Powerful Kinetic Diastereoselection in Ruthenium-Catalysed Ring-Closing Metathesis of (Homoallyl)vinylcyclopropanes

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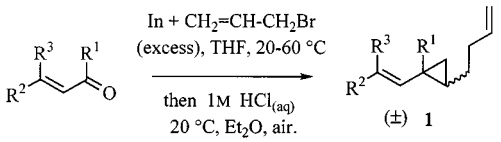
Homoallyl-substituted vinyl cyclopropanes **1a–c**, which are readily prepared by reaction of allylindium reagents with α,β-unsaturated ketones and aldehydes, undergo Ru-catalysed RCM reactions with Grubbs catalyst to give [4.1.0]bicyclooct-2-ene (norcarene) type bicyclic products. Noncyclisable '*trans*' homoallyl-substituted vinyl cyclopropanes **1b** and **1c** are separated from their '*cis*' diastereomers by RCM to **5b** and **5c** – but only with moderate efficiency due to a competing homo-cross metathesis ('dimerisation') to give **7b** and **7c,** respectively. However, the four diastereomers of the (homoallyl)distyrylcyclopropane **14a** obtained from indium-mediated reaction of dibenzylideneacetone and crotyl bromide undergo remarkable kinetic diastereoselection in their RCM reactions to give a 4,7-dimethyl[4.1.0]bicyclohept-2-ene-type product **15a**. This process allows recovery of a single diastereomer (> 95%) of **14a** without dimerisation being a significant side reaction. Furthermore, the RCM product **15a** is obtained rich in one diastereomer (ca. 90%). The kinetic diastereoselection and lack of dimerisation can be rationalised by considering developing transannular interactions and a pseudo-$A^{1,3}$ strain model.

Introduction

Transition metal catalysed ring closing metathesis (RCM) is arguably one of the most important organic synthetic reactions to have been extensively developed in the last decade.[1] The process is particularly effective at macrocyclisation,[2] allows nonclassical disconnection strategies[3] and can be rendered diastereo-[4] and enantio-selective.[5] The process can be catalysed by a variety of complexes derived from W, Re, Mo and Ru, the latter two being by far the most popular. Those based on Ru, especially "Grubbs' Catalyst",[6] have become very popular[7] due to their good activity, tolerance of nonalkene functionality and ease of handling.

We recently reported an unusual cyclopropane-forming reaction involving α,β-unsaturated ketones or aldehydes and allylindium reagents to generate homoallyl-substituted vinylcyclopropanes **1** (Scheme 1). The discovery and development of this reaction form the subject of the preceding paper.[8] In reactions involving either α,β-aldehydes or nonsymmetrical α,β-unsaturated ketones or monosubstituted allylindium reagents, the products **1** are obtained as a mixture of diastereomers.

In one case, the assignment of relative stereochemistry based on NOE experiments was ambiguous and herein we describe the use of RCM to solve this problem. This in turn led to the observation of subtle and rationalisable differences in reactivities of the diastereomers towards RCM. In certain cases, the kinetic diastereoselection allows the recovery of the unreactive substrate in high diastereomeric excess.[9] The study of the RCM reaction of **1** is of general interest in the expanding range of substrates tested for RCM reactivity since the tethering of two dienes through a conformationally restricting cyclopropane could possibly lead to increased rates (or yields) and selectivities. Furthermore, the bicyclo[n.1.0]alk-2-ene ring structure (n = 3–5, alk = hex, hept, oct) is a common structural motif in a number of phytochemicals, e.g. n = 3: thujone,[10] n = 4: chenopodene[11] and n = 5: africanone.[12] We therefore became interested in whether RCM reaction with **1** and homologues could be employed to generate the core ring structures of the latter two.



1a, R^1 = PhCH=CH- R^2 = Ph, R^3 = H,
1b, R^1, R^3 = H R^2 = Ph
1c, R^1 = H, R^2 = Ph, R^3 = Me
1d, R^1 = $(Me)_2C$=CH-, R^2, R^3 = Me

Scheme 1. Generalised scheme for the homoallyl cyclopropanation reaction of α,β-unsaturated ketones mediated by allylindium complexes. The cyclopropyl systems **1b** and **1c** are obtained as diastereomeric mixtures [C(1)/C(2)] whose ratios depend on the identity of R^1.

