Enyne Metathesis of Norbornene Derivatives: A Facile Approach to Polycyclic Heterocycles

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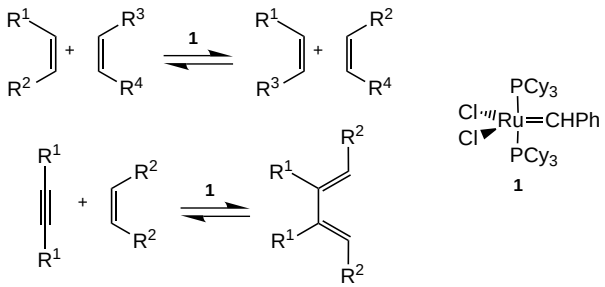
Abstract: Norbornene derivatives bearing propargyloxy substituents in the 5- and 6-positions undergo a cascade series of enyne metatheses when treated with Grubbs' catalyst and a terminal alkene, leading to heterocyclic dienes which undergo a stereoselective Diels–Alder reaction, giving access to a range of polycyclic heterocycles. The process is compatible with both terminal and internal alkynes, and depending upon the structure of the alkene can give symmetrical or unsymmetrical products. Mechanistic studies have shown that the initial metathesis reaction is between the strained norbornene and Grubbs' catalyst, rather than between the alkyne and Grubbs' catalyst.

Keywords: alkynes; Grubbs' catalyst; heterocycles; metathesis; norbornene; ruthenium

Introduction

The development of ruthenium complex **1** by Grubbs et al.[1] has sparked an explosion of interest in alkene metathesis reactions.[2] Grubbs' catalyst **1** is commercially available and stable both to air and to many functional groups found in metathesis substrates. The reactivity of Grubbs' catalyst can be tuned by modifying the ligands, particularly by the replacement of one or both phosphines by carbene type ligands,[3] and very recently a chiral analogue of catalyst **1** has also been reported.[4] The majority of the applications of Grubbs' catalyst involve a metathesis reaction between two alkenes, leading to two new alkenes (Scheme 1). However, Grubbs' catalyst will also induce a metathesis reaction between an alkene and an alkyne (enyne metathesis[5,6,7]), a process which leads to a diene as the product (Scheme 1). Enyne metatheses, although still not as widely exploited as alkene metatheses, are being increasingly used in organic synthesis.[8]

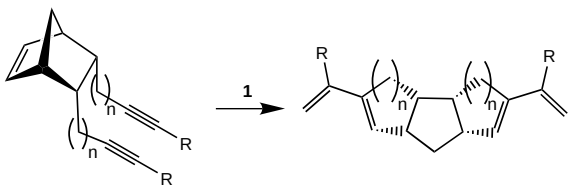


Scheme 1. Alkene and enyne metathesis reactions.

In previous work, we have shown that norbornene derivatives bearing amino acids,[9] amino esters,[10] peptides,[11] and nucleic acid bases[12] are excellent substrates for ring opening metathesis polymerisation (ROMP) reactions induced by Grubbs' catalyst and related complexes.[10,13] Norbornene derivatives are easily prepared by Diels–Alder reactions, and the release of strain[14] during the ring opening metathesis of the norbornene ring makes the process thermodynamically favourable and irreversible. Based on this precedent, we decided to investigate whether norbornene derivatives bearing suitably located alkyne substituents would also make good substrates for ring-opening/ring-closing enyne metathesis reactions as outlined in Scheme 2.[15,16,17] In this paper we give full details of the successful accomplishment of this concept.[18]

Results and Discussion

Initially, diyne **2** was selected as a substrate for metathesis reactions since it could be readily prepared from known diol[19] **3**, enyne metatheses would form unstrained six-membered rings, and there was literature



Scheme 2. Enyne metathesis of norbornene derivatives.

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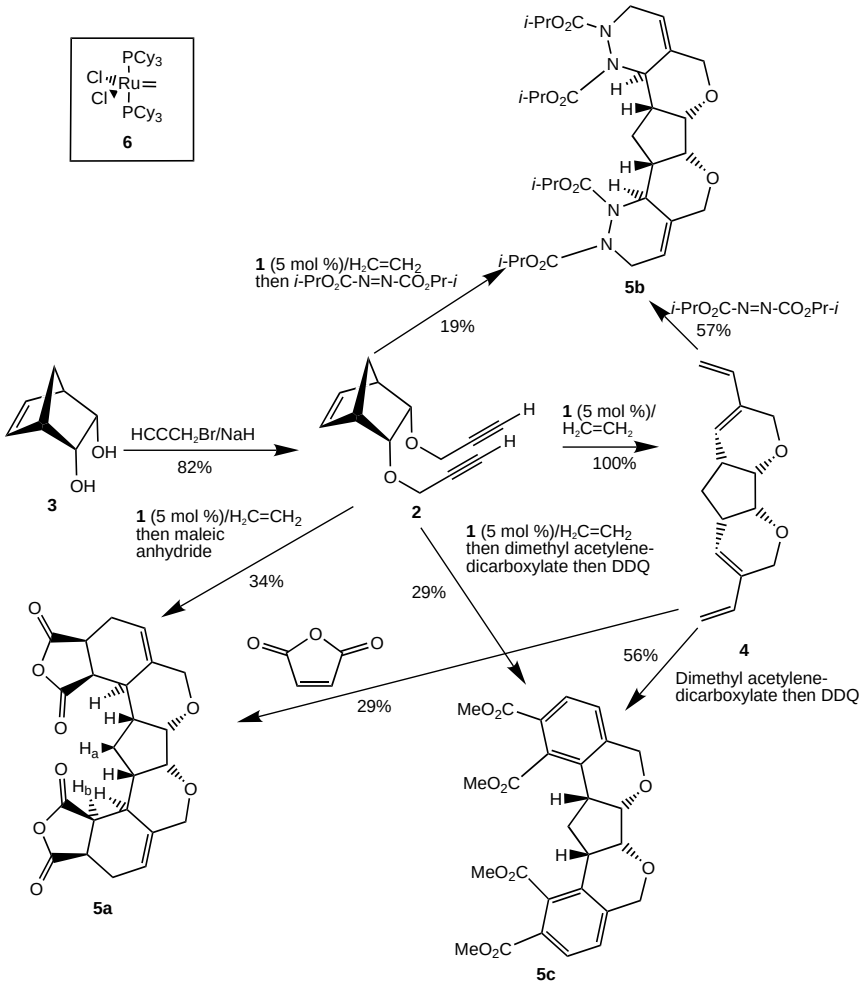
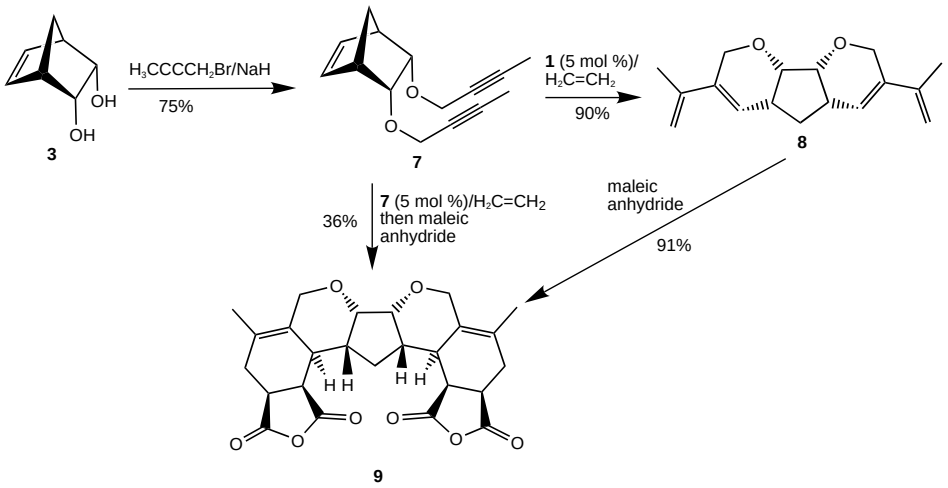
precedent for the ring-opening/ring-closing metathesis of the corresponding bis(allyloxy)norbornene.[16] Treatment of compound **2** with Grubbs' catalyst **1** (5 mol %) under an ethene[20] atmosphere gave the desired bis-diene **4** in 100% yield (Scheme 3). Compound **4** was found to undergo a Diels–Alder reaction with maleic anhydride to give heptacyclic bis-anhydride **5a** in 29% yield. Compound **5a** contains ten consecutive stereocentres and was obtained as a single stereoisomer. The stereochemistry of compound **5a** was determined based on the symmetry apparent in its NMR spectra, and the observation of an NOE between H_a and H_b which three-dimensional models showed was only consistent with the stereochemistry shown. This stereochemistry is also that expected since the *exo*-face of the dienes in compound **4** is more accessible than the *endo*-face, and Diels–Alder reactions have a kinetic preference to occur through an *endo*-transition state.

It was essential that the metathesis of compound **2** be carried out under an ethene atmosphere since one molecule of ethene is incorporated into bis-diene **4**. If an inert atmosphere was used instead, then under dilute conditions, compound **2** was recovered and under more concentrated conditions it underwent ROMP. The ethene also has a second role in the metathesis process: the conversion of Grubbs' catalyst **1** into the much more reactive[21] methylidene complex **6**, which then initiates the series of six consecutive ring-opening, ring-closing, and cross metatheses which eventually lead to compound **4**.

