50 (s, 9H, C(CH_3)$_3$), 1.48 (s, 3H, C(CH_3)$_2$), 1.01 (t, *J*=7.4, 3H, CH$_2$CH_3). ^{13}C NMR ($CDCl_3$), δ=151.5 (s, *C*O), 94.1 (s, *C*(CH$_3$)$_2$), 83.4 (s, *C*≡C), 80.6+80.3 (s, C≡*C*+*C*(CH$_3$)$_3$), 68.7 (t, *C*H$_2$O), 63.4 (d, *C*HOH), 48.5 (d, *C*H), 30.8 (t, *C*H$_2$CH$_3$), 28.3 (q, C(*C*H$_3$)$_3$), 26.3 (q, C(*C*H$_3$)$_2$), 24.8 (q, C(*C*H$_3$)$_2$), 9.34 (q, CH$_2$*C*H$_3$). MS (FAB$^+$) m/e: 284 (M$^+$+1, 20), 228 (40), 224(50), 210 (100).

3.8. tert-*Butyl (4*R*)-4-(3-hydroxy-1-nonyl)-2,2-dimethyl-1,3-oxazolane-3-carboxylate* ***9e***

According to the general procedure described above, reaction between **2** and heptanal **8e** afforded 2.81 g (83%) of **9e** as a yellow oil. IR (film, ν): 3450br., 2979m, 2946m, 2933m, 2872m, 1704s, 1683s, 1458m, 1392s, 1367s, 1263m, 1246m, 1210m, 1172m, 1139m, 1110m, 1089m, 1057m, 862m, 844m, 807w, 770m, 672w. ^{1}H NMR ($CDCl_3$), δ=4.56 (m, 1H, C*H*), 4.32 (t, *J*=5.4, 1H, C*H*OH), 3.94 (m, 2H, CH_2O), 2.83 (s, br., 1H, CHO*H*), 1.75 (m, 5H, [C(CH_3)$_2$+CH_2]), 1.53 (s, 12H, [C(CH_3)$_2$+C(CH_3)$_3$], 1.35 (m, 8H, CH_2), 0.91 (m, 3H, (CH$_2$)$_5$CH_3). ^{13}C NMR ($CDCl_3$), δ=151.4 (s, *C*O), 94.1 (s, *C*(CH$_3$)$_2$), 83.3 (s, *C*≡C), 77.6+77.0 (s, C≡*C*+*C*(CH$_3$)$_3$), 68.7 (t, *C*H$_2$O), 62.1 (d, *C*HOH), 48.5 (d, *C*H), 37.7 (t, *C*H$_2$), 31.6 (t, *C*H$_2$), 28.8 (t, *C*H$_2$), 28.3 (q, C(*C*H$_3$)$_3$), 26.3 (q, C(*C*H$_3$)$_2$), 25.0 (t, *C*H$_2$), 24.6 (q, C(*C*H$_3$)$_2$), 22.4 (*C*H$_2$), 14.0 (q, *C*H$_3$). MS (FAB$^+$) m/e: 340 (M$^+$+1, 21), 284 (34), 266 (100), 240 (39), 238 (39), 224 (54).

3.9. tert-*Butyl(4*R*)-4-[3-hydroxy-3-(2-thienyl)-1-propynyl]-2,2-dimethyl-1,3-oxazolane-3-carboxylate* ***9f***