Results and Discussion

Preliminary RCM Studies with Butenyl(homoallyl)- and (Pentenylvinyl)cyclopropanes

The homoallyl cyclopropanation (HAC) reaction of dibenzylidene acetone with allylindium reagents, generated in situ, reliably affords distyryl(homoallyl)cyclopropane **1a** in good yield (83%). We chose to study the RCM of **1a** first

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since it was envisaged as being the least likely substrate to induce complications.

Triene **1a** has two diastereotopic styryl groups which were considered to be unreactive towards the bulky Ru-carbene complex **2** (Grubbs′ catalyst [$(PCy_3)_2Ru(Cl_2)$=CHPh]) in an *intermolecular* sense. The vinyl unit at the terminus of the homoallyl chain, being monosubstituted and reasonably remote from the sterically demanding cyclopropyl quaternary centre, was viewed as potentially reactive enough for *intermolecular* reaction with the Ru-carbene **2** to initiate catalysis (Figure 1).

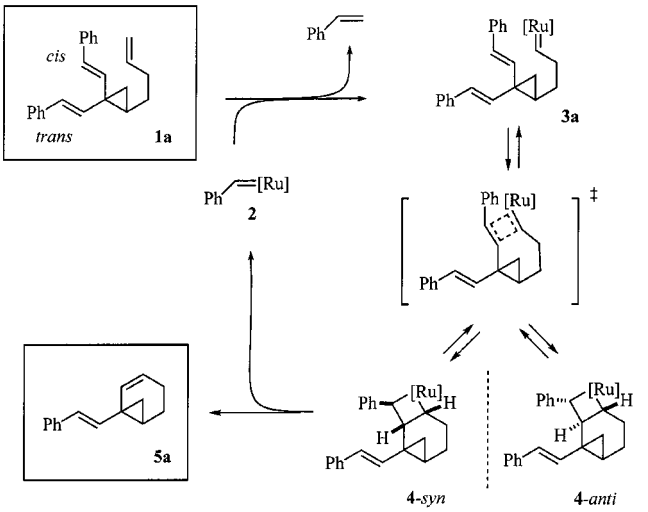


Figure 1. Hypothetical mechanism for Ru-benzylidene (**2**) catalysed RCM reaction of 2-homoallyl-1,1-distyrylcyclopropane **1a** to generate bicyclo[4.1.0]hept-2-ene **5a** and styrene *via* **3a** and then **4**-*syn*. The complex **4**-*anti* cannot undergo reversed retro-[2+2] since this would generate a *trans* cyclohexenyl ring.

According to the accepted mechanism,[13] the resulting metathesis process would generate carbene intermediate **3a**. This can then form ruthenacyclobutanes (**4a**-*syn)* and (**4a**-*anti)* by formal [2+2] cycloaddition – but only with the *cis*-disposed diastereotopic styryl group, since the *trans* styryl group is not within reach. Retro [2+2] of **4a** in the opposite sense, to generate the desired RCM product **5a**, can only occur with (**4a**-*syn)* since the same process with (**4a**-*anti)* would generate a *trans* double bond in a 6-membered ring. Usually Ru-catalaysed RCM reactions involve metathesis of two terminal alkenes and thus propagate through a methylene complex. However, in this example the styryl group results in the starting benzylidenecarbene complex **2** being the co-product of the retro [2+2]. This then can propagate reaction through repetition of an identical catalytic cycle (Figure 1).

Before performing the reactions, we had been concerned that competing side reactions might include a) cross-metathesis by **2** with unchanged **1a** to generate methylenecarbene **8** and presumably unreactive styrylated side-product **6a** and b) cross-metathesis of **1a** with intermediate **3a** to generate 'dimeric' **7a**. Furthermore, we had expected that as reaction proceeded, the increasing concentration of styrene would result in reaction of this with **2** to generate stilbene and **8** (Figure 2).

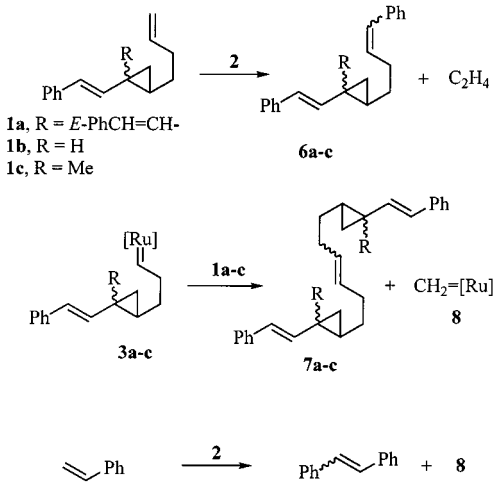


Figure 2. Potential undesired side reactions in the RCM reaction of **1a** (and by analogy the reactions of **1b**, **1c**) that would generate styrylated substrate (**6a**), 'dimeric' side-product **7a** *via* cross-metathesis with Ru-carbene complexes **2** and **3a** respectively, and stilbene.

