Modification of Terpenoid Derivatives with Ruthenium Catalysts Generated in situ

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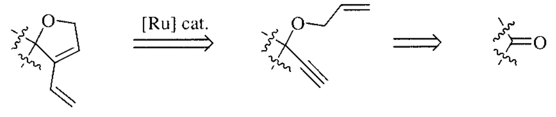
Keywords: Homogeneous catalysis / Rearrangement / Ruthenium / Terpenoids

Terpenoids derivatives containing geminal ethynyl and allyloxy groups are easily prepared from the corresponding ketones and aldehydes. The catalytic system generated in situ from $[RuCl_2(p\text{-cymene})]_2$, 1,3-bis(mesityl)imidazolinium chloride and cesium carbonate is able to transform these substrates into a new class of terpenoids via cycloisomerisation of the enyne structure.

Introduction

The selective formation of carbon−carbon bonds with concomitant construction of a conjugated diene system by enyne cycloisomerization represents a powerful tool in synthetic organic chemistry.[1−3] This catalytic reaction is mostly performed with alkene metathesis ruthenium catalysts,[4] and constitutes a key step for the synthesis or modification of natural products such as amino acids,[5a,5b] alkaloids,[5c,5d] steroids,[5e,5f] peptides[5g] and carbohydrates.[5h] On the other hand, terpenes and terpenoids represent a large class of natural compounds with noticeable and distinctive organoleptic properties.[6] Their simple chemical modification offers the possibility of producing unprecedented flavours or fragrances. Natural terpenoids have already been modified through organic transformations to produce insecticides,[7] and through metal-mediated reactions such as hydrogenation, isomerisation, oxidation, hydride reduction or hydroformylation.[8] The ring closing metathesis reaction has been used to form modified terpenoids from dienes,[9] but to the best of our knowledge no example of transformation by intramolecular enyne cycloisomerisation has been reported. However, after simple addition of C_5 units to terpenoids, the intramolecular enyne rearrangement catalysed by metathesis catalysts has the potential to generate a new class of nonnatural terpenoids.

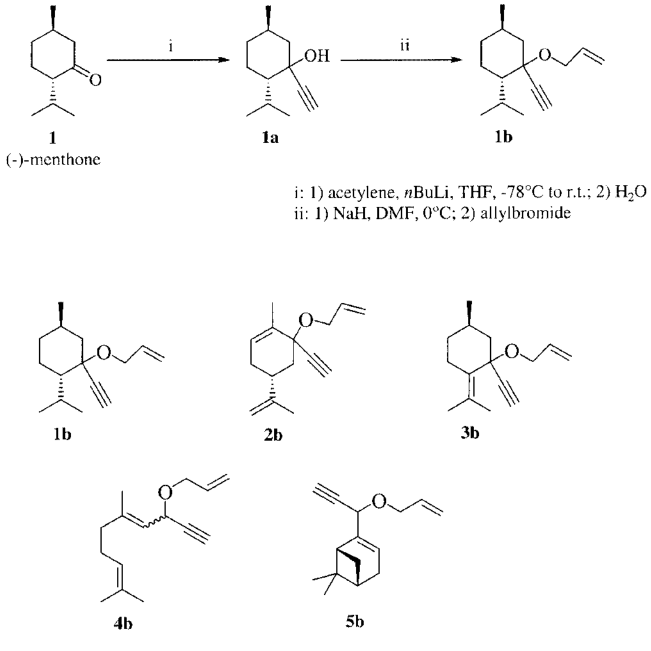
We now wish to report that terpenoids bearing a carbonyl functionality can easily be transformed with addition of a C_5 fragment into spiro compounds containing both a dihydrofuran ring and a diene moiety by enyne rearrangement in the presence of a simple three component ruthenium catalytic system generated in situ (Scheme 1).



Scheme 1. Retrosynthetic strategy

Results and Discussion

We have recently shown the efficiency of $[RuCl(=C=C=CPh_2)(p\text{-cymene})(PCy_3)][PF_6]$ to catalyse the skeleton rearrangement of allyl propargyl ethers into vinyldihydrofurans.[3] The use of the triflate salt, which was found to be a



Scheme 2. Preparation of allyl propargyl ethers **1b**−**5b**

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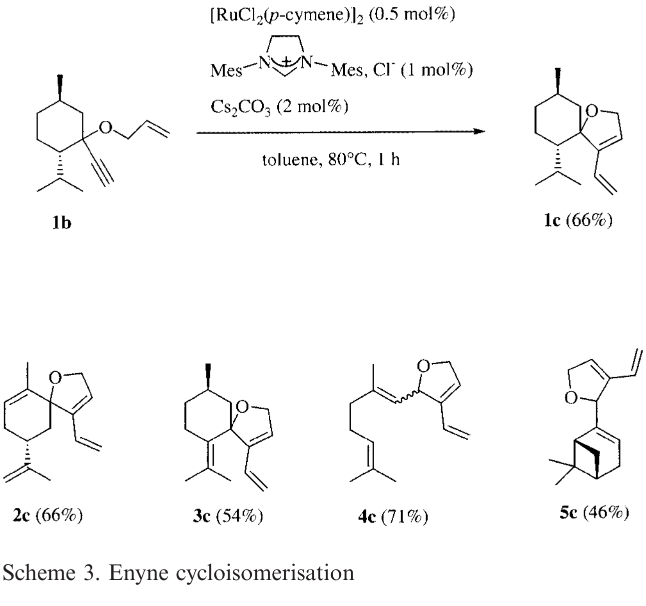
more active catalyst than the hexafluorophosphate salt for olefin metathesis,[10] made the metathesis of terpenoid enyne derivatives, possible. The preparation of the starting enynes derived from terpenoids was carried out in two steps from ketones or aldehydes by addition of lithium acetylide followed by allylation with allyl bromide (Scheme 2). Most of the intermediate propargylic alcohols **1a−5a** were already known and prepared according to similar procedures.[11] This two step transformation provided an efficient method to produce the new enynes **1b**, **2b**, **3b**, **4b** and **5b** arising from (−)-menthone (**1**), (−)-carvone (**2**), (+)-pulegone (**3**), citral (*cis* + *trans*) (**4**) and (−)-myrtenal (**5**) isolated in 85, 87, 65, 64, and 65% overall yields, respectively.