According to the general procedure described above, reaction between **2** and thiophene-2-carbaldehyde **8f** afforded 2.39 g (71%) of **9f** as a yellow oil. IR (film, ν): 3422br., 2979m, 2934w, 2879w, 1699s, 1457w, 1379s, 1367s, 1246m, 1170m, 1116m, 1090m, 1056m, 845w, 703w. ^{1}H NMR ($CDCl_3$), δ=7.27 (d, 1H, J=5Hz, C*H* arom.), 7.16 (d, 1H, J=3.2 Hz, C*H* arom.), 6.95 (dd, 1H, J=4.8 Hz, J′=1 Hz, C*H* arom.), 5.67 (s, br, 1H, C*H*OH), 4.64 (s, br., 1H, C*H*), 4.04 (d, 2H, J=4 Hz, CH_2O), 3.66 (s, br., 0.5H, CHO*H*), 3.46 (s, br., 0.5H, CHO*H*), 1.64 (s, 3H, C(CH_3)$_2$), 1.51, 1.48 (2s, 12H, [C(CH_3)$_3$+C(CH_3)$_2$]). ^{13}C NMR ($CDCl_3$), δ=151.4 (s, *C*O), 144.8 (s, *C* arom.), 126.5 (d, *C*H arom.), 125.7 (d, *C*H arom), 125.3 (d, *C*H arom.), 94.3 (s, *C*(CH$_3$)$_2$), 84.6 (s, *C*≡C), 81.4, 80.4 (s, *C*(CH$_3$)$_3$)+*C*≡C), 68.5 (t, *C*H$_2$O), 59.9 (d, *C*HOH), 48.6 (d, *C*H), 28.3 (q, C(*C*H$_3$)$_3$), 26.3 (q, C(*C*H$_3$)$_2$), 24.7 (q, C(*C*H$_3$)$_2$). MS (FAB$^+$) m/e: 338 (M$^+$+1, 1), 265 (21), 264 (100), 236 (10), 234 (15), 221 (13), 206 (21), 204 (11), 162 (55).

3.10. tert-*Butyl (4*R*)-4-{3-[(4*S*)-3-(*tert-*butyloxycarbonyl)-2,2-dimethyl-1,3-oxazolane-4-yl]-3-hydroxy-1-propynyl}-2,2-dimethyl-1,3-oxazolane-3-carboxylate* ***9g***

According to the general procedure described above, reaction between **2** and Garner's aldehyde **5** afforded 2.81 g (62%) of **9g** as a colourless oil. IR (film, ν): 3454br., 2979m, 1703s, 1378s, 1172m, 1090m. ^{1}H NMR ($CDCl_3$), δ=4.65–4.6 (m, 2H, 2 C*H*N), 4.05–4.0 (m, 5H, [C*H*OH+2CH_2O]), 1.64 (s, 6H, C(CH_3)$_2$), 1.53 (s, 24H, [C(CH_3)$_2$+C(CH_3)$_3$]. ^{13}C NMR ($CDCl_3$), δ=154.0 (s, *C*O), 151.4 (s, *C*O),

95.0 (s, *C*(CH_3)$_2$), 94.1 (s, *C*(CH_3)$_2$), 84.7 (s, *C*≡C), 81.3, 80.4 (s, C≡*C*+*C*(CH_3)$_3$), 68.6 (t, *C*H_2O), 64.7 (t, *C*H_2O), 63.4 (d, *C*HOH), 62.3 (d, *C*H), 48.5 (d, *C*H), 28.3 (q, C(*C*H_3)$_3$), 26.8, 24.2 (q, C(*C*H_3)$_2$). MS (FAB$^+$) m/e: 455 (M^++1, 12), 440 (22), 224 (22), 57 (100).

3.11. tert-*Butyl (4*R*)-4-(3-hydroxy-4-methyl-1-pentynyl)-2,2-dimethyl-1,3-oxazolane-3-carboxylate **9h***

According to the general procedure described above, reaction between **2** and isobutyraldehyde **8g** afforded 2.31 g (78%) of **9h** as a colourless oil. IR (film, ν): 3450br., 2977m, 2932m, 2873m, 1703s, 1686s, 1476m, 1458m, 1379s, 1367s, 1263m, 1247m, 1210m, 1173m, 1138m, 1111m, 1091m, 1056m, 863m, 846m, 806d, 770m, 673w. ^{1}H NMR ($CDCl_3$), δ=4.6–4.55 (m, 1H, C*H*), 4.2 (d, *J*=4.6, 1H, C*H*OH), 4.05–4.0 (m, 2H, C*H*$_2$O), 1.9–1.85 (m, 1H, C*H*(CH_3)$_2$), 1.64 (s, 3H, C(C*H*$_3$)$_2$), 1.51 (s, 12H, [C(C*H*$_3$)$_3$+C(C*H*$_3$)$_2$]), 1.0–0.95 (m, 6H, CH(C*H*$_3$)$_2$). ^{13}C NMR ($CDCl_3$), δ=151.4 (s, *C*O), 94.2 (s, *C*(CH_3)$_2$), 80.3 (s, *C*≡C), 77.6+77.0 (s, C≡*C*+*C*(CH_3)$_3$), 68.8 (t, *C*H_2O), 67.7 (d, *C*HOH), 48.6 (d, *C*H), 34.5 (d, *C*H(CH_3)$_2$), 28.4 (q, C(*C*H_3)$_3$), 25.6 (q, C(*C*H_3)$_2$), 23.5 (q, C(*C*H_3)$_2$), 18.8 (q, CH(*C*H_3)$_2$), 17.3 (q, CH(*C*H_3)$_2$). MS (CI, NH_3) m/e: 298 (M^++1, 27), 242 (34), 224 (100), 182 (24), 166 (16), 57 (12).