In the event, the reaction of triene **1a** proceeded as planned. Dilute solutions of **1a** (*ca.* 0.04 M) in CH_2Cl_2 were smoothly metathesised at ambient temperature by 3 mol-% Grubbs catalyst.[14] During the reaction we monitored progress by ^{1}H-NMR (and TLC) of samples taken at intervals over a period of 24 h. However, there was no evidence for cross metathesis (no styrylated **6a** or 'dimeric' **7a**) and indeed little or no trace of any stilbene. Prior to complete consumption of **1a**, the reaction mixture consisted essentially of unchanged **1a**, styrene and the desired RCM product **5a**. This was quite surprising – especially given the kinetic diastereoselection observed with more complicated substrates vide infra. After a workup that consisted solely of direct chromatography on silica-gel, the resultant norcarene-like bicyclo[4.1.0]hept-2-ene ring system (**5a**) was reproducibly obtained in 72–73% yields (Figure 3).

We had also been concerned by the known reactivity of vinylcyclopropanes (VCP) with transition metal complexes. It was therefore considered important to confirm that **5a** had indeed been formed and that some other undesired VCP rearrangement had not occurred during or after the RCM reaction. Although elemental analysis, HR-MS and routine 1D and 2D ^{1}H and ^{13}C NMR were fully consistent with the RCM product being **5a**, we also determined $^1J_{CC}$ and $^1J_{CH}$ coupling constants (Figure 3). The low $^1J_{CC}$ values within the ring and with carbons attached to the ring and the high $^1J_{CH}$ values (high s-character) are very characteristic NMR features for cyclopropane systems (Figure 3). These, together with the NOE connectivities (500 MHz PNOSY) satisfied us that the divinylcyclopropane in **5a** was still intact.

The PNOSY experiments were very informative regarding the conformation of **5a**. Study of Dreiding models indicate that there are two limiting twist-boat structures (Figure 3) with intermediate conformers being rather strained.

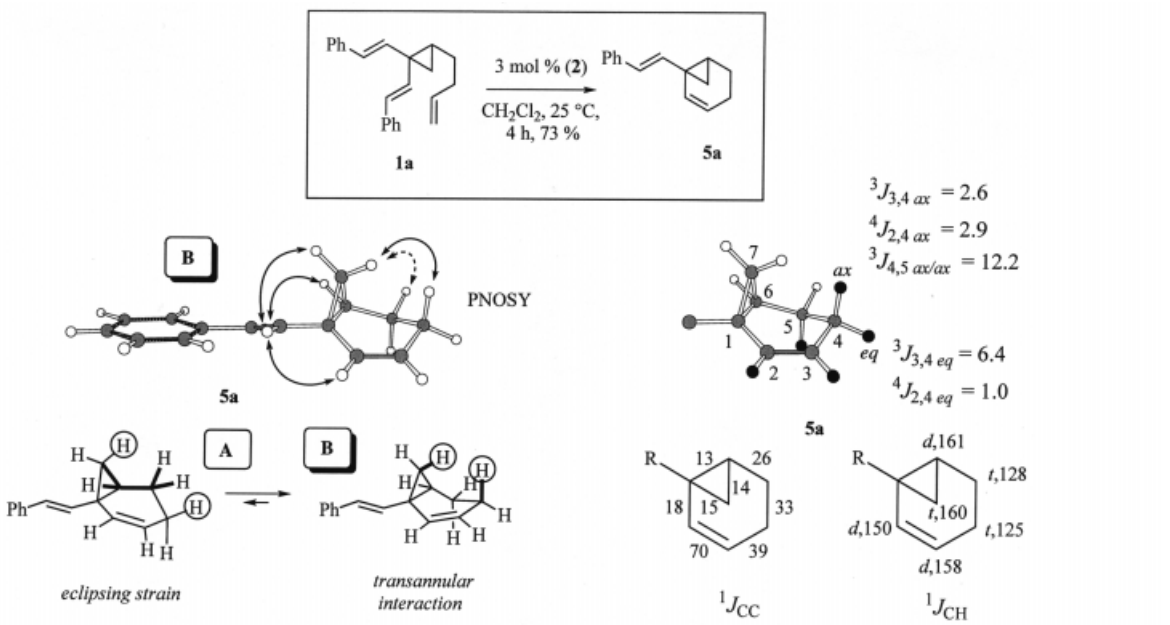
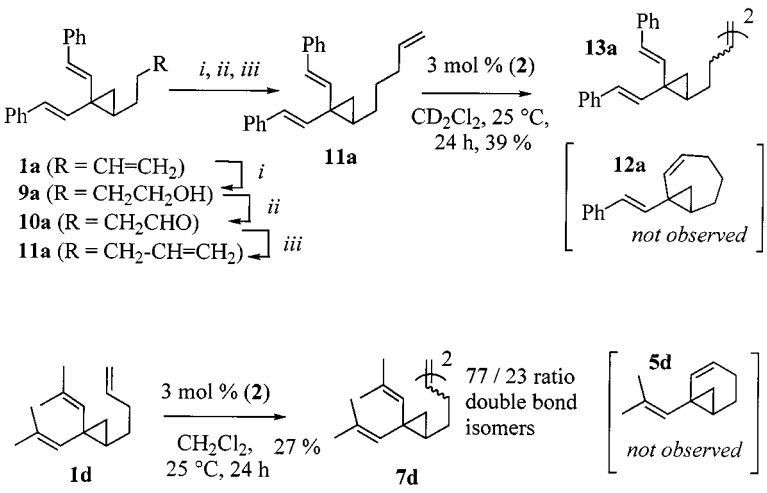