Since Grubbs' catalyst is known not to react with electron-deficient alkenes, and to be compatible with carbonyl based functional groups, it was also possible to carry out the transformation of compound **2** into compound **5a** in a one-pot process simply by adding maleic anhydride to the metathesis reaction. This process is 100% atom economical, since all of the atoms present in the norbornene, ethene, and the anhydride are incorporated into compound **5a**. Bis-diene **4** also underwent Diels–Alder reactions with diisopropyl azodicarboxylate to give compound **5b**, and with dimethyl acetylenedicarboxylate to give a bis-dihydrobenzene derivative which could be oxidised with DDQ to give compound **5c** as shown in Scheme 3. Compounds



Scheme 3. Enyne metathesis/Diels–Alder reactions of compound **2.**



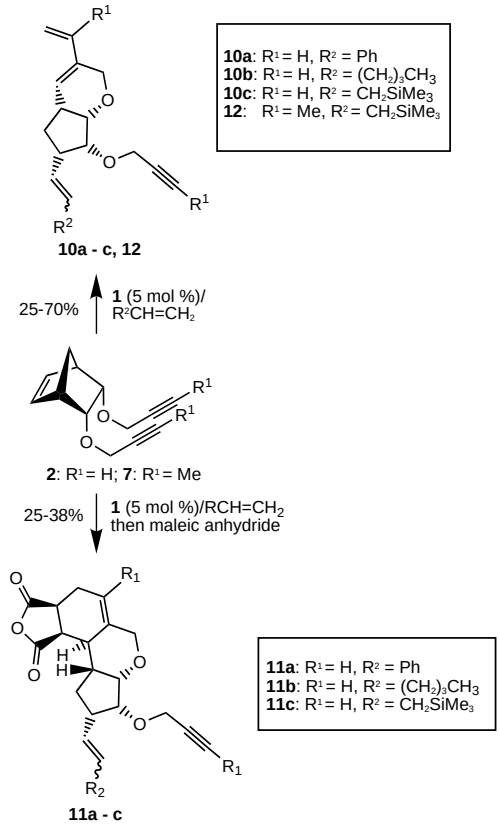
Scheme 4. Enyne metathesis/Diels–Alder reactions of compound **7.**

5b and **5c** could also be obtained directly from diyne **2** in a one-pot process as described for **5a**.

Most previous enyne metathesis reactions have involved terminal alkenes and/or alkynes. To further explore the scope of this chemistry, the use of norbornene derivative **7** in which neither the alkene nor the alkyne is terminal was investigated. Compound **7** was prepared by the alkylation of diol **3** using 1-bromobut-2-yne[22] as shown in Scheme 4. Treatment of compound **7** with Grubbs' catalyst (5 mol %) gave the desired bis-diene **8** in 90% yield. By adding maleic anhydride to the metathesis reaction, it was again possible to isolate bis-anhydride **9** in 36% yield directly from diyne **7**. Alternatively, compound **9** could be obtained from the bis-diene **8** in 91% yield.

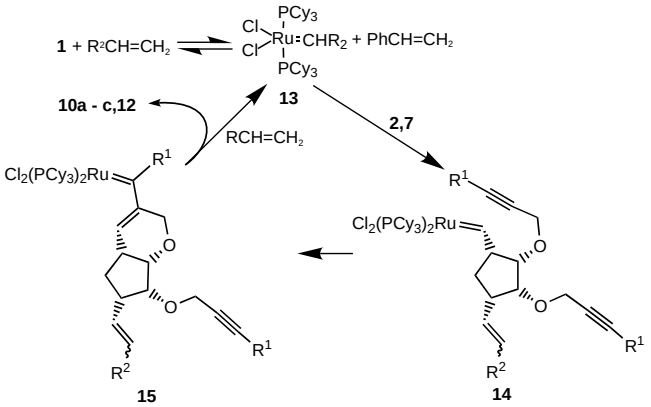
To further explore the scope and limitations of this cascade of enyne metathesis reactions, the use of alkenes other than ethene was investigated using norbornene derivative **2**. The use of internal alkenes (3-hexene) was totally unsuccessful. However, the use of terminal alkenes (at least 2.5 equivalents) did result in a metathesis cascade. The use of styrene, 1-hexene, or allyltrimethylsilane gave dienes **10a – c** as a 1:3 to 1:4 ratio of *cis* and *trans* isomers at the isolated double bond as shown in Scheme 5. For compounds **10b** and **10c**, the *cis* and *trans* isomers could be separated by flash chromatography. It was also possible to carry out the metathesis reactions and a subsequent Diels–Alder reaction (with maleic anhydride as the dienophile) *in situ*, leading to anhydrides **11a – c**. The stereochemistry of compounds **11a – c** is assigned by analogy with that of compound **5a**. This desymmetrising metathesis could also be applied to diyne **7**. Thus, treatment of compound **7** with allyltrimethylsilane gave diene **12** in 25% yield as a 1:1 ratio of *cis* and *trans* isomers at the isolated double bond.

The formation of compounds **10a – c** and **12** can be explained by a series of four consecutive metathesis reactions as shown in Scheme 6. Thus, Grubbs' catalyst



Scheme 5. Metathesis of compounds **2** and **7** in the presence of terminal alkenes.

first undergoes a cross metathesis reaction with the terminal alkene to generate a new metathesis initiator **13** (when the alkene is styrene, this is a degenerative metathesis). Catalyst **13** then reacts with the strained alkene of substrate **2** or **7**, to give ruthenium alkylidene **14** in which the isolated double bond has been formed. An intramolecular enyne metathesis reaction then



Scheme 6. Catalytic cycle for the formation of compounds **10a – c**.

forms the bicyclic framework, giving compound **15** and finally, another cross metathesis reaction with the terminal alkene gives compounds **10a – c** or **12** and reforms the metathesis catalyst **13**. To obtain evidence in support of this catalytic cycle, Grubbs' catalyst and allyltrimethylsilane were mixed in $CDCl_3$. After 40 minutes, a ^1H NMR spectrum was obtained on the mixture, which showed that in addition to unreacted catalyst **1**, alkylidene **13** ($R = CH_2SiMe_3$) and methylidene complex **6** were present in a 10:1 ratio (Figure 1). Hence, complex **13** which is needed to initiate the catalytic cycle shown in Scheme 6 is formed by the reaction between Grubbs' catalyst and allyltrimethylsilane. The relatively low reactivity of Grubbs' catalyst is also an important factor in this catalytic cycle, since under the reaction conditions it is not able to react with the internal alkene present in compounds **10a – c**, and hence cannot initiate a second cascade of metathesis reactions which would lead to bis-diene **4**.

To further extend the scope of this chemistry, the use of diyne **16** was investigated. If compound **16** underwent a metathesis cascade analogously to compound **2**, it would lead to a 7,5,7 fused ring system. As such, it represents a more challenging substrate for ring closing enyne metathesis. Diyne **16** was prepared from known[23] diol **17** (Scheme 7). The metathesis of compound **16** proved to be considerably more difficult than that of compounds **2** and **7**. Treatment of diyne **16** with 6 mol % of catalyst **1** under an ethene atmosphere gave a 1:1 mixture of compounds **18** and **19**, and none of the expected 7,5,7-tricylic product. In contrast, the metathesis of the corresponding bis-allyloxynorbornene is known[17] to give the 7,5,7-fused ring system when treated with catalyst **1**. It may be that the extra strain in the transition state associated with enyne metathesis as compared to alkene metathesis is just sufficient to prevent the formation of the second seven-membered ring. The formation of compound **18** is interesting, since it proves that, at least for this type of system, the initial

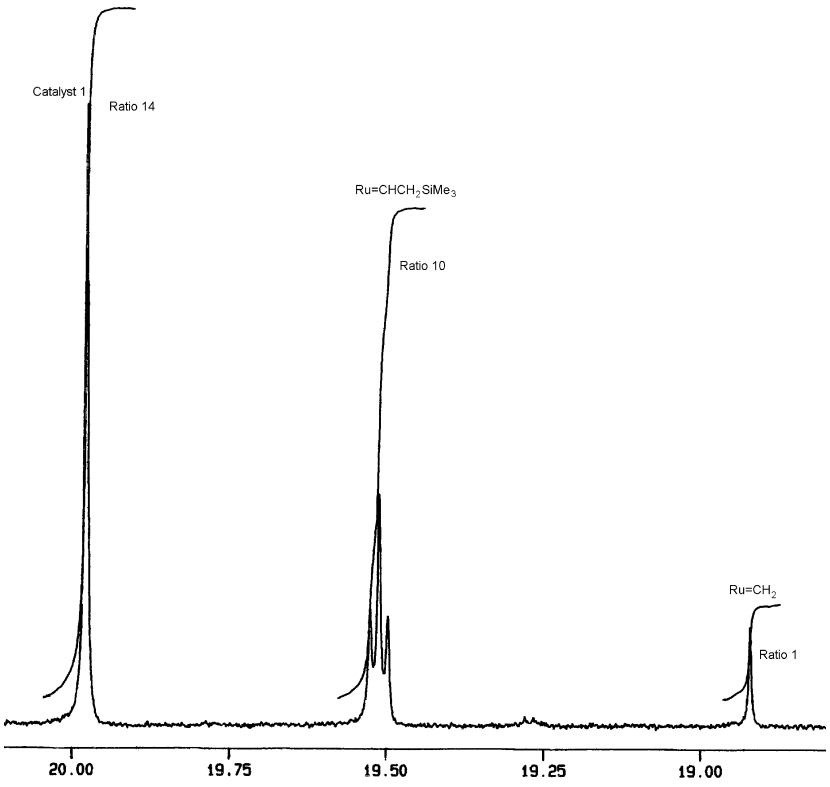
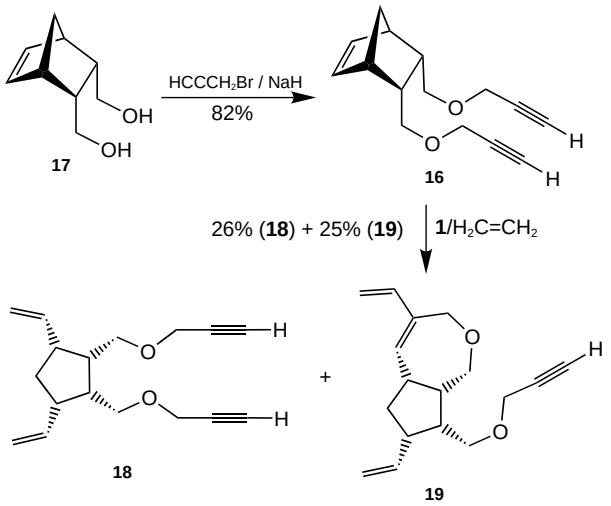


Figure 1. Extract of the ^1H NMR spectrum of a mixture of catalyst **1** and allyltrimethylsilane.