3.12. tert-*Butyl (4*R*)-4-[3-hydroxy-3-(3,4,5-trimethoxyphenyl)-1-propynyl]-2,2-dimethyl-1,3-oxazolane-3-carboxylate **9i***

According to the general procedure described above, reaction between **2** and 3,4,5-trimethoxybenzaldehyde **8h** afforded 4.04 g (96%) of **9i** as a yellow oil. IR (film, ν): 3444br., 2979m, 2937m, 2882m, 2839w, 1698s, 1594m, 1504m, 1461m, 1383s, 1332m, 1238m, 1169m, 1125s, 1096m, 1056m, 1008m, 846m, 808w, 771w, 668w, 523w. ^{1}H NMR ($CDCl_3$), δ=6.81 (s, 2H, C*H* arom.), 5.44 (s, br.,1H, C*H*OH), 4.66 (s, br., 1H, C*H*), 4.1–4.05 (m, 2H, C*H*$_2$O), 3.89 (s, 6H, 2×OCH_3), 3.86 (s, 3H, OCH_3), 2.51 (s, br., 1H, CHO*H*), 1.65 (s, 3H, C(C*H*$_3$)$_2$), 1.53, 1.48 (2s, 12H, [C(C*H*$_3$)$_3$+C(C*H*$_3$)$_2$]). ^{13}C NMR ($CDCl_3$), δ=153.2 (s, *C* arom.), 151.4 (s, *C*O), 137.8 (s, *C* arom.), 136.2 (s, *C* arom.), 103.7 (d, *C*H arom), 94.1 (s, *C*(CH_3)$_2$), 85.4 (s, *C*≡C), 81.8, 80.5 (s, *C*(CH_3)$_3$+*C*≡C), 68.6 (t, *C*H_2O), 64.5 (d, *C*HOH), 60.7 (q, O*C*H_3), 56.1 (q, O*C*H_3), 48.6 (d, *C*H), 28.3 (q, C(*C*H_3)$_2$), 26.9, 26.1 (q, C(*C*H_3)$_2$), 25.1, 24.3 (q, C(*C*H_3)$_2$). MS (EI) m/e: 421 (M^+, 27), 365 (14), 288 (22), 240 (30), 57 (100).

*3.13. Synthesis of α-acetylenic ketones **3a–i**. General procedure*

3.13.1. Method A

Over a cooled (0°C), mechanically stirred suspension of MnO_2 (6.7 g, 78 mmol) in CH_2Cl_2 (390 mL), a solution of the corresponding propargyllic alcohol **9a–i** (3 mmol) in CH_2Cl_2 (4.5 mL) was added dropwise. The reaction mixture was stirred at 0°C for 1 h, and then overnight at rt. The mixture was filtered over a $MgSO_4$ pad and washed successively with CH_2Cl_2 (100 mL), AcOEt (100 mL) and MeOH (100 mL). The solvents were removed under reduced pressure, and the residue filtered over a small SiO_2 column using hexanes:AcOEt as eluent. The results are summarised in Table 2.

3.13.2. Method B

To a solution of **9a–i** (5 mmol) in DMSO (18 mL), 2.1 g (7.5 mmol) of **12** were added at rt in one portion. After 10 min of vigorous stirring, the resulting suspension becomes a solution. The reaction mixture was stirred at rt for 4 h, then diluted with H_2O (75 mL) and extracted with AcOEt (3×40 mL). The combined extracts were washed with brine (25 mL), dried over $MgSO_4$ and the solvent

evaporated under reduced pressure. The resulting residue was filtered through a small SiO_2 column using hexanes:AcOEt as eluent. The results are summarised in Table 2.