The propargylic alcohols **1a−5a** were obtained as a mixture of stereoisomers in the ratios 1:2 (**1a** and **3a**), or 1:1 (**2a**, **4a**, and **5a**), as detected from the ^{1}H NMR signal of the ethynyl proton. Consequently, the corresponding allyl ethers and cyclized compounds were obtained as mixtures of stereoisomers. The citral derivatives **4a**, **4b**, **4c** were obtained as a 1:1 mixture of the *cis* and *trans* isomers, identical to the initial ratio in the starting citral (GC-MS detection).

A complete conversion of the enynes **1b, 2b** and **4b** into **1c**, **2c** and **4c** was obtained after heating in toluene at 80 °C for 24 h in the presence of 2.5 mol % of $[RuCl(=C=C=CPh_2)(p\text{-cymene})(PCy_3)][OTf]$, after an initial activation of the precatalyst by irradiation with a UV lamp (λ = 300 nm) for 30 min.[3]

Recent studies have shown that new catalytic systems generated in situ from a source of ruthenium, a precursor of diaminocarbene and a base, were more efficient for enyne metathesis than the well-defined allenylidene catalyst precursors.[12,13] Indeed, a much more active catalytic system was generated by mixing $[RuCl_2(p\text{-cymene})]_2$, 1,3-bis(mesityl)imidazolinium chloride and cesium carbonate in the molar ratio 1:2:4.[13] In toluene at 80 °C in the presence of a catalytic system containing 0.5 mol % of the ruthenium complex, the complete transformation of 0.5 mmol of the enynes **1b**, **2b**, **3b** or **4b** was achieved within 1, 2, 2 and 1 h (Scheme 3) to give the corresponding spirocycles **1c**, **2c**, **3c** or **4c**, which were isolated in 66, 66, 54 and 71% yield, respectively. Under similar conditions, the conversion of the enyne **5b** derived from the more bulky (−)-myrtenal (**5**) was very slow, but the use of the catalyst arising from 2.5 mmol % of $[RuCl_2(p\text{-cymene})]_2$ allowed a conversion of 84% after 21 h at 80 °C and the corresponding cyclic compound **5c** was isolated with 46% yield.



Scheme 3. Enyne cycloisomerisation

Conclusion

The catalyst, easily prepared from a ruthenium source and a bulky heterocarbene ligand makes possible the preparation of modified terpenoids containing additional spirocyclic structure including a conjugated diene arrangement suitable for further cycloaddition reactions.[12−14] The facile introduction of five carbon atoms to terpene ketones and aldehydes by successive addition of the ethynyl (C_2) and allyl group (C_3) leads to new propargylic enynes, and then after rearrangement by catalytic cycloisomerisation to a new class of higher terpenoids (from monoterpenoids to sesquiterpenoids). As the stereoselectivity of the formation of terpenoid derivatives bearing a propargylic alcohol functionality can be controlled by the addition of alkynylcerate,[15] the formation of spirocycles in enantiomerically enriched forms can be envisaged.

Experimental Section

General Remarks: All experiments were carried out in Schlenk tubes under an inert atmosphere of nitrogen. The solvents were dried and distilled prior to use. ^{1}H and ^{13}C NMR were recorded with a Bruker AC 200 MHz spectrometer and GC-MS were performed with a CE Instrument GC 8000 Top (capillary column OV1, 25 m × 0.35 mm, 0.1−0.15 μm) chromatograph linked to a Automass II Finnigan MAT (70 eV) apparatus.

General Procedure for the Preparation of Allyl Propargyl Ethers 1b−5b: Acetylene (3−5 equiv.) was dissolved in tetrahydrofuran (2 mL per mmol of ketone) at −78 °C and *n*-butyllithium (1.6 M in *n*-hexane, 1.2 equiv.) was added dropwise. After 30 min at −78 °C, the ketone **1−3** or the aldehyde **4**,**5** was slowly added to the acetylide suspension and the reaction was stirred at −78 °C for 1 h and then allowed to warm up at room temperature. After quenching with 1 N HCl and extraction, the corresponding propargylic alcohol was isolated in good yield after flash chromatography over silica gel. Subsequent treatment with NaH (1.2 equiv.) at 0 °C in dimethylformamide for 30 min and addition of 1.3 equivalent of allyl bromide afforded the enynes **1b−5b** after flash column chromatography on silica gel.