Scheme 7. Formation and metathesis of diyne **16**.

metathesis occurs at the alkene rather than at the alkyne.[7,20] The amount of product **19** formed could be increased to 48% by adding a second batch of catalyst **1** to the reaction one day after it had started, however even under these conditions it was not possible to isolate any tricyclic product. This result does however demonstrate that **18** and **19** are formed from a common intermediate (the ruthenium complex corresponding to ring-opening of the norbornene ring) and that compound **18** can restart the metathesis cascade leading to compound **19** by cross metathesis with catalyst **6**.

Conclusions

It has been demonstrated that in the presence of ethene, Grubbs' catalyst will initiate a cascade of ring-opening metatheses, ring-closing-enyne metatheses and cross metatheses of norbornene derivatives bearing pendant alkynes, giving a one-pot synthesis of bis-dienes which are suitable for further manipulation. When the ethene is replaced by a terminal alkene, the low reactivity of Grubbs' catalyst towards unstrained internal alkenes causes the cascade to terminate at the mid-point, leading to highly functionalised mono-dienes. It has also been shown that these dienes undergo stereoselective Diels–Alder reactions either in a subsequent step or *in situ* with the metathesis cascade, leading to polyheterocyclic systems. The nature of the products and isolated intermediates suggests that (at least for these substrates) the metathesis cascade starts at the alkene rather than the alkyne. This reversal of the previously reported reactivity may be due to the strained and hence highly reactive nature of the alkene unit within a norbornene ring.

Experimental Section

Analytical thin layer chromatography was performed using Silica Gel 60 precoated plates with a fluorescent indicator. Flash column chromatography was performed using Silica Gel 60 (230 – 400 mesh). Dichloromethane was dried by distillation from calcium hydride. THF was dried and purified by distillation from metallic sodium. Melting points were recorded on a Büchi oil-based apparatus and are uncorrected. Infrared spectra were run on a Perkin-Elmer Paragon 1000 spectrometer and peaks are reported as strong (s), medium (m), weak (w) or broad (br). Liquid samples were recorded neat and solids as nujol mulls. NMR spectra were obtained using Bruker Avance digital NMR spectrometers operating at 360, 400, or 500 MHz for protons and 90, 100, or 125 MHz for carbon. All spectra were recorded at room temperature in $CDCl_3$ unless otherwise stated and are referenced to the solvent peak. The number of hydrogens attached to each carbon atom was determined by DEPT-90 and DEPT-135 experiments. Where compounds were analysed as mixtures of *cis*- and *trans*-isomers, all of the peaks corresponding to the major (*trans*-) isomer are reported along with those peaks corresponding to the *cis*-isomer which are not coincident with or hidden by peaks for the *trans*-isomer. Low resolution mass spectra were recorded using chemical ionisation (CI) with ammonia as reagent gas unless otherwise stated. Only molecular ions, the base peak and significant fragment ions are reported along with their relative intensities. High resolution mass measurements were made using electrospray ionisation (ES).

Diyne 2

To a solution of diol **3** (950 mg, 7.54 mmol) in dimethylformamide (10 mL) was added NaH (60% in mineral oil; 905 mg, 3 equiv.) at 0 °C. The resulting mixture was stirred for one hour at 0 °C, then propargyl bromide (80% in toluene; 4.485 g, 4 equiv.) was added. The mixture was then warmed to room temperature and stirred for 18 hours. After hydrolysis with water (15 mL) the mixture was extracted with diethyl ether (4×15 mL) and evaporated under vacuum to leave the crude product as a yellowish viscous liquid which could be purified by distillation or by flash chromatography (CH_2Cl_2/Et_2O, 98:2) to give diyne **2** as a colourless oil; yield: 1.243 g (82%). IR (neat): $\nu_{max} = 3299$ (s), 3061 (w), 2116 (w), 1575 cm^{-1} (w); ^1H NMR: $\delta = 6.19 - 6.18$ (2H, m, =CH), 4.23 – 4.22 (2H, m, CHO), 4.17 (4H, d, $J = 2.3$ Hz, CH_2O), 3.07 – 3.06 (2H, m, =CHCH), 2.36 (2H, t, $J = 2.4$ Hz, ≡CH), 1.44 (1H, dt, $J = 9.6$, 2.2 Hz, CH_2), 1.14 (1H, d, $J = 9.6$ Hz, CH_2); ^{13}C NMR: $\delta = 133.8$ (CH), 79.4 (C), 77.4 (CH), 72.7 (CH), 56.5 (CH_2), 45.2 (CH), 41.1 (CH_2); MS (CI): $m/z = 220$ ($M + NH_4^+$, 16), 203 (MH^+, 100); HRMS (ES): calcd. for $C_{13}H_{15}O_2$ (MH^+): 203.1072; found: 203.1072.

Bis-diene 4

A solution of diyne **2** (100 mg, 0.50 mmol) in dry dichloromethane (37 mL) was cooled to −78 °C and ethene was passed through the solution for 10 minutes. A solution of catalyst **1** (20.34 mg, 0.0250 mmol) in dry dichloromethane (3 mL) was then added and after 15 minutes the mixture was warmed to room temperature and stirred for 4 hours. The solvent was then

removed under vacuum and the residue subjected to flash chromatography (CH_2Cl_2) to give compound **4** as a white solid; yield: 113 mg (100%): mp decomposed at 165 °C; IR (nujol): $\nu_{max} = 3085$ (s), 1720 (m), 1681 (m), 1644 (s), 1604 cm^{-1} (s); ^1H NMR: $\delta = 6.18$ (2H, dd, $J = 11.0, 17.8$ Hz, =CCH), 5.76 (2H, dq, $J = 5.8$, 1.0 Hz, C=CH), 4.91 (2H, dd, $J = 17.9$, 0.6 Hz, $=CH_{2(trans)}$), 4.90 (2H, d, $J = 11.0$ Hz, $=CH_{2(cis)}$), 4.50 (2H, dd, $J = 15.1$, 0.8 Hz, OCH_2), 4.2–4.15 (2H, m, CHO), 4.12 (2H, dt, $J = 15.1$, 2.4 Hz, OCH_2), 2.4–2.3 (2H, m, C<u>H</u>-CH=), 1.96 (1H, dtt, $J = 11.8$, 6.4, 1.2 Hz, CH_2), 1.49 (1H, q, $J = 12.1$ Hz, CH_2); ^{13}C NMR: $\delta = 136.3$ (CH), 135.7 (C), 127.2 (CH), 111.9 (CH_2), 77.3 (CH), 65.0 (CH_2), 40.1 (CH), 36.3 (CH_2); MS (CI): $m/z =$ 248 ($M + NH_4^+$, 6.4), 231 (MH^+, 89%), 230 (M^+, 10), 147 (46), 91 (100); HRMS (ES): calcd. for $C_{15}H_{19}O_2$ (MH^+): 231.1385; found: 231.1382.

Anhydride 5a from Diyne 2

To a solution of diyne **2** (100 mg, 0.50 mmol) in dry ethyl acetate (37 mL) and under an ethene atmosphere at −78 °C was added a solution of catalyst **1** (20.55 mg, 0.0250 mmol) in dry ethyl acetate (3 mL). When gas absorption ended (*ca.* 15 min.), the cold bath was removed and the mixture was stirred at room temperature until NMR showed that all the starting material had been consumed (*ca.* 20 hours). A solution of maleic anhydride (107 mg, 1.10 mmol) in ethyl acetate was added and the mixture was stirred for 20 hours at room temperature. The solvent was then removed under vacuum and the residue was purified by flash chromatography (CH_2Cl_2) to give anhydride **5a** as an off-white solid; yield: 72 mg (34%). The product could also be purified by recrystallisation from CH_2Cl_2/Et_2O in 28% yield; mp decomposed at 205 °C; IR (nujol): $\nu_{max} = 1848$ (s), 1777 (s), 1636 cm^{-1} (s); ^1H NMR: $\delta = 5.70$ (2H, d, $J = 3.6$ Hz, =CH), 4.28 (2H, d, $J = 14.5$ Hz, CH_2O), 4.15 (2H, d, $J = 5.8$ Hz, CHO), 3.98 (2H, d, $J = 14.5$ Hz, CH_2O), 3.36 (4H, br s, O=C-CHCH-C=O), 2.71 (2H, dd, $J = 15.7$, 7.1 Hz, =CHC<u>H</u>$_2$), 2.60 (3H, br s, $CHCH_2CH$), 2.34 (2H, br s, =C-CH), 2.3–2.2 (2H, m, $=CHCH_2$), 1.5–1.4 (1H, m, CH_2); ^{13}C NMR: $\delta = 172.7$ (C), 171.0 (C), 136.5 (C), 119.0 (CH), 79.0 (CH), 67.0 (CH_2), 43.1 (CH), 39.6 (CH), 37.8 (CH), 36.1 (CH), 33.0 (CH_2), 23.2 (CH_2); MS (CI): $m/z = 444$ ($M + NH_4^+$, 5), 60 (100); HRMS (ES): calcd. for $C_{23}H_{26}NO_8$ ($M + NH_4^+$): 444.1658; found: 444.1657.

Anhydride 5a from Bis-diene 4

To a solution of bis-diene **4** (50 mg, 0.22 mmol) in ethyl acetate (5 mL) at room temperature was added maleic anhydride (108 mg, 1.10 mmol). The mixture was stirred at room temperature for 21 hours. The solvent was then removed under vacuum and the residue was dissolved in dichloromethane and filtered twice through a celite pad. Evaporation of the solvent gave anhydride **5a** as a white solid; yield: 27 mg (29%). Spectroscopic data were as reported above.