3.14. tert-*Butyl (4*R*)-2,2-dimethyl-4-(3-oxo-3-phenyl-1-propynyl)-1,3-oxazolane-3-carboxylate **3a***

The reaction between **9a** and the oxidising reagent afforded, according to Method A, 0.87 g (88%) and, according to Method B, 1.56 g (95%) of **3a** as a colourless solid. M.p. 77–78°C. $[\alpha]_D^{20}$ −141.6 (c=1.11 MeOH). IR (KBr, ν): 2980m, 2932m, 2230m, 1704s, 1650s, 1598s, 1581w, 1477s, 1451m, 1377s, 1367s, 1314w, 1264s, 1210m, 1112m, 1090m, 1056m, 857m, 838m, 806w, 769m, 703m. ^{1}H NMR (DMSO, T=60°C), δ=8.14 (m, 2H, C*H* arom.), 7.85–7.65 (m, 3H, C*H* arom.), 5.04 (dd, *J*=5.8 Hz, *J′*=2.6 Hz, 1H, C*H*), 4.35–4.2 (m, 2H, CH_2O), 1.69 (s, 3H, C(CH_3)$_2$), 1.58 (s, 3H, C(CH_3)$_2$), 1.56 (s, 9H, C(CH_3)$_3$). ^{13}C NMR (DMSO, T=60°C), δ=176.5 (s, *C*O), 150.5 (s, N*C*O), 136.1 (s, *C* arom.), 134.2, 128.5 (d, *C*H arom.), 93.8 (s, *C*(CH$_3$)$_2$), 93.5 (s, *C*≡C), 79.9 (s, *C*(CH$_3$)$_3$), 79.1 (s, C≡*C*), 67.3 (t, *C*H$_2$O), 48.1 (d, *C*H), 27.7 (q, C(*C*H$_3$)$_3$), 25.9 (q, C(*C*H$_3$)$_2$), 24.0 (q, C(*C*H$_3$)$_2$). MS (EI) m/e: 214 (M$^+$−PhCO-, 100), 105 (36), 57 (86).

3.15. tert-*Butyl (4*R*)-4-(3-benzo[*d*][1,3]dioxol-5-yl-3-oxo-1-propynyl)-2,2-dimethyl-1,3-oxazolane-3-carboxylate **3b***

The reaction between **9b** and the oxidising reagent afforded, according to Method A, 0.87 g (78%) and, according to Method B, 1.75 g (94%) of **3b** as a colourless solid. M.p. 99–100°C. $[\alpha]_D^{24}$ −113.1 (c=0.61 MeOH). IR (KBr, ν): 2981m, 2934m, 2220m, 1700s, 1640m, 1602m, 1504m, 1488m, 1447s, 1377s, 1367s, 1261s, 1210m, 1166m, 1098m, 1038m, 933m, 900w, 850m, 830w, 806w, 770w, 747m, 717w, 703m. ^{1}H NMR (DMSO, T=60°C), δ=7.84 (d, *J*=8, 1H, C*H* arom.), 7.55 (s, 1H, C*H* arom.), 7.15 (d, *J*=8 Hz, 1H, C*H* arom.), 6.26 (s, 2H, OCH_2O), 5.05–5.0 (m, 1H, C*H*), 4.3–4.2 (m, 2H, CH_2O), 1.68 (s, 3H, C(CH_3)$_2$), 1.57 (s, 12H, C(CH_3)$_3$+C(CH_3)$_2$). ^{13}C NMR (DMSO, T=60°C), δ=174.6 (s, *C*O), 152.7 (s, *C* arom.), 150.5 (s, N*C*O), 148.0 (s, *C* arom.), 131.1 (s, *C* arom.), 126.3, 108.0, 107.2 (3d, *C*H arom.), 102.2 (t, O*C*H$_2$O), 93.5 (s, *C*(CH$_3$)$_2$), 92.9 (s, *C*≡C), 80.0 (s, *C*(CH$_3$)$_3$), 79.0 (s, C≡*C*), 67.4 (t, *C*H$_2$O), 48.2 (d, *C*H), 27.7 (q, C(*C*H$_3$)$_3$), 26.1 (q, C(*C*H$_3$)$_2$), 24.1 (q, C(*C*H$_3$)$_2$). MS (EI) m/e: 373 (M$^+$, 1), 317 (10), 259 (14), 258 (49), 149 (28), 57 (100).