Figure 3. Ru-catalysed RCM of **1a** to generate 1-styryl-bicyclo[4.1.0]hept-2-ene **5a**. That the cyclopropyl structure was intact was confirmed by analysis of $^1J_{CC}$ and $^1J_{CH}$ coupling constants (extracted by analysis of ^{13}C satellites in $^{13}C\{^1H\}$ NMR and ^1H-coupled ^{13}C NMR respectively). The low $^1J_{CC}$ coupling constants within the cyclopropane ring carbons (13–15 Hz) and the nonring carbons to which they are joined (18 and 26 Hz) and high $^1J_{CH}$ coupling constants at C(6)–H_2 and C(7)–H are indicative of high s-character ($^1J_{CH}$ = ca. 500/[s/(s+p)]). Selected PNOSY contacts and ^1H coupling constants give information regarding the preferred (**B**) conformation of the cyclohexenyl ring.

In one conformation (**A**, left hand side) there is an unfavourable eclipsing of the homoallylic methylene with the cyclopropyl unit – but this avoids transannular interaction of the allylic methylene with the cyclopropane. In the other conformer (**B**, right hand side) the homoallylic methylene is staggered with respect to both the cyclopropyl unit and the allylic methylene, however, this arrangement results in a pseudo 'flag-bowsprit' transannular interaction. Nonetheless, the latter conformer (**B**) is dominant in solution since the '*endo*' cyclopropane proton projecting over the endocyclic face exhibits a strong NOE with the allylic proton *syn* to the cyclopropane and only a very weak NOE with the (*syn*) homoallylic proton. The reverse would be observed if the eclipsing conformer (**A**) were dominant. Simple AM1 calculations indeed indicate that **A** is *ca.* 1 kcal mol^{-1} less stable than **B**.

Further evidence to support the conclusion that **B** is dominant in solution comes from a study of the ^1H-NMR coupling constants around the norcarene ring (Figure 3). These were extracted by extensive simulation of the 500 MHz ^1H-NMR spectrum. In particular, the allylic proton C(4)H_{ax} exhibiting NOE contact with the cyclopropane couples weakly (^3J = 2.6 Hz) with C(3)H and strongly with C(2)H (^4J = 2.9 Hz), whilst C(4)H_{eq} couples more strongly with C(3)H (^3J = 6.4 Hz) and weakly with C(2)H (^4J = 1.0 Hz). The magnitude of the ^3J couplings are consistent with those predicted by a modified Karplus analysis[15] based on the dihedral angles (Φ = 85/32°) between C(4)$H_{ax/eq}$ and C(3)H as indicated by AM1 calculations. Furthermore, the magnitude of the ^4J couplings are consistent with those predicted by analysis of the orthogonality of C(4)$H_{ax/eq}$ to the π-system[16] and there is a ^4J "W" coupling between C(4)H_{eq} and C(6)H. A final piece of evidence is the observation that C(4)H_{ax} exhibits a large diaxial coupling (^3J = 12.2 Hz) with C(5)H_{ax}. Analysis of analogous coupling patterns proved very informative in the determination of the relative stereochemistry of the more complicated 3,7-dimethylbicyclo[4.1.0]hept-2-ene ring systems (**15a**) discussed later.