Compound 5b from Diyne 2

To a solution of diyne **2** (50 mg, 0.25 mmol) in dry dichloromethane (18 mL) and under an ethene atmosphere at −78 °C, was added a solution of catalyst **1** (20.55 mg, 0.0250 mmol) in dry dichloromethane (3 mL). When gas absorption ended (*ca.* 15 min) the cold bath was removed and the mixture was stirred at room temperature until NMR showed that all of the starting material had been consumed (ca. 6 hours). Diisopropyl azodicarboxylate (111.2 mg, 0.55 mmol) was added and the mixture was heated to reflux and stirred for 20 hours. The solvent was then evaporated under vacuum and the residue purified by flash chromatography (CH_2Cl_2) to give compound **5b** as a white crystalline solid; yield: 33 mg (19%); mp 124–127 °C; IR (nujol): $\nu_{max} = 1704$ cm^{-1} (s); ^1H NMR (DMSO-d_6 100 °C): $\delta = 5.6–5.5$ (2H, m, =CH), 4.91 (2H, hept, $J = 6.2$ Hz, $OCHMe_2$), 4.9–4.8 (4H, m, $OCHMe_2$ + CHO), 4.61 (2H, dd, $J = 12.4$, 1.7 Hz, CH_2O), 4.33 (2H, d, $J = 17.3$ Hz, CH_2N), 4.10 (2H, d, $J = 12.4$ Hz, CH_2O), 3.99 (2H, d, $J = 6.2$ Hz, NCHC<u>H</u>), 3.61 (2H, d, $J = 17.0$ Hz, CH_2N), 2.2–2.1 (3H, m, NCH + CH_2), 2.0–1.9 (1H, m, CH_2), 1.27 [12H, d, $J = 6.2$ Hz, $(CH_3)_2$], 1.21 [12H, d, $J = 6.1$ Hz, $(CH_3)_2$]; ^{13}C NMR (DMSO-d_6 100 °C): $\delta =$ 155.1 (C), 154.5 (C), 135.2 (C), 116.8 (CH), 80.1 (CH), 70.1 (CH), 69.4 (CH_2), 69.3 (CH), 57.4 (CH), 43.4 (CH), 42.1 (CH_2), 31.1 (CH_2), 22.0 (CH_3), 21.9 (CH_3); MS: (CI): $m/z = 652$ ($M +$ NH_4^+, 35), 635 (MH^+, 100); HRMS (ES): calcd. for $C_{31}H_{47}N_4O_{10}$ (MH^+): 635.3292; found: 635.3286;

Compound 5b from Bis-diene 4

To a solution of bis-diene **4** (50 mg, 0.22 mmol) in dichloromethane (5 mL) was added diisopropyl azodicarboxylate (175.8 mg, 4 equiv.) and the mixture was heated to reflux and stirred for 20 hours. The solvent was then evaporated under vacuum and the residue purified by flash chromatography (CH_2Cl_2) to give compound **5b** as a white crystalline solid; yield: 80 mg (58%). Spectroscopic data as reported above.

Compound 5c from Diyne 2

To a solution of diyne **2** (150 mg, 0.75 mmol) in dry dichloromethane (55 mL) and under an ethene atmosphere at −78 °C, a solution of catalyst **1** (20.55 mg, 0.0250 mmol) in dry dichloromethane (3 mL) was added. When gas absorption ended (*ca.* 15 min) the cold bath was removed and the mixture was stirred at room temperature for 2 hours after which time NMR showed that all of the starting material had been consumed. The solvent was then removed under vacuum and the residue was redissolved in toluene (15 mL), dimethyl acetylenedicarboxylate (527 mg, 5 equiv.) was added and the reaction was heated at reflux for 16 hours. After this time, DDQ (425 mg, 2.5 equiv.) was added and the mixture was heated at reflux for a further 48 hours. The reaction was allowed to cool to room temperature and the solvent was evaporated under vacuum. The residue was purified by flash chromatography (EtOAc) to give compound **5c** as a viscous liquid; yield: 103 mg (29%). IR (neat): $\nu_{max} = 2953$ (m), 1728 (s), 1584 cm^{-1} (w); ^1H NMR: $\delta =$ 7.74 (2H, d, $J = 8.0$ Hz, ArCH), 7.08 (2H, d, $J = 8.0$ Hz, ArCH), 4.95 (2H, d, $J = 15.3$ Hz, CH_2O), 4.66 (2H, d, $J = 15.3$ Hz, CH_2O), 4.45 (2H, d, $J = 5.0$ Hz, CHO), 3.95 (6H, s, OCH_3), 3.81 (6H, s, OCH_3), 3.2–3.1 (2H, m, ArC-CH), 2.4–2.3 (1H, m, CH_2), 1.72 (1H, q, $J = 12.5$ Hz, CH_2); ^{13}C NMR: $\delta = 169.8$ (C), 166.4 (C), 140.4 (ArC), 135.9 (ArC), 133.2 (ArC), 127.2 (ArC), 128.2 (ArCH), 126.0 (ArCH), 78.6 (CH), 68.0 (CH_2), 53.1 (CH_3), 52.9 (CH_3), 39.4 (CH_2), 38.4 (CH); MS (CI): $m/z = 528$ ($M + NH_4^+$, 38), 213 (100); HRMS (ES): calcd. for $C_{27}H_{30}NO_{10}$ ($M + NH_4^+$): 528.1870; found 528.1864.

Compound 5c from Bis-diene 4

To a solution of bis-diene **4** (40 mg, 0.17 mmol) in toluene (5 mL) was added dimethyl acetylenedicarboxylate (123.6 mg, 5 equiv.) and the reaction was heated to reflux and stirred for 21 hours. After this time DDQ (95 mg, 2.4 equiv.) was added and the reaction was heated at reflux for a further 20 hours. After the reaction was cooled to room temperature, the solvent was evaporated under vacuum and the residue was purified by flash chromatography (CH_2Cl_2/MeOH, 3:1) to give compound **5c** as a viscous liquid; yield: 24 mg (27%). Spectroscopic data as reported above.

Diyne 7

To a solution of diol **3** (300 mg, 2.38 mmol) in dimethylformamide (3 mL) at 0 °C was added NaH (60% in mineral oil; 285.7 mg, 3 equiv.). The mixture was stirred for 1 hour at 0 °C, then 1-bromobut-2-yne (0.950 g, 3 equiv.) was added. The mixture was then warmed to room temperature and stirred for 16 hours. After hydrolysis with water (5 mL), the mixture was extracted with diethyl ether (4 × 5 mL) and evaporated under vacuum and the residue was purified by flash chromatography (CH_2Cl_2/EtOAc, 85:15) to give diyne **7** as a colourless oil; yield: 410 mg (75%). IR (neat): $\nu_{max} = 3065$ (w), 2970 (s), 2293 (w), 2241 (m), 1712 (s), 1634 cm^{-1} (m); ^1H NMR: $\delta = 6.18-6.17$ (2H, m, =CH), 4.18–4.17 (2H, m, CHO), 4.10 (4H, q, $J =$ 2.3 Hz, OCH_2), 3.39 (2H, br s, CH), 1.79 (6H, t, $J = 2.3$ Hz, CH_3), 1.41 (1H, dt, $J = 9.5, 2.2$ Hz, CH_2), 1.13 (1H, d, $J = 9.5$ Hz, CH_2); ^{13}C NMR: $\delta = 134.8$ (CH), 82.5 (C), 78.1 (CH), 75.9 (C), 58.0 (CH_2), 46.2 (CH), 42.2 (CH_2), 21.1 (CH_3); MS (CI): $m/z =$ 248 ($M + NH_4^+$, 100), 231 (MH^+, 15); HRMS (ES): calcd. for $C_{15}H_{19}O_2$ (MH^+): 231.1385; found: 231.1387.

Bis-diene 8

A solution of diyne **7** (50 mg, 0.22 mmol) in dry dichloromethane (18 mL) was cooled to −78 °C and ethene was passed through the solution for 10 minutes. A solution of catalyst **1** (9.04 mg, 5 mol %) in dry dichloromethane (2 mL) was then added and after 15 minutes the mixture was warmed to room temperature and stirred for 4 hours. The solvent was then removed under vacuum and the residue subjected to flash chromatography (CH_2Cl_2) to give diene **8** as a white crystalline solid; yield: 50 mg (90%); mp 99–101 °C; IR (nujol): $\nu_{max} =$ 3088 (m), 1638 (m), 1609cm^{-1} (m); ^1H NMR: $\delta = 5.86$ (2H, d, $J = 3.7$ Hz, =CH), 4.80 (2H, s, $=CH_2$), 4.72 (2H, s, $=CH_2$), 4.54 (2H, d, $J = 1.5$ Hz, CH_2O), 4.2–4.1 (4H, m, CH_2O + CHO), 2.33–2.31 (2H, m, C<u>H</u>CH=), 2.02–1.96 (1H, m, CH_2), 1.81 (6H, s, CH_3), 1.52 (1H, q, $J = 12.2$ Hz, CH_2); ^{13}C NMR: $\delta =$ 139.1 (C), 135.2 (C), 121.7 (CH), 109.4 (CH_2), 75.5 (CH), 64.6 (CH_2), 38.8 (CH), 35.2 (CH_2), 19.1 (CH_3); MS (CI): $m/z = 276$ ($M + NH_4^+$, 51), 259 (MH^+, 100); HRMS (ES): calcd. for $C_{17}H_{23}O_2$ (MH^+): 259.1698; found: 259.1698.

Anhydride 9 from Diyne 7

A solution of diyne **7** (120 mg, 0.52 mmol) in dry ethyl acetate (35 mL) and under an ethene atmosphere was cooled to −78 °C. A solution of catalyst **1** (21.44 mg, 5 mol %) in dry ethyl acetate (5 mL) was then added and after gas evolution ended, the reaction was warmed to room temperature and stirred for 17 hours. A solution of maleic anhydride (112.49 mg, 2.2 equiv.) in ethyl acetate (3 mL) was added to the reaction which was then stirred at room temperature for 24 hours. The solvent was removed under vacuum, the residue redissolved in chloroform and filtered through a Celite pad. The solvent was again evaporated under vacuum and the residue was purified by recrystallisation (CH_2Cl_2/Et_2O) to give compound **9** as an off-white solid; yield: 85 mg (36%); mp decomposes at 178 °C. IR (nujol): $\nu_{max} = 1843$ (w), 1773 (s), 1636 cm^{-1} (w); ^1H NMR: $\delta = 4.55$ (2H, d, $J = 14.5$ Hz, OCH_2), 4.10 (2H, d, $J = 5.4$ Hz, CHO), 3.85 (2H, d, $J = 14.5$ Hz, OCH_2), 3.4–3.2 (4H, m, O=CCHCHC=O), 2.6–2.5 (5H, m, CH-C=+ C<u>H</u>C<u>H</u>$_2$C<u>H</u>), 2.3–2.2 (4H, m, C<u>H</u>$_2$-CH=), 1.63 (6H, s, CH_3), 1.5–1.4 (1H, m, CHC<u>H</u>$_2$CH); ^{13}C NMR: $\delta = 174.1$ (C), 172.6 (C), 128.8 (C), 127.8 (C), 79.9 (CH), 65.5 (CH_2), 44.7 (CH), 40.9 (CH), 39.2 (CH_2), 38.1 (CH), 35.5 (CH), 31.0 (CH_2), 19.37 (CH_3); MS (CI): $m/z = 472$ ($M + NH_4^+$, 100), 455 (MH^+, 25); HRMS (ES): calcd. for $C_{25}H_{30}NO_8$ ($M + NH_4^+$): 472.1971; found: 472.1969.