3.16. tert-*Butyl (4*R*)-2,2-dimethyl-4-[3-(2-furyl)-3-oxo-1-propynyl]-1,3-oxazolane-3-carboxylate **3c***

The reaction between **9c** and the oxidising reagent afforded, according to Method A, 0.73 g (77%) and, according to Method B, 1.46 g (92%) of **3c** as a colourless solid. M.p.: 165–166°C. $[\alpha]_D^{20}$ −191.7 (c=0.42 MeOH). IR (KBr, ν): 3123m, 2992w, 2972m, 2886w, 2229m, 1697s, 1637s, 1561w, 1466m, 1397s, 1365m, 1336m, 1308m, 1262m, 1242m, 1175m, 1151m, 1125m, 1095m, 1061m, 1029m, 983w, 849m, 827w, 801m, 770w, 747w, 674w. ^{1}H NMR (DMSO, T=27°C), δ=8.23 (s, 1H, C*H* arom.), 7.60 (s, br., 1H, C*H* arom.), 6.91 (t, *J*=1.6 Hz, 1H, C*H* arom.), 5.0 (t, *J*=4.2 Hz, 1H, C*H*), 4.20–4.15 (m, 2H, CH_2O), 1.66 (s, 3H, C(CH_3)$_2$), 1.55 (s, br., 12H, C(CH_3)$_2$+C(CH_3)$_3$). ^{13}C NMR (DMSO, T=27°C), δ=163.2 (s, *C*O), 152.3 (s, N*C*O), 150.7 (s, *C* arom.), 150.0 (d, *C*H arom.), 122.2 (d, *C*H arom.), 113.3 (d, *C*H arom.), 93.8 (s, *C*(CH$_3$)$_2$), 93.5 (s, *C*≡C), 80.1 (s, *C*(CH$_3$)$_3$), 78.5 (s, C≡*C*), 67.5 (t, *C*H$_2$O), 48.3 (d, *C*H), 28.0 (q, C(*C*H$_3$)$_3$), 26.5 (q, C(*C*H$_3$)$_2$), 24.3 (q, C(*C*H$_3$)$_2$). MS (FAB$^+$) m/e: 320 (M$^+$+1, 10), 265 (17), 264 (100), 220 (53), 218 (22), 206 (56), 204 (55).

3.17. tert-*Butyl (4*R*)-2,2-dimethyl-4-(3-oxo-1-pentynyl)-1,3-oxazolane-3-carboxylate **3d**

The reaction between **9d** and the oxidising reagent afforded, according to Method A, 0.60 g (72%) and, according to Method B, 1.29 g (92%) of **3d** as a yellow oil. $[\alpha]_D^{20}$ −63.8 (c=1.17 MeOH). IR (film, ν): 2981m, 2938m, 2882m, 2215m, 1704s, 1682s, 1478m, 1459m, 1377s, 1367s, 1264m, 1245m, 1171m, 1098m, 1077m, 1058m, 970d, 859m, 842m, 807w, 770m, 672w. ^{1}H NMR (DMSO, T=60°C), δ=4.90 (dd, *J*=6.2 Hz, *J*′=2.4 Hz, 1H, C*H*), 4.22 (dd, *J*=8.8 Hz, *J*′=6.2 Hz, 1H, CH_2O), 4.09 (dd, *J*=8.8 Hz, *J*′=2.4 Hz, 1H, CH_2O), 2.65 (q, *J*=7.4, 2H, CH_2CH$_3$), 1.65 (s, 3H, C(CH_3)$_2$), 1.56 (s, 12H, [C(CH_3)$_3$+C(CH_3)$_2$]), 1.17 (t, *J*=7.4 Hz, 3H, CH$_2$CH_3). ^{13}C NMR (DMSO, T=60°C), δ=187.1 (s, *C*O), 150.4 (s, N*C*O), 93.5 (s, *C*(CH$_3$)$_2$), 91.0 (s, *C*≡C), 80.1+79.8 (s, C≡*C*+*C*(CH$_3$)$_3$), 67.3 (t, *C*H$_2$O), 47.9 (d, *C*H), 37.8 (t, *C*H$_2$CH$_3$), 27.7 (q, C(*C*H$_3$)$_3$), 25.8 (q, C(*C*H$_3$)$_2$), 24.0 (q, C(*C*H$_3$)$_2$), 7.4 (q, CH$_2$*C*H$_3$). MS (FAB$^+$) m/e: 282 (M$^+$+1, 8), 226 (32), 182 (52), 168 (30), 166 (35), 154 (92), 144 (48), 138 (52), 136 (100), 124 (56), 107 (59), 100 (74).