1-Allyloxy-1-ethynyl-2-isopropyl-5-methylcyclohexane (1b): (−)-Menthone (**1**, 2.6 g, 17.1 mmol) was treated as described in the general procedure to give, after column chromatography on silica gel (eluent: heptane/diethyl ether, 50:1), the enyne **1b** in 85% yield (3.2 g, 14.5 mmol) as a colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.83 (d, ^3J = 6.6 Hz, 3 H, CH_3), 0.92 and 0.93 [2 d, ^3J = 7.0 Hz, 6 H, $CH(CH_3)_2$], 1.04−1.18 [m, 1 H, $CH_2CH(CH_3)$], 1.25−1.80 (m, 6 H, 3 × CH_2), 2.13−2.24 [m, 1 H, $CHCH(CH_3)_2$], 2.43 (s, 1 H, $C{\equiv}CH$), 2.40 [hept × d, ^3J = 6.9, $^3J'$ = 1.8 Hz, 1 H,

$CHC\mathit{H}(CH_3)_2]$, 3.82−4.20 (m, 2 H, $OC\mathit{H}_2CH{=}CH_2$), 5.09 (dm, ^3J = 10.4 Hz, *cis* 1 H, $OCH_2CH{=}C\mathit{H}_2$), 5.30 (dm, ^3J = 18.3 Hz, *trans* 1 H, $OCH_2CH{=}C\mathit{H}_2$), 5.81−6.01 (m, 1 H, $OCH_2C\mathit{H}{=}CH_2$) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.6 (2 × CH_3), 20.3 [$(CH_3)_2CHCH\mathit{C}H_2CH_2$], 21.9 [$CH_2CH_2\mathit{C}H(CH_3)$], 23.9 [$CH_2CH_2CH(\mathit{C}H_3)$], 28.5 [$(CH_3)_2\mathit{C}HCHCH_2CH_2$], 34.9 [$CH_2\mathit{C}H_2CH(CH_3)$], 44.3 [$\mathit{C}H_2C(OR)$], 51.4 [$(CH_3)_2CH\mathit{C}HCH_2CH_2$], 64.1 ($OCH_2$), 73.3 [$\mathit{C}(OR)(C{\equiv}CH)$], 76.8 [$C(OR)(C{\equiv}\mathit{C}H)$], 85.9 [$C(OR)(\mathit{C}{\equiv}CH)$], 114.9 ($OCH_2CH{=}\mathit{C}H_2$), 135.6 ($OCH_2\mathit{C}H{=}CH_2$) ppm. MS (EI): *m/z* (%) = 220 (<1) [M^+], 135 (49), 107 (19), 95 (22), 79 (26), 69 (78), 55 (42), 40 (100).

6-Allyloxy-6-ethynyl-4-isopropenyl-1-methylcyclohex-1-ene (2b): (−)-Carvone (**2**, 2.7 g, 18.1 mmol) was treated as described in the general procedure to give, after column chromatography on silica gel (eluent: heptane/diethyl ether, 40:1), the enyne **2b** in 87% yield (3.4 g, 15.7 mmol) as a colourless oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.69−1.74 [m, 3 H, $CH{=}C(C\mathit{H}_3)$], 1.77−1.84 [m, 3 H, $H_2C{=}C(C\mathit{H}_3)$], 1.86−2.35 [m, 4 H, $C\mathit{H}_2CH(C(CH_3){=}CH_2)C\mathit{H}_2C$(O-allyl)], 2.50 (s, 1 H, $C{\equiv}CH$), 2.35−2.62 [m, 1 H, $C\mathit{H}C(CH_3){=}CH_2$], 3.92−4.25 (m, 2 H, $OC\mathit{H}_2CH{=}CH_2$), 4.68−4.80 [m, 2 H, $C(CH_3){=}C\mathit{H}_2$], 5.10 (dm, ^3J = 10.3 Hz, *cis* 1 H, $OCH_2CH{=}C\mathit{H}_2$), 5.27 (dm, ^3J = 17.2 Hz, *trans* 1 H, $OCH_2CH{=}C\mathit{H}_2$), 5.50−5.65 [m, 1 H, $CH_2C\mathit{H}{=}C(CH_3)$], 5.82−6.03 (m, 1 H, $OCH_2C\mathit{H}{=}CH_2$) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.5 [$CH{=}C(\mathit{C}H_3)$], 20.6 [$H_2C{=}C(\mathit{C}H_3)$], 30.7 ($C{=}CH\mathit{C}H_2CH$), 39.2 [$\mathit{C}HC(CH_3){=}CH_2$], 39.6 [$CH\mathit{C}H_2C(OH)$], 64.5 ($OCH_2$), 73.7 [$\mathit{C}(OH)(C{\equiv}CH)$], 74.9 ($\mathit{C}{\equiv}CH$), 84.4 ($C{\equiv}\mathit{C}H$), 109.2 [$H_2\mathit{C}{=}C(CH_3)$], 115.82 ($OCH_2CH{=}\mathit{C}H_2$), 125.5 [$CH_2\mathit{C}H{=}C(CH_3)$], 135.11 ($OCH_2\mathit{C}H{=}CH_2$), 135.2 [$CH{=}\mathit{C}(CH_3)$], 148.3 [$H_2C{=}\mathit{C}(CH_3)$] ppm. MS (EI): *m/z* (%) = 216 (<1) [M^+], 158 (36); 143 (34), 129 (33), 117 (81), 105 (46), 91 (67), 77 (89), 65 (29), 53 (47), 41 (100). $C_{15}H_{20}O$ (216.3): calcd. C 83.28, H 9.32; found C 83.08, H 9.52.