Anhydride 9 from Bis-diene 8

To a solution of bis-diene **8** (50 mg, 0.194 mmol) in ethyl acetate (6 mL) at room temperature was added maleic anhydride (42 mg, 0.428 mmol). The mixture was stirred at room temperature for 21 hours, then the solvent was removed under vacuum. The residue was dissolved in chloroform and filtered through a Celite pad. The solvent was evaporated under vacuum to give anhydride **9** as a white solid; yield: 80 mg (91%). An analytical sample could be obtained by recrystallisation from CH_2Cl_2/Et_2O.

Diene 10a

To a solution of diyne **2** (100 mg, 0.50 mmol) and styrene (260 mg, 5 equiv.) in dry dichloromethane (37 mL) under an inert atmosphere at room temperature was added a solution of catalyst **1** (20.34 mg, 0.025 mmol) in dry dichloromethane (3 mL). The mixture was stirred at room temperature for 16 hours and the solvent was then removed under vacuum. The residue was purified by flash chromatography (CH_2Cl_2) to leave compound **10a** as a 3:1 ratio of *trans*- and *cis*-isomers as a colourless oil; yield: 27 mg (35%). IR (neat): $\nu_{max} = 3301$ (s), 2936 (m), 2892 (m), 1647 cm^{-1} (m); ^1H NMR (*trans*-isomer): $\delta = 7.3-7.1$ (5H, m, ArCH), 6.43 (1H, dd, $J = 9.6$, 15.8 Hz, C<u>H</u>=CH_2), 6.25–6.15 (2H, m, CH=CHPh), 5.81 (1H, d, $J =$ 4.5 Hz, -C=CH), 5.0–4.9 (2H, m, $=CH_2$), 4.48 (1H, d, $J =$ 15.4 Hz, =C-CH_2O), 4.21 (1H, t, $J = 1.9$ Hz, CHO), 4.2–4.15 (1H, m, =C-CH_2O), 4.2–4.1 (2H, m, ≡C-CH_2O), 3.97 (1H, t, $J = 3.8$ Hz, CHO), 3.1–3.0 (1H, m, C<u>H</u>-CH=), 2.34 (1H, t, $J =$ 2.2 Hz, HC≡), 2.3–2.2 (2H, m, $CHCH_2$), 1.6–1.5 (1H, m, CH_2); (*cis*-isomer): $\delta = 7.3-7.1$ (5H, m, ArCH), 6.43 (1H, dd, $J = 9.6$, 15.8 Hz, C<u>H</u>=CH_2), 6.25–6.15 (1H, m, Ph-CH), 5.96 (1H, t, $J =$ 11.2 Hz, PhCH=C<u>H</u>), 5.81 (1H, d, $J = 4.5$ Hz, -C=CH), 5.0–4.9 (2H, m, $=CH_2$), 4.51 (1H, d, $J = 15.4$ Hz, =C-CH_2O), 4.21 (1H, t, $J = 1.9$ Hz, CHO), 4.2–4.15 (1H, m, =C-CH_2O), 4.2–4.1 (2H, m, ≡C-CH_2O), 3.97 (1H, t, $J = 3.8$ Hz, CHO), 3.4–3.35 (1H, m, C<u>H</u>-CH=), 2.34 (1H, t, $J = 2.2$ Hz, HC≡), 2.3–2.2 (2H, m, C<u>H</u>C<u>H</u>$_2$), 1.6–1.5 (1H, m, CH_2); ^{13}C NMR: $\delta = 138.0$ ($C_{(cis)}$), 136.3 ($CH_{(trans)}$), 134.6 ($C_{(trans)}$), 134.5 ($C_{(trans)}$), 132.9 ($CH_{(trans)}$), 130.4 ($CH_{(trans)}$), 129.1 ($CH_{(cis)}$), 128.7 ($CH_{(cis)}$), 128.5 ($CH_{(trans)}$), 128.4 ($CH_{(cis)}$), 127.2 ($CH_{(trans)}$), 126.9 ($CH_{(cis)}$), 126.7 ($CH_{(trans)}$), 112.0 ($CH_{2(trans)}$), 81.3 ($CH_{(cis)}$), 81.0 ($CH_{(trans)}$), 80.2 ($C_{(trans)}$),

77.9 ($CH_{(cis)}$), 77.5 ($CH_{(trans)}$), 75.1 ($CH_{(trans)}$), 64.7 ($CH_{2(cis)}$), 64.6 ($CH_{2(trans)}$), 57.4 ($CH_{2(cis)}$), 57.2 ($CH_{2(trans)}$), 44.8 ($CH_{(trans)}$), 37.4 ($CH_{2(trans)}$), 36.4 ($CH_{(trans)}$); MS (CI): *m/z* = 324 ($M+NH_4^+$, 100), 307 (MH^+, 27); HRMS (ES): calcd. for $C_{21}H_{26}NO_2$ ($M+NH_4^+$): 324.1964; found: 324.1960.

Diene 10b

To a solution of diyne **2** (100 mg, 0.50 mmol) and 1-hexene (210 mg, 5 equiv.) in dry dichloromethane (37 mL) under an inert atmosphere at room temperature was added a solution of catalyst **1** (20.34 mg, 0.025 mmol) in dry dichloromethane (3 mL). The mixture was stirred at room temperature for 17 hours and the solvent was then removed under vacuum. The residue was purified by flash chromatography (CH_2Cl_2) to give compound **10b** as a colourless oil; yield: 55 g (49%). The *cis*- and *trans*-isomers could be separated during the chromatography. Data for the *trans*-isomer: IR (neat): ν_{max} = 3308 (s), 2958 (s), 2929 (s), 2872 (s), 2248 (m), 1648 (w), 1606 cm^{-1} (w); ^1H NMR: δ = 6.18 (1H, dd, *J* = 11.0, 18.0 Hz, H_2C=C<u>H</u>), 5.78 (1H, d, *J* = 5.2 Hz, CH-C<u>H</u>=C), 5.60 (1H, dd, *J* = 9.7, 15.2 Hz, CH-C<u>H</u>=CH), 5.26 (1H, dt, *J* = 6.8, 15.2 Hz, CH_2C<u>H</u>=), 4.91 (1H, d, *J* = 17.6 Hz, =$CH_{2(trans)}$), 4.90 (1H, d, *J* = 11.3 Hz, =$CH_{2(cis)}$), 4.45 (1H, d, *J* = 15.2 Hz, =C-CH_2O), 4.20 (1H, dd, *J* = 2.4, 16.1 Hz, OCH_2C≡), 4.17 (1H, dd, *J* = 2.4, 16.1 Hz, OCH_2C≡), 4.11 (1H, d, *J* = 15.0 Hz, =C-CH_2O), 4.13–4.09 (1H, m, CHO), 3.90 (1H, t, *J* = 4.0 Hz, CHO), 2.82 (1H, ddd, *J* = 5.8, 9.0, 14.6 Hz, C<u>H</u>-CH=CH), 2.34 (1H, t, *J* = 2.4 Hz, HC≡), 2.3–2.2 (1H, m, C<u>H</u>-CH=C), 2.17 (1H, dt, *J* = 9.1, 13.0 Hz, $CHC\underline{H}_2CH$), 1.94–1.90 (2H, m, =$CHC\underline{H}_2$), 1.42 (1H, ddd, *J* = 5.9, 9.4, 13.0 Hz, $CHC\underline{H}_2CH$), 1.3–1.15 (4H, m, $CH_3C\underline{H}_2C\underline{H}_2$), 0.80 (3H, t, *J* = 7.0 Hz, CH_3); ^{13}C NMR: δ =136.4 (CH), 134.4 (C), 132.4 (CH), 131.4 (CH), 128.8 (CH), 111.8 (CH_2), 80.8 (CH), 80.3 (C), 77.9 (CH), 74.9 (CH), 64.6 (CH_2), 57.0 (CH_2), 44.2 (CH), 37.4 (CH_2), 36.1 (CH), 32.5 (CH_2), 32.2 (CH_2), 22.6 (CH_2), 14.4 (CH_3); MS (CI): *m/z* = 322 ($M+NH_4^+$, 17), 304 (M^+, 100); HRMS (ES): calcd. for $C_{19}H_{30}NO_2$ ($M+NH_4^+$): 304.2277; found: 304.2282;. Data for the *cis*-isomer: IR (neat): ν_{max} = 3309 (s), 2957 (s), 2930 (s), 2872 (s), 2247 (w), 1606 cm^{-1} (m); ^1H NMR: δ = 6.18 (1H, dd, *J* = 11.0, 18.0 Hz, H_2C=C<u>H</u>), 5.78 (1H, d, *J* = 5.4 Hz, CH-C<u>H</u>=C), 5.62 (1H, t, *J* = 10.5 Hz, CH-C<u>H</u>=CH), 5.28 (1H, dt, *J* = 10.9, 7.3 Hz, H_2C-C<u>H</u>=), 4.91 (1H, d, *J* = 11.2 Hz, =$CH_{2(cis)}$), 4.90 (1H, d, *J* = 17.7 Hz, =$CH_{2(trans)}$), 4.44 (1H, d, *J* = 15.4 Hz, =CCH_2O), 4.22 (1H, dd, *J* = 2.4, 16.1 Hz, ≡$CC\underline{H}_2O$), 4.12 (1H, dd, *J* = 2.3, 16.1 Hz, ≡C-$C\underline{H}_2O$), 4.3–4.1 (2H, m, =CH_2O + CHO), 3.93 (1H, t, *J* = 4.0 Hz CHO), 3.2–3.1 (1H, m, C<u>H</u>-CH=), 2.34 (1H, t, *J* = 2.4 Hz, ≡CH), 2.31–2.28 (1H, m, C<u>H</u>-CH=), 2.17 (1H, dt, *J* = 12.9, 8.8 Hz, $CHC\underline{H}_2CH$), 2.0–1.9 (2H, m, =$CHC\underline{H}_2$), 1.39 (1H, ddd, *J* = 6.1, 9.6, 13.0 Hz, $CHC\underline{H}_2CH$), 1.3–1.2 (4H, m, $C\underline{H}_2C\underline{H}_2CH_3$), 0.80 (3H, t, *J* = 6.8 Hz, CH_3); ^{13}C NMR: δ = 136.3 (CH), 134.5 (C), 131.6 (CH), 129.8 (CH), 128.7 (CH), 111.8 (CH_2), 80.9 (CH), 80.3 (C), 77.7 (CH), 74.8 (CH), 64.6 (CH_2), 57.2 (CH_2), 37.9 (CH), 37.6 (CH_2), 36.4 (CH), 32.4 (CH_2), 27.2 (CH_2), 22.7 (CH_2), 14.4 (CH_3).