3.18. tert-*Butyl (4*R*)-2,2-dimethyl-4-(3-oxo-1-nonyl)-1,3-oxazolane-3-carboxylate **3e**

The reaction between **9e** and the oxidising reagent afforded, according to Method A, 0.68 g (68%) and, according to Method B, 1.56 g (93%) of **3e** as an orange oil. $[\alpha]_D^{20}$ −92.3 (c=0.95 MeOH). IR (film, ν): 2980m, 2959m, 2933m, 2873m, 2216m, 1701s, 1678s, 1477w, 1459m, 1376s, 1366s, 1263m, 1243m, 1209w, 1171m, 1091m, 1054m, 860m, 843m, 807w, 769m. ^{1}H NMR (DMSO, T=60°C), δ=4.89 (dd, *J*=6.0 Hz, *J*′=2.4 Hz, 1H, C*H*), 4.22 (dd, *J*=9.0 Hz, *J*′=6.2 Hz, 1H, CH_2O), 4.08 (dd, *J*=9.0 Hz, *J*′=2.2 Hz, 1H, CH_2O), 2.62 (t, *J*=7.2, 2H, COCH_2), 1.70–1.65 (m, 6H, 3 CH_2), 1.65 (s, 3H, C(CH_3)$_2$), 1.57 (s, 9H, C(CH_3)$_3$), 1.38 (s, br., 5H, CH_2+C(CH_3)$_2$), 0.97 (t, *J*=7.0 Hz, 3H, CH$_2$CH_3). ^{13}C NMR (DMSO, T=60°C), δ=186.6 (s, *C*O), 150.3 (s, N*C*O), 93.4 (s, *C*(CH$_3$)$_2$), 90.9 (s, *C*≡C), 80.2, 79.7 (s, C≡*C*+*C*(CH$_3$)$_3$), 67.3 (t, *C*H$_2$O), 47.9 (d, *C*H), 44.5 (t, *C*H$_2$), 30.4 (t, *C*H$_2$), 27.6 (t, *C*H$_2$), 27.5 (q, C(*C*H$_3$)$_3$), 25.8 (q, C(*C*H$_3$)$_2$), 24.0 (q, C(*C*H$_3$)$_2$), 23.2 (t, *C*H$_2$), 21.3 (t, *C*H$_2$), 13.2 (q, CH$_2$*C*H$_3$). MS (EI) m/e: 337 (M$^+$, 6), 236 (24), 57 (100).

3.19. tert-*Butyl (4*R*)-2,2-dimethyl-4-[3-oxo-1-propynyl-3-thienyl]-1,3-oxazolane-3-carboxylate **3f**

The reaction between **9f** and the oxidising reagent afforded, according to Method A, 0.74 g (74%) and, according to Method B, 1.52 g (91%) of **3f** as a colourless solid. M.p.: 119–120°C. $[\alpha]_D^{20}$ −155.2 (c=0.96, MeOH). IR (KBr, ν): 2972m, 2936m, 2884m, 2232m, 1696s, 1622s, 1514w, 1413m, 1384s, 1338w, 1283m, 1260m, 1239m, 1170m, 1148m, 1112m, 1090m, 1057m, 846w, 751m, 731w. ^{1}H NMR (DMSO, T=60°C), δ=8.21 (d, J=4.8 Hz, 1H,C*H* arom.), 8.05 (d, J=3.2 Hz, 1H, C*H* arom.), 7.40–7.35 (m, 1H, C*H* arom.), 5.00–4.95 (m, 1H, C*H*), 4.25–4.20 (m, 2H, CH_2O), 1.68 (s, 3H, C(CH_3)$_2$), 1.57 (s, br., 12H, [C(CH_3)$_3$+C(CH_3)$_2$]). ^{13}C NMR (DMSO, T=60°C), δ=168.3 (s, *C*O), 150.5 (s, N*C*O), 143.6 (s, *C* arom.), 136.8 (s, *C* arom.), 135.4 (s, *C* arom.), 128.6 (s, *C* arom.), 93.6 (s, *C*≡C), 92.3 (s, *C*(CH$_3$)$_2$), 80.0 (s, *C*(CH$_3$)$_3$), 78.7 (s, *C*≡C), 67.4 (t, *C*H$_2$O), 48.1 (d, *C*H), 27.7 (q, C(*C*H$_3$)$_3$), 26.1 (q, C(*C*H$_3$)$_2$), 24.1 (q, C(*C*H$_3$)$_2$). MS (FAB$^+$) m/e: 336 (M$^+$+1, 4), 281 (20), 280 (100), 236 (73), 234 (27), 222 (90), 220 (73).