In the course of attempting to generate crystalline derivatives of **1a** we had performed a regio- and chemo-selective hydroboration-oxidation sequence leading to primary alcohol **9a** (Scheme 2). A simple oxidation (Swern conditions) to afford aldehyde **10a** and then Wittig-type methylenation furnished triene **11a** which is the homologue of **1a**. Under the same conditions as were employed for the RCM of **1a**, we found that **11a** failed completely to generate the desired [5.1.0]bicyclooct-2-ene ring system **12a**. The reaction of triene **11a** (0.16 M in in CD_2Cl_2) was followed by ^1H NMR over a period of 24 h. During this period there was no trace of styrene, instead we observed a cleanly occurring, but slow, cross-metathesis to give 'dimeric' **13a** (Scheme 2) as confirmed by MS. The reaction slowed dramatically after 5 h and after ca. 24 h (39% conversion of **11a**) turnover had effectively ceased. The phorone-derived (homoallyl)vinylcyclopropane **1d** behaved analogously and failed to be converted into RCM product **5d**. MS and NMR analysis of the crude reaction mixture again indicated exclusive homo cross-metathesis to afford 'dimeric' **7d** which was subsequently isolated by column chromatography in 27% yield as a 3/1 mixture of double bond geometric isomers. Unreacted triene **1d** was recovered in 38% yield. It therefore appears that the *intramolecular* metathesis with a *cis*-disposed alkene is disfavoured, relative to *intermolecular* cross-meta-



Scheme 2. Upper sequence: synthesis and attempted Ru-catalysed RCM of **11a** (the homologue of **1a**) to generate 1-styrylated bicyclo[5.1.0]-oct-2-ene **12a**. No **12a** was observed under the standard reaction conditions, instead a slow cross-metathesis occurred to generate **13a**. Conditions: *i*. 9-BBN, THF, then H_2O_2/NaOH, 75% *ii*. DMSO/$(COCl)_2$, Et_3N, CH_2Cl_2, 68%. *iii*, KH, $[PPh_3PCH_3][I]$, 18-crown-6, THF, 67%. Lower reaction: attempted RCM of the phorone-derived homoallylcyclopropane **1d** also suffered from almost exclusive competing cross-metathesis to generate **7d**. This is likely the result of slow intramolecular [2+2] of the sterically demanding ruthenium carbene complex with the trisubstituted double bond.

thesis, in the rutheniumcarbene intermediates generated from **1d** and **11a**. In the first case (**1d**) the intramolecular [2+2] cycloaddition would involve a hindered tri-substituted alkene ($Me_2C{=}CH{-}$)[17] whilst in the second (**11a**), although not obvious from the study of Dreiding models, the extra methylene (relative to **1a**) presumably engenders a strained geometry in the 7-membered ring formed on cycloaddition.

Selective RCM of '*cis*' Diastereomers of (Homoallylstyryl)cyclopropanes in the Presence of '*trans*'

Having demonstrated that the RCM reaction could be effected very smoothly on the triene **1a** we became interested in the possibility of utilising it to upgrade the diastereomeric excess (*de*) of dienes **1b** (R = H) and **1c** (R = Me) obtained by HAC reaction of allylindium reagents with cinnamaldehyde and benzylidene acetone respectively. The presence of two stereogenic centres in (±)-**1b** and (±)-**1c** results in two diastereomers (*cis* and *trans*) which are obtained with 27% *de trans* and 2% *de cis* respectively. As discussed earlier, due to the restricting geometry of the cyclopropane unit, intermediate rutheniumcarbenes **3** can only undergo intramolecular [2+2] cycloaddition with a *cis*-disposed styryl group (Figure 1). Consequently the carbenes *trans*-**3b** and *trans*-**3c** cannot undergo RCM to generate **5b** and **5c** in which the cyclopropane is concatenated *trans* within the cyclohexenyl ring. Here, of course, there is now a potential problem since the remoteness of the terminal vinyl groups in dienes **1b** and **1c** mean that the *cis*/*trans* isomers are likely to be equally reactive towards benzylidene-Ru complex **2**. Thus the fate of the carbene complexes (*trans*-**3b** and *trans*-**3c**) will determine whether the overall catalytic reactions are successful or side reactions (Figure 2) will compete. Unlike **1a**, the reactions proved problematic. After exposure of **1c** (initially a *ca*. 1/1 mixture of *cis* to *trans*) to 3 mol-% **2** in CH_2Cl_2 at 25 °C for 96 h, the volatiles (styrene and RCM-product **5c** in CH_2Cl_2 by MS analysis) were removed in vacuo and the reaction residue purified by chromatography. Material balance and NMR/MS analysis indicated that despite prolonged reaction periods (compare with 4 h for triene **1a**) there was incomplete conversion of diene *cis*-**1c** and extensive dimerisation (MS) to generate **7c** (as a *ca*. 2/1 ratio of double bond isomers) with no evidence (by NMR or MS) for styrylated **6c** which would be generated by cross-metathesis with styrene. To gain more information, we monitored the RCM reactions of 0.025 M and 0.024 M solutions of dienes **1b** and **1c** in CD_2Cl_2 (septum-capped NMR tubes) by ^1H NMR (270 MHz). In both reactions, NMR signals due to ethylene and styrene were clearly evident soon after addition of 3 mol-% **2**.