1-Allyloxy-1-ethynyl-2-isopropylidene-5-methylcyclohexane (3b): (+)-Pulegone (**3**, 1.4 g, 9.2 mmol) was treated as described in the general procedure to give, after column chromatography on silica gel (eluent: heptane/diethyl ether, 40:1), the enyne **3b** in 65% yield (1.3 g, 6 mmol) as a colourless oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.54 (s, 3 H, CH_3), 1.62−1.65 [m, 6 H, $C{=}C(C\mathit{H}_3)_2$], 1.71−1.73 [m, 1 H, $CH_2C\mathit{H}(CH_3)$], 1.96−2.11 [m, 4 H, $C\mathit{H}_2CH_2C{=}C(CH_3)_2$, $C(OH)C\mathit{H}_2CH(CH_3)$], 2.38−2.40 (m, 1 H, $C{\equiv}CH$), 3.90−4.12 (m, 2 H, $OC\mathit{H}_2CH{=}CH_2$), 4.73 (dd, ^3J = 8.5, ^2J = 2.1 Hz, *cis* 1 H, $OCH_2CH{=}C\mathit{H}_2$), 4.99−5.10 [m, 1 H, $CH_2C\mathit{H}_2C{=}C(CH_3)_2$], 5.16 (dm, ^3J = 16.9 Hz, *trans* 1 H, $OCH_2CH{=}C\mathit{H}_2$), 5.24−5.30 [m, 1 H, $CH_2C\mathit{H}_2C{=}C(CH_3)_2$], 5.75−5.96 (m, 1 H, $OCH_2C\mathit{H}{=}CH_2$) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.5/17.5 (2 × CH_3), 23.1 (CH_3), 25.5 ($\mathit{C}HCH_3$), 26.0/26.2 [$\mathit{C}H_2C{=}C(CH_3)_2$], 32.3 [$CH_2CH_2CH(CH_3)CH_2$], 39.1 [$CH_2CH_2CH(CH_3)\mathit{C}H_2$], 64.5/64.7 ($C{\equiv}\mathit{C}H$), 68.5/68.6 ($O\mathit{C}H_2CH{=}CH_2$), 73.1 (C quat.), 82.2/82.3 ($\mathit{C}{\equiv}CH$), 117.4 ($OCH_2CH{=}\mathit{C}H_2$), 131.5/131.8 [$\mathit{C}{=}C(CH_3)_2$], 134.1/134.2 ($OCH_2\mathit{C}H{=}CH_2$), 140.7/140.8 [$C{=}\mathit{C}(CH_3)_2$] ppm. MS (EI): *m/z* (%) = 218 (<1) [M^+], 145 (34), 91 (59), 77 (29), 69 (100), 55 (27), 39 (29).

3-Allyloxy-5,9-dimethyldeca-4,8-dien-1-yne (4b): Citral (**4**, 2.6 g, 17.2 mmol) was treated as described in the general procedure to give, after column chromatography on silica gel (eluent: heptane/diethyl ether, 50:1), the enyne **4b** in 64% yield (2.4 g, 11 mmol) as a colourless oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.52−1.75 (m, 9 H, 3 × CH_3), 1.93−2.17 (m, 4 H, 2 × CH_2), 2.41/2.42 (2 × d, ^4J = 2.1 Hz, 1 H, $C{\equiv}CH$), 3.89−4.18 (m, 2 H, $OC\mathit{H}_2CH{=}CH_2$), 4.75 [dd, ^3J = 8.5, ^4J = 2.1 Hz, 1 H, $C\mathit{H}(OR)(C{\equiv}CH)$], 4.96−5.34 [m, 4 H, $C\mathit{H}{=}C(CH_3)_2$, $CH(OH)C\mathit{H}{=}C(CH_3)CH_2$, $OCH_2CH{=}C\mathit{H}_2$], 5.77−5.99 (m, 1 H, $OCH_2C\mathit{H}{=}CH_2$) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.6/17.5 [$CH{=}C(\mathit{C}H_3)CH_2$], 23.2 (*cis* CH_3), 25.5 (*trans* CH_3), 26.0/26.3 ($C{=}CH\mathit{C}H_2$), 32.4/39.2 ($C{=}CHCH_2\mathit{C}H_2$), 64.5/64.7 [$\mathit{C}H(OR)(C{\equiv}CH)$], 68.6/68.8 ($O\mathit{C}H_2CH{=}CH_2$), 73.2 ($C{\equiv}\mathit{C}H$), 82.3/82.4 ($\mathit{C}{\equiv}CH$), 117.55 ($OCH_2CH{=}\mathit{C}H_2$), 122.0/122.85 [$CH(OR)\mathit{C}H{=}C(CH_3$], 123.4/123.6 [$(CH_3)_2C{=}\mathit{C}HCH_2$], 131.6/132.0 [$CH{=}\mathit{C}(CH_3)_2$], 134.1/134.2 ($OCH_2\mathit{C}H{=}CH_2$), 140.9/141.0 [$CH{=}\mathit{C}(CH_3)CH_2$] ppm. MS (EI): *m/z* (%) = 218 (<1) [M^+], 144 (66), 116 (19), 90 (36), 68 (45), 53 (14), 41 (100). $C_{15}H_{22}O$ (218.3): calcd. C 82.52, H 10.16; found C 82.58, H 10.16.