3.20. tert-*Butyl (4*R*)-4-{3-[(4*S*)-3-(*tert-*butyloxycarbonyl)-2,2-dimethyl-1,3-oxazolane-4-yl]-3-oxo-1-propynyl}-2,2-dimethyl-1,3-oxazolane-3-carboxylate* ***3g***

The reaction between **9g** and the oxidising reagent afforded, according to Method A, 0.70 g (52%) and, according to Method B, 1.71 g (76%) of **3g** as a colourless oil. $[\alpha]_D^{20}$ −165.1 (c=0.45 MeOH). IR (film, ν): 2965m, 2938m, 2870m, 2214m, 1714s, 1682m, 1477w, 1470m, 1372s, 1262m, 1210m, 1175m, 1098m, 1068m, 1052m, 849m, 807d, 766m. ^{1}H NMR (DMSO, T=60°C), δ=4.94 (dd, *J*=6.2 Hz, *J′*=2.2 Hz, 1H, C*H*), 4.54 (dd, *J*=7.4 Hz, *J′*=3.4 Hz, 1H, C*H′*), 4.30–4.25 (m, 2H, CH_2O+CH_2O′), 4.1–4.05 (m, 2H, CH_2O+CH_2O′), 1.69 (s, 3H, C(CH_3)$_2$′), 1.62 (s, 3H, C(CH_3)$_2$), 1.57 (s, 3H, C(CH_3)$_2$′), 1.56 (s, 9H, C(CH_3)$_3$), 1.51 (s, 3H, C(CH_3)$_2$). ^{13}C NMR (DMSO, T=60°C), δ=186.7 (s, *C*O), 150.4 (s, N*C*O), 94.1 (s, *C*(CH$_3$)$_2$), 93.6 (s, *C*≡C), 79.9 (s, C≡*C*), 79.8, 78.4 (s, 2 *C*(CH$_3$)$_3$), 67.2 (t, *C*H$_2$O), 66.0 (d, *C*H′), 64.6 (t, *C*H$_2$O′), 48.0 (d, *C*H), 27.7, 27.6 (q, 2 C(*C*H$_3$)$_3$), 25.9 (q, C(*C*H$_3$)$_2$), 23.9 (q, C(*C*H$_3$)$_2$). MS (CI, NH$_3$) m/e: 453 (M$^+$+1, 1), 353 (26), 298 (16), 297 (100), 239 (30), 85 (10), 83 (14), 57 (11).

3.21. tert-*Butyl (4*R*)-2,2-dimethyl-4-(4-methyl-3-oxo-1-pentynyl)-1,3-oxazolane-3-carboxylate* ***3h***

The reaction between **9h** and the oxidising reagent afforded, according to Method A, 0.60 g (68%) of a 1:1 mixture of **3h** and **11** as a colourless oil. According to Method B, 1.22 g (83%) of **3h** as colourless oil. $[\alpha]_D^{20}$ −148.9 (c=1.06 MeOH). IR (film, ν): 2977m, 2935m, 2877m, 2215m, 1705s, 1679s, 1478m, 1466m, 1377s, 1263m, 1245m, 1171m, 1092m, 1056m, 958w, 947w, 855m, 838m, 806w, 770m, 736w, 675w. ^{1}H NMR (CDCl$_3$ T=50°C), δ=4.75–4.70 (m, 1H, C*H*), 4.10–4.05 (m, 2H, CH_2O), 2.65–2.60 (m, 1H, C*H*(CH$_3$)$_2$), 1.68 (s, 3H, C(CH_3)$_2$), 1.57 (s, 3H, C(CH_3)$_2$), 1.55 (s, 9H, C(CH_3)$_3$), 1.24 (d, *J*=7.0 Hz, 6H, CH(CH_3)$_2$). ^{13}C NMR (CDCl$_3$ T=50°C), δ=191.1 (s, *C*O), 151.2 (s, N*C*O), 94.6 (s, *C*(CH$_3$)$_2$), 91.3 (s, *C*≡C), 80.9 (s, *C*(CH$_3$)$_3$), 80.1 (s, C≡*C*), 68.0 (t, *C*H$_2$O), 48.6 (d, *C*H), 43.0 (d, *C*H(CH$_3$)$_2$), 28.2 (q, C(*C*H$_3$)$_3$), 26.2 (q, C(*C*H$_3$)$_2$), 24.6 (q, C(*C*H$_3$)$_2$), 17.7 (q, CH(*C*H$_3$)$_2$). MS (EI) m/e: 268(5), 240(18), 222(14), 197(8), 196(100), 182(17), 180(33), 57(15).