Diene 10c

To a solution of diyne **2** (100 mg, 0.50 mmol) and allyltrimethylsilane (286 mg, 5 equiv.) in dry dichloromethane (37 mL) under an inert atmosphere at room temperature was added a solution of catalyst **1** (20.34 mg, 0.025 mmol) in dry dichloromethane (3 mL). The mixture was stirred at room temperature for 17 hours and the solvent was then removed under vacuum. The residue was purified by flash chromatography (CH_2Cl_2) to give compound **10c** as a colourless oil; yield: 52 mg (70%). The *cis* and *trans*-isomers could be separated by a second flash column (eluting with CH_2Cl_2). Data for the *trans*-isomer: IR (neat): ν_{max} = 3308 (s), 2955 (s), 2248 (m), 1683 (m), 1648 cm^{-1} (m); ^1H NMR: δ = 6.28 (1H, dd, *J* = 11.0, 18.0 Hz, H_2C=C<u>H</u>), 5.88 (1H, d, *J* = 5.3 Hz, CH-C<u>H</u>=C), 5.55 (1H, dd, *J* = 15.2, 9.6 Hz, CH-C<u>H</u>=CH), 5.34 (1H, dt, *J* = 15.2, 7.9 Hz, CH_2C<u>H</u>=), 5.01 (1H, d, *J* = 17.5 Hz, =$CH_{2(trans)}$), 5.00 (1H, d, *J* = 11.4 Hz, =$CH_{2(cis)}$), 4.54 (1H, d, *J* = 15.4 Hz, =C-CH_2O), 4.33 (1H, dd, *J* = 2.4, 16.1 Hz, ≡C-CH_2O), 4.27 (1H, dd, *J* = 2.4, 16.14 Hz, ≡C-CH_2O), 4.23–4.17 (1H, m, =C-CH_2O), 4.18 (1H, dd, *J* = 4.2, 8.6 Hz, CHO), 3.99 (1H, t, *J* = 4.0 Hz, CHO), 2.90 (1H, dq, *J* = 9.0, 5.9 Hz, C<u>H</u>-CH=CH), 2.43 (1H, t, *J* = 2.4 Hz, ≡CH), 2.4–2.3 (1H, m, C<u>H</u>-CH=C), 2.24 (1H, dt, *J* = 12.8, 8.9 Hz, $CHC\underline{H}_2CH$), 1.50 (1H, ddd, *J* = 5.7, 9.3, 12.8 Hz, $CHC\underline{H}_2CH$), 1.44 (2H, dd, *J* = 1.0, 7.9 Hz, CH_2Si), 0.01 [9H, s, $Si(CH_3)_3$]; ^{13}C NMR: δ = 137.9 (CH), 136.0 (C), 132.5 (CH), 130.3 (CH), 128.4 (CH), 113.3 (CH_2), 82.3 (CH), 79.4 (CH), 81.9 (C), 76.3 (CH), 66.1 (CH_2), 58.6 (CH_2), 46.0 (CH), 39.4 (CH_2), 37.7 (CH), 24.4 (CH_2) 0.0 (CH_3); MS (CI): *m/z* = 334 ($M+NH_4^+$, 100), 264 (98); HRMS (ES): calcd. for $C_{19}H_{29}O_2Si$ (MH^+): 317.1937; found: 317.1942. Data for the *cis*-isomer: IR (neat): ν_{max} = 3309 (s), 2954 (s), 2246 (w), 1645 (m), 1606 cm^{-1} (w); ^1H NMR: δ = 6.25 (1H, dd, *J* = 11.1, 18.0 Hz, H_2C=C<u>H</u>), 5.85 (1H, d, *J* = 5.4 Hz, CH-C<u>H</u>=C), 5.62 (1H, t, *J* = 10.6 Hz, CH-C<u>H</u>=CH), 5.37 (1H, dt, *J* = 10.6, 7.8 Hz, CH_2C<u>H</u>=), 4.98 (1H, d, *J* = 17.7 Hz, =$CH_{2(trans)}$), 4.97 (1H, d, *J* = 11.3 Hz, =$CH_{2(cis)}$), 4.52 (1H, d, *J* = 15.3 Hz, =CCH_2O), 4.29 (1H, dd, *J* = 2.4, 16.1 Hz, ≡CCH_2O), 4.19 (1H, dd, *J* = 2.4, 16.1 Hz, ≡CCH_2O), 4.23–4.16 (2H, m, =C-CH_2O + CHO), 4.00 (1H, t, *J* = 4.0 Hz, CHO), 3.2–3.1 (1H, m, C<u>H</u>-CH=CH), 2.41 (1H, t, *J* = 2.4 Hz, ≡CH), 2.35-2.30 (1H, m, C<u>H</u>-CH=C), 2.23 (1H, dt, *J* = 12.9, 8.8 Hz, $CHC\underline{H}_2CH$), 1.46 (1H, ddd, *J* = 5.9, 9.7, 12.9 Hz, $CHC\underline{H}_2CH$), 1.39 (1H, dd, *J* = 1.5, 7.3 Hz, CH_2Si), 1.35 (1H, dd, *J* = 1.5, 7.3 Hz, CH_2Si), 0.00 [9H, s, $Si(CH_3)_3$]; ^{13}C NMR: δ = 137.7 (CH), 135.8 (C), 130.9 (CH), 130.2 (CH), 126.6 (CH), 113.2 (CH_2), 82.2 (CH), 81.7 (C), 79.2 (CH), 76.2 (CH), 66.0 (CH_2), 58.6 (CH_2), 39.4 (CH_2), 38.9 (CH), 37.8 (CH), 19.9 (CH_2), 0.0 (CH_3).

Anhydride 11a

To a solution of diyne **2** (100 mg, 0.50 mmol) and styrene (260 mg, 5 equiv.) in dry dichloromethane (37 mL) under an inert atmosphere at room temperature was added a solution of catalyst **1** (20.34 mg, 0.025 mmol) in dry dichloromethane (3 mL). The mixture was stirred at room temperature for 16 hours, after which time a solution of maleic anhydride (108 mg, 2.2 equiv.) in ethyl acetate (5 mL) was added. The reaction was stirred at room temperature for a further 24 hours, and the solvent was then removed under vacuum. The residue was purified by flash chromatography (CH_2Cl_2) to leave compound **11a** as a 3:1 ratio of *trans*- and *cis*-isomers as a colourless oil; yield: 50 mg (25%). IR (neat): ν_{max} = 3026 (m), 2854 (s), 1845 (m), 1778 (s), 1710 cm^{-1} (s); ^1H NMR: δ (*trans*-isomer) = 7.3–7.1 (5H, m, ArCH), 6.4–6.3 (2H, m, PhCH=CH), 5.66 (1H, m, CH_2C<u>H</u>=), 4.30 (1H, dd, *J* = 15.9,

2.3 Hz, $OCH_2C\equiv$), 4.19 (1H, dd, $J=15.9$, 2.3 Hz, $OCH_2C\equiv$), 4.35 – 4.15 (1H, m, CHO), 4.1 – 3.8 (3H, m, CHO + $=CCH_2O$), 3.4 – 3.3 (2H, m, O=CCHCHC=O), 2.8 – 2.6 (3H, m, C<u>H</u>-CH_2-C<u>H</u> + =CH-C<u>H_2</u>), 2.5 – 2.4 (1H, m, CH-C=), 2.4 – 2.3 (1H, m, CH-C<u>H_2</u>-CH), 2.29 (1H, t, $J=2.4$ Hz, ≡CH), 2.21 (1H, dd, $J=3.1$, 15.3 Hz, =CH-C<u>H_2</u>), 1.62 (1H, dt, $J=7.1$, 12.2 Hz, CH-C<u>H_2</u>-CH); δ (*cis*-isomer) = 7.3 – 7.1 (5H, m, ArCH), 6.47 (1H, d, $J=11.6$ Hz, Ph-CH=), 5.82 (1H, dd, $J=9.8$, 11.6 Hz, Ph-CH=C<u>H</u>), 5.66 (1H, m, CH_2C<u>H</u>=), 4.30 (1H, dd, $J=15.9$, 2.3 Hz, $OCH_2C\equiv$), 4.19 (1H, dd, $J=15.9$, 2.3 Hz, $OCH_2C\equiv$), 4.35 – 4.15 (1H, m, CHO), 4.08 – 3.85 (3H, m, CHO + $=CCH_2O$), 3.4 – 3.3 (2H, m, O=CCHCHC=O), 2.8 – 2.6 (3H, m, C<u>H</u>-CH_2-C<u>H</u> + =CH-C<u>H_2</u>), 2.5 – 2.4 (1H, m, CH-C=), 2.4 – 2.3 (1H, m, CH-C<u>H_2</u>-CH), 2.29 (1H, t, $J=2.4$ Hz, ≡CH), 2.21 (1H, dd, $J=3.1$, 15.3 Hz, =CH-C<u>H_2</u>), 1.62 (1H, dt, $J=12.2$, 7.1 Hz, CH-C<u>H_2</u>-CH); ^{13}C NMR: δ = 174.5 ($C_{(trans)}$), 172.1 ($C_{(trans)}$), 139.3 ($C_{(trans)}$), 137.9 ($C_{(trans)}$), 131.6 ($CH_{(trans)}$), 131.2 ($CH_{(cis)}$), 130.6 ($CH_{(trans)}$), 129.9 ($CH_{(cis)}$), 128.9 ($CH_{(trans)}$), 128.8 ($CH_{(cis)}$), 128.7 ($CH_{(trans)}$), 127.5 ($CH_{(cis)}$), 127.2 ($CH_{(trans)}$), 126.6 ($CH_{(cis)}$), 119.8 ($CH_{(trans)}$), 119.7 ($CH_{(cis)}$), 83.0 ($CH_{(trans)}$), 82.8 ($CH_{(cis)}$), 82.4 ($CH_{(trans)}$), 82.3 ($CH_{(cis)}$), 80.9 ($C_{(trans)}$), 80.85 ($C_{(cis)}$), 74.32 ($CH_{(trans)}$), 74.28 ($CH_{(cis)}$), 68.13 ($CH_{2(trans)}$), 68.08 ($CH_{2(cis)}$), 59.35 ($CH_{2(trans)}$), 59.31 ($CH_{2(cis)}$), 42.8 ($CH_{(trans)}$), 42.7 ($CH_{(trans)}$), 40.47 ($CH_{(cis)}$), 44.04 ($CH_{(cis)}$), 38.95 ($CH_{(trans)}$), 38.66 ($CH_{(cis)}$), 37.18 ($CH_{2(trans)}$), 36.48 ($CH_{2(trans)}$), 33.20 ($CH_{(trans)}$), 24.20 ($CH_{2(trans)}$); MS (EI): $m/z=404$ (M^+, 73), 273 (100); HRMS (ES): calcd. for $C_{25}H_{28}NO_5$ ($M+NH_4^+$): 422.1967; found: 422.1969.