2-(1-Allyloxyprop-2-ynyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene (5b): (−)-Myrtenal (**5**, 2.0 g, 13.5 mmol) was treated as described in the general procedure to give, after column chromatography on silica gel (eluent: heptane/diethyl ether, 40:1), the enyne **5b** in 65% yield (1.9 g, 8.8 mmol) as a colourless oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.80 (s, 3 H, CH_3), 1.11−1.16 [m, 1 H, $C(CH_3)_2C\mathit{H}(CH_2)CH_2$], 1.25 (s, 3 H, CH_3), 2.00−2.17 [m, 1 H, $C(CH_3)_2C\mathit{H}(CH_2)C{=}CH$], 2.21−2.44 (m, 5 H, $C{\equiv}CH$, CH_2, CH_2), 3.87−4.09 (m, 2 H, $OC\mathit{H}_2CH{=}CH_2$), 4.42−4.47 [m, 1 H, $C\mathit{H}$(O-allyl)($C{\equiv}CH$)], 5.07−5.29 (m, 2 H, $OCH_2CH{=}C\mathit{H}_2$), 5.57−5.71 (m, 1 H, $C{=}C\mathit{H}CH_2$), 5.75−5.95 (m, 1 H, $OCH_2C\mathit{H}{=}CH_2$) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.8/21.0 (CH_3), 25.9 (CH_3), 31.2/31.4 (CH_2), 37.7/37.9 [$\mathit{C}(CH_3)_2$], 40.6/41.2 [$HC{=}C\mathit{C}H[C(CH_3)_2](CH_2)$], 42.0/42.2 [$CH_2\mathit{C}H[C(CH_3)_2](CH_2)$], 42.6/42.7 ($CH_2$), 68.4/68.5 ($C{\equiv}\mathit{C}H$), 70.7/71.1 ($OCH_2$), 74.0/74.3 [$\mathit{C}H(OR)(C{\equiv}CH)$], 80.6/80.8 ($\mathit{C}{\equiv}CH$), 117.0/117.2 ($OCH_2CH{=}\mathit{C}H_2$), 121.3/121.8 ($C{=}\mathit{C}HCH_2$), 134.2 ($OCH_2\mathit{C}H{=}CH_2$), 144.2/144.4 ($\mathit{C}{=}CH$) ppm. MS (EI): *m/z* (%) = 216 (<1) [M^+], 143 (12), 128 (29), 115 (100), 105 (20), 91 (35), 77 (27), 67 (22), 53 (19), 40 (34). $C_{15}H_{20}O$ (216.3): calcd. C 83.28, H 9.32; found C 82.93, H 9.24.

General Procedure for the Preparation of Cyclic Compounds 1c−5c: $[RuCl_2(p\text{-cymene})]_2$ (0.5 to 1.25 mmol %), 1,3-bis(mesityl)imidazolinium chloride and cesium carbonate (molar ratio: 1/2/4) were dissolved in toluene (5 mL per mmol of enyne) and the mixture was stirred for 5 min at room temperature. The enyne (**1b−5b**) was added to the orange-red solution and the mixture was stirred at 80 °C until GC-MS analysis indicated the complete conversion to the cyclic product. The solvent was then removed and the residue was dissolved in heptane, filtered and evaporated to dryness. For reaction times and purification, see below.

6-Isopropyl-9-methyl-4-vinyl-1-oxaspiro[4.5]dec-3-ene (1c): Starting from the enyne **1b** (150 mg, 0.7 mmol) and by using 0.5 mol % of the ruthenium dimer, the total conversion was observed after 1 h and after a bulb-to-bulb distillation, **1c** (100 mg, 0.5 mmol, 66%) was obtained as a colourless oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.70−0.90 (m, 9 H, 3 × CH_3), 1.01−1.09 [m, 1 H, $CH_2C\mathit{H}(CH_3)$], 1.16−1.89 [m, 8 H, 3 × CH_2, $C\mathit{H}CH(CH_3)_2$, $CHC\mathit{H}(CH_3)_2$], 4.48−4.56 (m, 2 H, $OC\mathit{H}_2CH{=}C$), 5.08 (d, ^3J = 11.2 Hz, *cis* 1 H, $CH{=}C\mathit{H}_2$), 5.40 (d, ^3J = 17.0 Hz, *trans* 1 H, $CH{=}C\mathit{H}_2$), 5.82 (m, 1 H, $C\mathit{H}{=}CH_2$), 6.04−6.20 (m, 1 H, $OCH_2C\mathit{H}{=}C$) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.1 (2 × CH_3), 21.4 [$(CH_3)_2CHCH\mathit{C}H_2CH_2$], 22.4 [$CH_2CH_2CH(\mathit{C}H_3)$], 23.5 [$CH_2CH_2\mathit{C}H(CH_3)$], 27.0 [$(CH_3)_2\mathit{C}HCHCH_2CH_2$], 35.2 [$CH_2\mathit{C}H_2CH(CH_3)$], 45.6 [$\mathit{C}H_2C(OR)$], 47.3 [$(CH_3)_2CH\mathit{C}HCH_2CH_2$], 72.1 ($OCH_2$), 93.0 (C *spiro*), 115.6 ($CH{=}\mathit{C}H_2$), 123.51 ($OCH_2\mathit{C}H{=}C$), 129.3 ($\mathit{C}H{=}CH_2$), 143.7 [$CH{=}\mathit{C}(CH{=}CH_2)$] ppm. MS (EI): *m/z* (%) = 220 (33) [M^+], 135 (100), 91 (15), 79 (28), 69 (18), 55 (29), 41 (35).