3.21.1. Spectroscopic data for ***11***

^{1}H NMR (CDCl$_3$), δ=6.46 (s, br., 1H, C=CH_2), 6.07 (s, br., 1H, C=CH_2), 4.75–4.70 (m, 1H, C*H*), 4.15–4.10 (m, 2H, CH_2O), 1.94 (s, 3H, CCH_3), 1.68 (s, 3H, C(CH_3)$_2$), 1.56 (s, 3H, C(CH_3)$_2$), 1.53 (s, 9H, C(CH_3)$_3$). ^{13}C NMR (CDCl$_3$), δ=179.5 (s, *C*O), 151.1 (s, N*C*O), 145.1 (s, *C*=CH$_2$), 130.9 (t, C=*C*H$_2$), 94.7 (s, *C*(CH$_3$)$_2$), 91.0 (s, *C*≡C), 80.7 (s, *C*(CH$_3$)$_3$), 79.1 (s, C≡*C*), 67.9 (t, *C*H$_2$O), 48.6 (d, *C*H), 28.3 (q, C(*C*H$_3$)$_3$), 26.4 (q, C(*C*H$_3$)$_2$), 24.6 (q, C(*C*H$_3$)$_2$), 15.9 (q, CH(*C*H$_3$)$_2$). MS (EI) m/e: 266(5), 238(9), 220(18), 195(8), 194(100), 180(9), 179(8), 178(50), 136(6), 57(30).

3.22. tert-*Butyl (4*R*)-2,2-dimethyl-4-[3-oxo-1-propynyl-3-(3,4,5-trimethoxyphenyl)]-1,3-oxazolane-3-carboxylate* ***3i***

The reaction between **9i** and the oxidising reagent afforded, according to Method A, 0.99 g (79%) and, according to Method B, 1.96 g (94%) of **3i** as a yellowish oil. $[\alpha]_D^{20}$ −126.5 (c=0.83, MeOH). IR (film, ν): 2979m, 2939m, 2882m, 2840w, 2223m, 1696s, 1644s, 1582s, 1503m, 1463m, 1415s, 1376s, 1332s, 1232m, 1209m, 1173m, 1128s, 1062m, 1002m, 916w, 862m, 846m, 771w, 744m, 676w. ^{1}H NMR (DMSO, T=60°C), δ=7.47 (s, 2H, C*H* arom.), 5.04 (dd, *J*=5.8 Hz, *J′*=2.6 Hz, 1H, C*H*), 4.25–4.20 (m, 2H, CH_2O), 3.97 (s, 6H, 2×OMe), 3.92 (s, 3H, OMe), 1.69 (s, 3H, C(CH_3)$_2$), 1.59 (s, 3H, C(CH_3)$_2$), 1.55 (s, 9H, C(CH_3)$_3$). ^{13}C NMR (DMSO, T=60°C), δ=175.3 (s, *C*O), 152.8 (2s, *C* arom.), 150.6 (s, N*C*O), 143.8 (s, *C* arom.), 131.3 (s, *C* arom.), 107.0 (2s, *C* arom.), 93.6, 93.4 (2s, C≡*C*+*C*(CH$_3$)$_2$), 80.0, 78.9

(2s, C≡*C*+*C*(CH_3)$_3$), 67.5 (t, *C*H_2O), 60.1 (q, O*C*H_3), 56.1 (2q, O*C*H_3), 48.2 (d, *C*H), 27.7 (q, C(*C*H_3)$_3$), 26.2 (q, C(*C*H_3)$_2$), 24.1 (q, C(*C*H_3)$_2$). MS (FAB$^+$) m/e: 420 (M^++1, 14), 419 (M+, 35), 365 (14), 364 (69), 363 (20), 320 (17), 306 (20), 304 (31), 195 (100).[34]

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