Anhydride 11b

To a solution of diyne **2** (100 mg, 0.50 mmol) and 1-hexene (210 mg, 5 equiv.) in dry dichloromethane (37 mL) under an inert atmosphere at room temperature was added a solution of catalyst **1** (20.34 mg, 0.025 mmol) in dry dichloromethane (3 mL). The mixture was stirred at room temperature for 16 hours, after which time a solution of maleic anhydride (108 mg, 2.2 equiv.) in ethyl acetate (5 mL) was added. The reaction was stirred at room temperature for a further 20 hours, and the solvent was then removed under vacuum. The residue was purified by flash chromatography (CH_2Cl_2) to leave compound **11b** as a 3:1 ratio of *trans*- and *cis*-isomers as a colourless oil; yield: 70 mg (38%). IR (neat): $\nu_{max}=3305$ (s), 2928 (s), 2859 (s), 1845 (m), 1777 (s), 1728 cm^{-1} (s); ^{1}H NMR: δ = 5.65 (1H, br s, C=CH), 5.5 – 5.3 (2H, m, CH=CH), 4.3 – 4.1 (3H, m, CHO + $OCH_2C\equiv$), 4.05 (1H, d, $J=13.3$ Hz, $=CCH_2O$), 3.9 – 3.8 (2H, m, $=CCH_2O$ + CHO), 3.37 – 3.36 (2H, m, O=C-CH-CH-C=O), 2.7 – 2.65 (2H, m, CH_2C<u>H</u> + C<u>H_2</u>-CH=C), 2.5 – 2.45 (2H, m, C<u>H</u>-CH=CH + C<u>H</u>-C=CH), 2.29 (1H, t, $J=2.4$ Hz, ≡CH), 2.27 – 2.21 (2H, m, C<u>H_2</u>-CH=C + CH-C<u>H_2</u>-CH), 2.0 – 1.9 (2H, m, C<u>H_2</u>-CH=CH), 1.5 – 1.4 (1H, m, CH-C<u>H_2</u>-CH), 1.27 – 1.25 (4H, m, CH_3C<u>H_2CH$_2$</u>), 0.9 – 0.8 (3H, m, CH_3); ^{13}C NMR: δ = 174.5 ($C_{(trans)}$), 172.0 ($C_{(trans)}$), 139.5 ($C_{(trans)}$), 132.4 ($CH_{(trans)}$), 131.8 ($CH_{(cis)}$), 129.1 ($CH_{(trans)}$), 128.5 ($CH_{(cis)}$), 119.7 ($CH_{(trans)}$), 82.8 ($CH_{(trans)}$), 82.7 ($CH_{(cis)}$), 82.5 ($CH_{(trans)}$), 81.0 ($C_{(trans)}$), 74.0 ($CH_{(trans)}$), 68.1 ($CH_{2(trans)}$), 59.3 ($CH_{2(trans)}$), 59.2 ($CH_{2(cis)}$), 43.6 ($CH_{(trans)}$), 42.7 ($CH_{(trans)}$), 40.5 ($CH_{(trans)}$), 38.7 ($CH_{(trans)}$), 38.2 ($CH_{(cis)}$), 36.9 ($CH_{2(trans)}$), 36.5 ($CH_{2(cis)}$), 33.1 ($CH_{(trans)}$), 32.7 ($CH_{2(trans)}$), 32.3 ($CH_{2(cis)}$), 32.0 ($CH_{2(trans)}$), 28.0 ($CH_{2(cis)}$), 24.2 ($CH_{2(trans)}$), 22.7 ($CH_{2(trans)}$), 22.5 ($CH_{2(cis)}$), 14.4 ($CH_{3(cis)}$), 14.3 ($CH_{3(trans)}$); MS (CI): $m/z=402$ ($M+NH_4^+$, 100), 385 (MH^+, 28); HRMS (ES): calcd. for $C_{23}H_{32}NO_5$ ($M+NH_4^+$): 402.2280; found: 402.2268.

Anhydride 11c

To a solution of diyne **2** (100 mg, 0.50 mmol) and allyltrimethylsilane (285 mg, 5 equiv.) in dry dichloromethane (37 mL) under an inert atmosphere at room temperature was added a solution of catalyst **1** (20.34 mg, 0.025 mmol) in dry dichloromethane (3 mL). The mixture was stirred at room temperature for 6 hours, after which time a solution of maleic anhydride (108 mg, 2.2 equiv.) in ethyl acetate (5 mL) was added. The reaction was stirred at room temperature for a further 20 hours, and the solvent was then removed under vacuum. The residue was purified by flash chromatography (CH_2Cl_2) to leave compound **11c** as a 3:1 ratio of *trans*- and *cis*-isomers as a colourless oil; yield: 64 mg (31%). IR (neat): $\nu_{max}=3304$ (s), 2954 (s), 2858 (s), 1778 (s), 1710 cm^{-1} (s); ^{1}H NMR: δ = 5.73 (1H, dd, $J=2.1$, 4.2 Hz, C=CH), 5.5 – 5.4 (2H, m, CH=CH), 4.4 – 4.2 (3H, m, $=C$-CH_2O + CHO), 4.12 (1H, dd, $J=13.2$, 2.4 Hz, $OCH_2C\equiv$), 4.0 – 3.9 (2H, m, $OCH_2C\equiv$ + CHO), 3.5 – 3.4 (2H, m, O=C-CH-CH-C=O), 2.9 – 2.7 (2H, m, C<u>H_2</u>-CH=C + $CHCH_2C$<u>H</u>), 2.6 – 2.5 (2H, m, =CC<u>H</u>$CHCH_2C$<u>H</u>), 2.4 – 2.3 (3H, m, ≡CH + C=CHC<u>H_2</u> + CHC<u>H_2</u>CH), 1.6 – 1.5 (1H, m, CHC<u>H_2</u>CH), 1.46 (2H, d, $J=6.9$ Hz, $SiCH_2$), 0.02 [9H, s, $Si(CH_3)_3$]; ^{13}C NMR: δ = 176.1 ($C_{(trans)}$), 173.6 ($C_{(trans)}$), 141.1 ($C_{(trans)}$), 129.8 ($CH_{(trans)}$), 128.9 ($CH_{(cis)}$), 129.1 ($CH_{(trans)}$), 127.8 ($CH_{(cis)}$), 121.2 ($CH_{(trans)}$), 84.4 ($CH_{(trans)}$), 84.3 ($CH_{(cis)}$), 84.3 ($CH_{(trans)}$), 84.2 ($CH_{(cis)}$), 82.6 ($C_{(trans)}$), 75.6 ($CH_{(trans)}$), 69.6 ($CH_{2(trans)}$), 60.8 ($CH_{2(trans)}$), 60.7 ($CH_{2(cis)}$), 45.5 ($CH_{(trans)}$), 44.2 ($CH_{(trans)}$), 42.0 ($CH_{(trans)}$), 40.3 ($CH_{(trans)}$), 39.6 ($CH_{(cis)}$), 38.3 ($CH_{2(trans)}$), 34.6 ($CH_{(trans)}$), 34.5 ($CH_{(cis)}$), 25.7 ($CH_{2(trans)}$), 24.8 ($CH_{2(cis)}$), 21.0 ($CH_{2(trans)}$), 0.0 ($CH_{3(trans)}$); MS (CI): $m/z=432$ ($M+NH_4^+$, 52), 415 (MH^+, 18), 90 (100); HRMS (ES): calcd. for $C_{23}H_{34}NO_5Si$ ($M+NH_4^+$): 432.2206; found: 432.2200.