9-Isopropenyl-6-methyl-4-vinyl-1-oxaspiro[4.5]deca-3,6-diene (2c): Starting from the enyne **2b** (100 mg, 0.46 mmol) and by using 0.5 mol % of the ruthenium dimer, the total conversion was observed after 2 h and after a bulb-to-bulb distillation, **2c** (66 mg, 0.3 mmol, 66%) was obtained as a colourless oil. ^{1}H NMR (200 MHz, CDCl$_3$): δ = 1.56 [s, 3 H, CH=C(CH_3)], 1.67 [s, 3 H, H$_2$C=C(CH_3)], 1.75–2.12 [m, 4 H, CH_2CH[C(CH$_3$)=CH$_2$)CH_2C(O-ring)], 2.39–2.57 [m, 1 H, C*H*C(CH$_3$)=CH$_2$], 4.59–4.72 [m, 4 H, OCH$_2$, C(CH$_3$)=CH_2], 5.06 (d, ^3J = 11.0 Hz, *cis* 1 H, OCH$_2$CH=CCH=CH_2), 5.44 (d, ^3J = 17.6 Hz, *trans* 1 H, OCH$_2$CH=CCH=CH_2), 5.57–5.68 [m, 1 H, CH$_2$C*H*=C(CH$_3$)], 5.87 (m, 1 H, OCH$_2$CH=CC*H*=CH$_2$), 6.06–6.25 [m, 1 H, CH$_2$C*H*=C(vinyl)] ppm. ^{13}C NMR (50 MHz, CDCl$_3$): *δ* = 17.2 [CH=C(*C*H$_3$)], 20.6 [H$_2$C=C(*C*H$_3$)], 30.1 (C=CH*C*H$_2$CH), 39.1 [*C*HC(CH$_3$)=CH$_2$], 40.7 (CH*C*H$_2$Cspira), 73.2 (OCH$_2$), 90.1 (C spira), 109.0 [H$_2$*C*=C(CH$_3$)], 116.1 (CH=*C*H$_2$), 123.1 [OCH$_2$*C*H=C(vinyl)], 125.6 [CH$_2$*C*H=C(CH$_3$)], 129.4 (*C*H=CH$_2$), 135.4 [CH=*C*(CH$_3$)], 143.6 [C(vinyl)], 148.5 [H$_2$C=*C*(CH$_3$)] ppm. MS (EI): *m*/*z* (%) = 216 (9) [M$^+$], 201 (15), 198 (14), 148 (30), 133 (100), 119 (29), 105 (58), 91 (75), 81 (16), 77 (68), 65 (49), 53 (45), 39 (72). C$_{15}$H$_{20}$O (216.3): calcd. C 83.28, H 9.32; found C 83.39, H 9.35.

6-Isopropylidene-9-methyl-4-vinyl-1-oxaspiro[4.5]dec-3-ene (3c): Starting from the enyne **3b** (250 mg, 1.1 mmol) and by using 0.5 mol % of ruthenium dimer, the total conversion was observed after 2 h and after a bulb-to-bulb distillation, **3c** (135 mg, 0.6 mmol, 54%) was obtained as a colourless oil. ^{1}H NMR (200 MHz, CDCl$_3$): *δ* = 1.47–1.52 (m, 3 H, CH$_3$), 1.59–1.67 [m, 6 H, C=C(CH_3)$_2$], 1.75–1.79 [m, 1 H, CH$_2$C*H*(CH$_3$)], 1.99–2.20 [m, 4 H, CH_2CH$_2$C=C(CH$_3$)$_2$, C(O-ring)CH_2CH(CH$_3$)], 4.34–4.49 (m, 2 H, OCH_2CH=C), 5.00 (d, ^3J = 10.9 Hz, *cis* 1 H, CH=CH_2), 5.35 (d, ^3J = 16.8 Hz, *trans* 1 H, CH=CH_2), 5.79–5.88 (m, 1 H, C*H*=CH$_2$), 5.99–6.15 (m, 1 H, OCH$_2$C*H*=C) ppm. ^{13}C NMR (50 MHz, CDCl$_3$): *δ* = 16.0/16.2 (2 × CH$_3$), 20.7 (CH$_3$), 25.4 (*C*HCH$_3$), 25.9/26.0 [*C*H$_2$C=C(CH$_3$)$_2$], 34.1 [CH$_2$*C*H$_2$CH(CH$_3$)CH$_2$], 38.8 [CH$_2$CH$_2$CH(CH$_3$)*C*H$_2$], 69.8 (OCH$_2$), 92.0 (C spira), 114.7 (CH=*C*H$_2$), 121.9 (OCH$_2$*C*H=C), 130.1 (*C*H=CH$_2$), 132.5 [*C*=C(CH$_3$)$_2$], 140.2 [C=*C*(CH$_3$)$_2$], 143.7 [CH=*C*(CH=CH$_2$)] ppm. MS (EI): *m*/*z* (%) = 218 (41) [M$^+$], 203 (100), 175 (16), 147 (21), 133 (23), 119 (31), 105 (51), 91 (71), 79 (50), 67 (36), 55 (42), 41 (72).