Diene 12

To a solution of diyne **7** (50 mg, 0.22 mmol) and allyltrimethylsilane (139 mg, 5 equiv.) in dry dichloromethane (18 mL) under an inert atmosphere at room temperature was added a solution of catalyst **1** (9.0 mg, 0.011 mmol) in dry dichloromethane (3 mL). The solution was stirred at room temperature for 18 hours after which time additional catalyst **1** (9.0 mg, 0.011 mmol) was added and the solution stirred for a further 24 hours. The solvent was then removed under vacuum and the residue was purified by flash chromatography (CH_2Cl_2) to leave compound **12** as a 1:1 mixture of *trans*- and *cis*-isomers as a colourless oil; yield: 20 mg (25%). IR (neat): $\nu_{max}=2952$ (s), 1938 (w), 1716 (m), 1638 (m), 1609 cm^{-1} (m); ^{1}H NMR: δ (*trans*-isomer) = 5.94 (1H, d, $J=5.3$ Hz, C=CH), 5.56 (1H, dd, $J=15.1$, 9.7 Hz, CH-C<u>H</u>=CH), 5.4 – 5.3 (1H, m, CH_2-C<u>H</u>=), 4.87 (1H, s, $=CH_2$), 4.78 (1H, s, $=CH_2$), 4.55 (1H, d, $J=15.2$ Hz, OCH_2-C=), 4.3 – 4.0 (3H, m, OCH_2-C= + $OCH_2C\equiv$), 4.0 – 3.9 (2H, m, OCHCHO), 3.0 – 2.8 (1H, m, C<u>H</u>-CH=C), 2.4 – 2.3 (1H, m, C<u>H</u>-CH=C), 2.3 – 2.2 (1H, m, CHC<u>H_2</u>CH), 1.91 (3H, s, CH_3-C=), 1.85 (3H, t, $J=2.3$ Hz, CH_3-C≡), 1.4 – 1.3 (3H, m, CHC<u>H_2</u>CH + $SiCH_2$), 0.03 [9H, s, $Si(CH_3)_3$]; δ_H (*cis*-isomer) = 5.94 (1H, d, $J=5.3$ Hz, C=CH), 5.64 (1H, t $J=10.7$ Hz, CH-C<u>H</u>=CH), 5.4 – 5.3 (1H, m, CH_2-C<u>H</u>=), 4.87 (1H, s,

=CH_2), 4.78 (1H, s, =CH_2), 4.55 (1H, d, J = 15.2 Hz, OCH_2-C=), 4.3 – 4.05 (3H, m, OCH_2-C= + OCH_2C≡), 3.95 – 3.9 (2H, m, OCHCHO), 3.2 – 3.1 (1H, m, C<u>H</u>-CH=C), 2.4 – 2.3 (1H, m, C<u>H</u>-CH=C), 2.3 – 2.2 (1H, m, CHC<u>H_2</u>CH), 1.88 (3H, s, CH_3-C=), 1.85 (3H, t, J = 2.3 Hz, CH_3-C≡), 1.4 – 1.3 (3H, m, CHC<u>H_2</u>CH + $SiCH_2$), 0.00 [9H, s, $Si(CH_3)_3$]; ^{13}C NMR: δ_C = 140.23 ($C_{(cis)}$), 140.19 ($C_{(trans)}$), 134.9 ($C_{(cis)}$), 134.8 ($C_{(trans)}$), 133.8 ($CH_{(trans)}$), 131.0 ($CH_{(cis)}$), 129.5 ($CH_{(cis)}$), 126.2 ($CH_{(trans)}$), 124.5 ($CH_{(cis)}$), 124.3 ($CH_{(trans)}$), 118.01 ($CH_{2(trans)}$), 110.2 ($CH_{2(cis)}$), 82.9 ($C_{(trans)}$), 82.3 ($C_{(cis)}$), 80.4 ($CH_{(cis)}$), 80.3 ($CH_{(trans)}$), 77.3 ($CH_{(cis)}$), 77.2 ($CH_{(trans)}$), 76.4 ($C_{(cis)}$), 75.4 ($C_{(trans)}$), 70.8 ($CH_{2(trans)}$), 65.2 ($CH_{2(cis)}$), 57.4 ($CH_{2(cis)}$), 57.2 ($CH_{2(trans)}$), 44.0 ($CH_{(trans)}$), 37.7 ($CH_{2(cis)}$), 37.6 ($CH_{2(trans)}$), 37.1 ($CH_{(cis)}$), 36.0 ($CH_{(cis)}$), 35.7 ($CH_{(trans)}$), 22.4 ($CH_{2(trans)}$), 20.2 ($CH_{3(trans)}$), 18.1 ($CH_{2(cis)}$), 3.7 ($CH_{(trans)}$), 3.6 ($CH_{(cis)}$), −1.8 ($CH_{3(cis)}$), −1.9 ($CH_{3(trans)}$); MS (CI): m/z = 362 ($M + NH_4^+$, 6), 345 (MH^+, 10), 90 (100); HRMS (ES): calcd. for $C_{21}H_{36}NO_2Si$ ($M + NH_4^+$): 362.2515; found: 362.2516.

Di-yne 16

To a stirring solution of diol **17** (1.200 g, 7.86 mmol) in DMF (10 mL) at 0 °C was added NaH (54.6 mg, 22.8 mmol). After 1 hour, propargyl bromide (4.638 g, 22.5 mmol) was added. The mixture was warmed to room temperature and stirred for 23 hours, then it was partitioned between water (10 mL) and ether (10 mL). The aqueous layer was extracted with Et_2O (4 × 12 mL), dried ($MgSO_4$) and evaporated under vacuum. The residue was purified by column chromatography (CH_2Cl_2/MeOH, 99.5:0.5) affording dipropargyl ether **16** as a colourless oil; yield: 520 mg (61%). The product could be purified by distillation with a yield of 82%. IR (neat): ν_{max} = 3295 (s), 2961 (s), 1677 cm^{-1} (s); ^{1}H NMR: δ = 6.09 – 6.08 (2H, m, CH=CH), 4.03 – 4.02 (4H, m, OCH_2C≡), 3.3 – 3.1 (4H, m, OC<u>H_2</u>CH), 2.87 – 2.86 (2H, m, =HC-C<u>H</u>), 2.45 – 2.37 (2H, m, OCH_2C<u>H</u>), 2.35 (2H, t, J = 2.3 Hz, ≡CH), 1.4 – 1.2 (2H, m, CHC<u>H_2</u>CH); ^{13}C NMR: δ = 135.7 (CH), 80.4 (C), 74.5 (CH), 70.6 (CH_2), 58.5 (CH_2), 49.3 (CH_2), 46.7 (CH), 41.8 (CH); MS (CI): m/z = 248 ($M + NH_4^+$, 100); 231 (MH^+, 20); HRMS (ES): calcd. for $C_{15}H_{19}O_2$ ($M + H^+$): 231.1385; found: 231.1384.

Metathesis of 16 to give 18 and 19

A solution of diyne **16** (100 mg, 0.44 mmol) in dry dichloromethane (20 mL) was cooled to −78 °C and ethene was passed through the solution for 10 minutes. A solution of catalyst **1** (21.44 mg, 6 mol %) in dry dichloromethane (2 mL) was then added and after 15 minutes the mixture was warmed to room temperature and stirred for 20 hours. The solvent was then removed under vacuum and the residue subjected to flash chromatography (CH_2Cl_2, then EtOAc) to give compounds **18** (yield: 29 mg, 26%) and **19** (yield: 28 mg, 25%) as colourless oils.

Data for compound **18**: IR (neat): ν_{max} = 3075 (m), 2929 (s), 2872 (s), 1719 (s), 1674 (m), 1638 cm^{-1} (s); ^{1}H NMR: δ = 5.82 (2H, ddd, J = 8.5, 10.1, 18.6 Hz, =CH), 4.94 (2H, ddd, J = 1.0, 2.0, 17.1 Hz, =$CH_{2(trans)}$), 4.89 (2H, ddd, J = 0.7, 2.0, 10.1 Hz, =$CH_{2(cis)}$), 4.06 (2H, dd, J = 2.3, 15.8 Hz, OCH_2C≡), 4.01 (2H, dd, J = 2.3, 15.8 Hz, OCH_2C≡), 3.49 (2H, dd, J = 6.5, 9.4 Hz, OC<u>H_2</u>CH), 3.45 (2H, dd, J = 5.2, 9.4 Hz, OC<u>H_2</u>CH), 2.7 – 2.6 (2H, m, C<u>H</u>-CH=), 2.4 – 2.3 (2H, m, OCH_2C<u>H</u>), 2.34 (2H, t, J = 2.4 Hz, ≡CH), 1.91 (1H, dt, J = 13.1, 8.2 Hz, CHC<u>H_2</u>CH), 1.52 (1H, dt, J = 13.1, 10.0 Hz, CHC<u>H_2</u>CH); ^{13}C NMR: δ = 140.4 (CH_2), 114.5 (CH), 80.1 (C), 74.1 (CH), 68.4 (CH_2), 58.1 (CH_2), 45.3 (CH), 45.2 (CH), 37.1 (CH_2); MS (CI): m/z = 276 ($M + NH_4^+$, 100), 259 (MH^+, 1.1); HRMS (ES): calcd. for $C_{17}H_{23}O_2$ (MH^+): 259.1698; found: 259.1696.

Data for compound **19**: IR (neat): ν_{max} = 2934 (s), 1721 (s), 1677 (m), 1638 cm^{-1} (m); ^{1}H NMR: δ = 6.15 (1H, dd, J = 10.2, 17.8 Hz, =C-C<u>H</u>=CH_2), 5.8 – 5.7 (1H, m, CH-C<u>H</u>=CH_2), 5.62 (1H, d, J = 4.7 Hz, C=C<u>H</u>-CH), 5.0 – 4.9 (2H, m, =CH_2), 4.9 – 4.8 (2H, m, =CH_2), 4.47 (1H, d, J = 15.8 Hz, CH_2O), 4.29 (1H, d, J = 15.8 Hz, CH_2O), 4.1 – 3.9 (4H, m, 2 × OCH_2), 3.4 – 3.3 (2H, m, OCH_2), 3.0 – 2.6 (2H, m, C<u>H</u>CH_2C<u>H</u>), 2.4 – 2.3 (1H, m, C<u>H</u>CH_2O), 2.32 (1H, s, ≡CH), 2.3 – 2.2 (1H, m, C<u>H</u>CH_2O), 2.2 – 2.1 (1H, m, CHC<u>H_2</u>CH), 1.5 – 1.4 (1H, m, CHC<u>H_2</u>CH); ^{13}C NMR: δ = 140.0 (CH), 139.4 (CH), 136.4 (CH), 135.2 (CH_2), 115.4 (C), 110.8 (CH_2), 74.8 (C), 70.8 (CH_2), 69.5 (CH_2), 68.6 (CH_2), 58.5 (CH_2), 47.9 (CH), 45.7 (CH), 45.4 (CH), 40.3 (CH), 39.5 (CH_2) 26.2 (CH); MS (CI, isobutane): m/z = 259 (MH^+, 62), 221 (86), 203 (91), 91 (98), 79 (100).

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