2-(2,6-Dimethylhepta-1,5-dienyl)-3-vinyl-2,5-dihydrofuran (4c): Starting from the enyne **4b** (100 mg, 0.46 mmol) and by using 0.5 mol % of ruthenium dimer, the total conversion was observed after 1 h and after a bulb-to-bulb distillation, **4c** (71 mg, 0.3 mmol, 71%) was obtained as a colourless oil. ^{1}H NMR (200 MHz, CDCl$_3$): δ = 1.61–1.80 (m, 9 H, 3 × CH$_3$), 1.99–2.18 (m, 4 H, CH_2CH_2), 2.80–3.04 (m, 2 H, OCH_2CH=C), 4.79–4.91 (m, 1 H, *cis* CH=CH_2), 5.05–5.21 [m, 3 H, *trans* CH=CH_2, (CH$_3$)C=C*H*C*H*(O-ring)], 5.22–5.66 [m, 2 H, (CH$_3$)$_2$C=C*H*, C*H*=CH$_2$], 6.63–6.75 (m, 1 H, OCH$_2$C*H*=C) ppm. ^{13}C NMR (50 MHz, CDCl$_3$): *δ* = 17.7 [CH=C(*C*H$_3$)CH$_2$], 19.3 (*cis* CH$_3$), 22.2 (*trans* CH$_3$), 25.7 (C=CH*C*H$_2$), 39.7 (C=CHCH$_2$*C*H$_2$), 63.6 (OCH$_2$), 77.9 [CH(O-ring)], 115.7 (CH=*C*H$_2$), 117.9 [(CH$_3$)C=*C*HCH(O-cycle)], 121.4 (*C*H=CH$_2$), 122.3 [(CH$_3$)$_2$C=*C*HCH$_2$], 124.0 (OCH$_2$*C*H=C), 135.1 [CH=*C*(CH$_3$)$_2$], 135.9 [CH=*C*(CH$_3$)CH$_2$], 148.2 [CH=*C*(CH=CH$_2$)] ppm. MS (EI): *m*/*z* (%) = 218 (21) [M$^+$], 205 (14), 137 (17), 95 (21), 81 (32), 69 (100), 55 (35), 41 (93). C$_{15}$H$_{22}$O (218.3): calcd. C 82.52, H 10.16; found C 82.17, H 10.24.

2-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)-3-vinyl-2,5-dihydrofuran (5c): Starting from the enyne **5b** (300 mg, 1.4 mmol) and by using 1.25 mol % of the ruthenium dimer, 84% of conversion was observed after 21 h and after flash column chromatography (eluent: heptane/diethyl ether, 40:1), **5c** (138 mg, 0.6 mmol, 46%) was obtained as a colourless oil. ^{1}H NMR (200 MHz, CDCl$_3$): *δ* = 0.84 (s, 3 H, CH$_3$), 1.02–1.12 [m, 1 H, C(CH$_3$)$_2$C*H*(CH$_2$)CH$_2$], 1.27 (s, 3 H, CH$_3$), 1.97–2.19 [m, 1 H, C(CH$_3$)$_2$C*H*(CH$_2$)C=CH], 2.23–2.50 (m, 4 H, 2 × CH$_2$), 4.56–4.62 (m, 2 H, OCH_2CH=CCH=CH$_2$), 4.76–4.97 (m, 1 H, C*H*OCH$_2$), 5.01–5.36 (m, 2 H, OCH$_2$CH=CCH=CH_2), 5.50–5.66 (m, 1 H, CHC=C*H*CH$_2$), 5.85–5.98 (m, 1 H, OCH$_2$CH=CC*H*=CH$_2$), 6.21–6.42 [m, 1 H, CH$_2$C*H*=C(vinyl)] ppm. ^{13}C NMR (50 MHz, CDCl$_3$): *δ* = 20.9/21.2 (CH$_3$), 25.8/26.0 (CH$_3$), 31.3/31.5 (CH$_2$), 37.5 [*C*(CH$_3$)$_2$], 40.3/40.6 [HC=C*C*H[C(CH$_3$)$_2$](CH$_2$)], 42.2 [CH$_2$*C*H[C(CH$_3$)$_2$](CH$_2$)], 42.8/43.0 (CH$_2$), 71.4 (OCH$_2$), 85.5 [*C*H(OR)], 114.5 (CH=*C*H$_2$), 117.7 (C=*C*HCH$_2$), 122.1 (OCH$_2$*C*H=C), 132.5 (*C*H=CH$_2$), 136.8 [CH=*C*(vinyl)], 145.7 (*C*=CHCH$_2$CH) ppm. MS (EI): *m*/*z* (%) = 215 (3) [M$^+$ − H], 172 (20), 154 (14), 128 (11), 67 (42), 53 (22), 41 (100). C$_{15}$H$_{20}$O (216.3): calcd. C 83.28, H 9.32; found C 82.99, H 9.41.

Acknowledgments

The authors are grateful to the Région Bretagne for a grant to JLN and to the European COST Programme (D12/0025/99).

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[1] M. Mori, *Top. Organomet. Chem.* **1998**, *1*, 133–154.

[2] [2a] A. Fürstner, F. Stelzer, H. Szillat, *J. Am. Chem. Soc.* **2001**, *123*, 11863–11869. [2b] A. Fürstner, H. Szillat, F. Stelzer, *J. Am. Chem. Soc.* **2000**, *122*, 6785–6786. [2c] N. Chatani, N. Furukawa, H. Sakurai, S. Murai, *Organometallics* **1996**, *15*, 901–903. [2d] N. Chatani, T. Morimoto, T. Muto, S. Murai, *J. Am. Chem. Soc.* **1994**, *116*, 6049–6050.

[3] M. Picquet, C. Bruneau, P. H. Dixneuf, *Chem. Commun.* **1998**, 2249–2250.

[4] [4a] S.-H. Kim, N. Bowden, R. H. Grubbs, *J. Am. Chem. Soc.* **1994**, *116*, 10801–10802. [4b] A. G. M. Barrett, S. P. D. Baugh, D. C. Braddock, K. Flack, V. C. Gibson, P. A. Procopiou, *Chem. Commun.* **1997**, 1375–1376. [4c] R. Stragies, M. Schuster, S. Blechert, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2518–2520. [4d] M. Mori, T. Kitamura, Y. Sato, *Synthesis* **2001**, 654–664.

[5] [5a] D. Sémeril, J. Le Nôtre, C. Bruneau, P. H. Dixneuf, A. F. Kolomiets, S. N. Osipov, *New J. Chem.* **2001**, *25*, 16–18. [5b] S. Kotha, N. Sreenivasachary, E. Brachmachary, *Tetrahedron Lett.* **1998**, *39*, 2805–2808. [5c] J. S. Clark, R. J. Townsend, A. J. Blake, S. J. Teat, A. Johns, *Tetrahedron Lett.* **2001**, *42*, 3235–3238. [5d] A. Kinoshita, M. Mori, *J. Org. Chem.* **1996**, *61*, 8356–8357. [5e] M. Rosillo, L. Casarrubios, G. Dominguez, J. Perez-Castells, *Tetrahedron Lett.* **2001**, *42*, 7029–7031. [5f] B. M. Trost, G. A. Doherty, *J. Am. Chem. Soc.* **2000**, *122*, 3801–3810. [5g] K. Undheim, J. Efskind, *Tetrahedron* **2000**, *56*, 4847–4857. [5h] M. A. Leeuwenburgh, C. Kulker, H. I. Duynstee, H. S. Overkleeft, G. van der Marel, J. H. van Boom, *Tetrahedron* **1999**, *55*, 8253–8262.

[6] S. Dev, A. P. S. Narula, J. S. Yadav, in *CRC Handbook of Terpenoids*; (Ed.: S. Dev); CRC: Boca Raton, **1982**, vol. 1, pp. 7–27.

[7] R. Tsao, J. R. Coats, *Chemtech* **1995**, *7*, 23–28.

[8] [8a] A. V. Malkov, P. Kocovsky, *Collect. Czech, Chem. Commun.* **2001**, *66*, 1257–1267. [8b] C. Chapuis, D. Jacoby, *Appl. Catal. A: General* **2001**, *221*, 93–117. [8c] M. Toyota, M. Rudyanto, M. Ihara, *Tetrahedron Lett.* **2000**, *41*, 8929–8932. [8d] V. Cadierno, M. P. Gamasa, J. Gimeno, *J. Organomet. Chem.* **2001**, *621*, 39–46. [8e] G. Lenoble, M. Urrutigoïty, P. Kalck, *J. Organomet. Chem.* **2002**, *643–644*, 12–18.

[9] [9a] V. P. Kamat, H. Hagiwara, T. Katsumi, T. Hoshi, T. Suzuki, M. Ando, *Tetrahedron* **2000**, *56*, 4397–4403. [9b] Y. Du, D. F. Wiemer, *Tetrahedron Lett.* **2001**, *42*, 6069–6072. [9c] D. C. Harrowven, M. C. Lucas, P. D. Howes, *Tetrahedron* **2001**, *57*, 9157–9162. [9d] G. Mehta, J. Nandakumar, *Tetrahedron Lett.* **2002**, *43*, 699–702. [9e] A. Srikrishna, M. Srinivasa Rao, *Synlett* **2002**, 340–342.

[10] M. Picquet, D. Touchard, C. Bruneau, P. H. Dixneuf, *New J. Chem.* **1999**, 141–143.

[11] [11a] M. Perry, Y. Maroni-Barnaud, *Bull. Soc. Chim. Fr.* **1969**, 3574–3580. [11b] J. Philippe, M.-L. Capmau, W. Chodkiewicz, *Bull. Soc. Chim. Fr.* **1971**, 2248–2255. [11c] K. Suga, S. Watanabe, T. Suzuki, *Can. J. Chem.* **1968**, 3041–3045.

[12] L. Ackermann, C. Bruneau, P. H. Dixneuf, *Synlett* **2001**, 397–399.

[13] D. Sémeril, M. Cléran, C. Bruneau, P. H. Dixneuf, *Adv. Synth. Catal.* **2001**, *343*, 184–187.

[14] [14a] S. Blechert, *Pure Appl. Chem.* **1999**, *71*, 1393–1399. [14b] M. Mori, N. Sakakibara, A. Kinoshita, *J. Org. Chem.* **1998**, *63*, 6082–6083. [14c] S. Kotha, N. Sreenivasachary, *Chem. Commun.* **2000**, 503–504. [14d] R. Duboc, C. Hénaut, M. Savignac, J. P. Genet, N. Bhatnagar, *Tetrahedron Lett.* **2001**, *42*, 2461–2464.

[15] C. Spins, C. Beaulieu, J. Lafrenière, *J. Org. Chem.* **2000**, *65*, 7091–7097.

Received May 16, 2002
[O02258]