Taking **1b** first (upper plot in Figure 4; starting *cis*/*trans* ratio *ca.* 37/63), the RCM products styrene and **5b**[18] grew steadily for 5 h after addition of catalyst (**2**). Concurrent with the RCM reaction was a roughly equal rate of conversion of **1b** to an *E*/*Z* mixture of 'dimeric' **7b** and 0.5 equiv. ethylene. After 7.5 h, turnover had slowed dramatically and after 21 h almost ceased. At this point ca. 55% of **1b** had been consumed to generate RCM product **5b** and 'dimeric' **7b** in ca. 25% and 15%[19] yields respectively.

The relatively low degree of dimerisation deserves comment: in the initial stages of catalysis, generation of non-cyclisable *trans*-**3b** must be statistically favoured (by *ca*. 1.7/1) over generation of *cis*-**1b** if, as seems reasonable, there is equal reactivity of the remote terminal alkene of *cis*/*trans*-**1b** towards **2**. Furthermore as reaction proceeds and the *de* of *trans*-**1b** increases, the formation of *trans*-**3b** over *cis*-**3b** becomes more and more statistically favoured (e.g. after 2 h, 38% conversion, the generation of *trans*-**3b** is favoured 5/1 over *cis*-**3b**). However, since *cis*-**1b** is consumed more rapidly than *trans*-**1b** (*ca.* 2.2/1), the noncyclisable *trans*-**3b** must mostly undergo regenerative ('*exo*') cross-metathesis

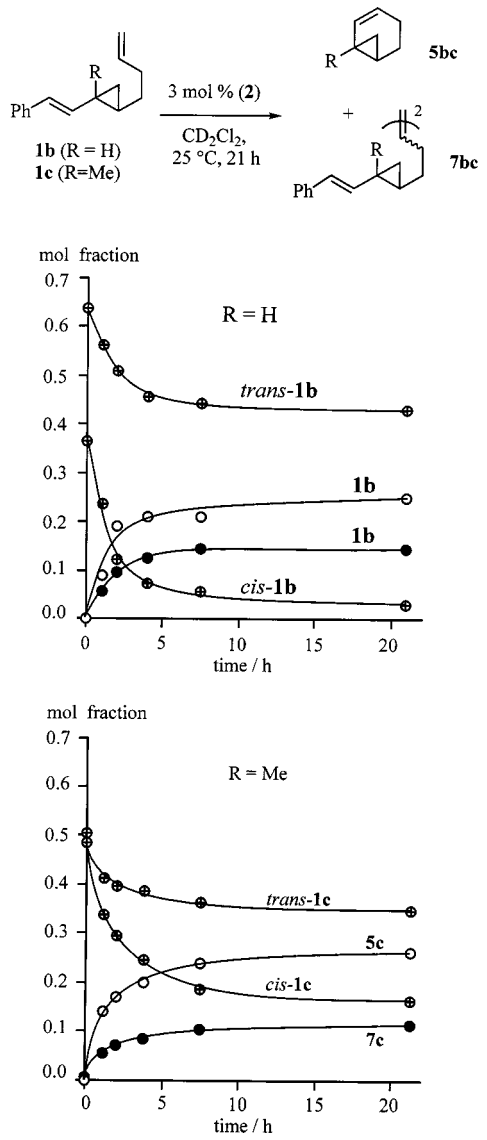


Figure 4. The RCM reactions of **1b** (ca. 27% *de* of *trans*) and **1c** (ca. 2% *de* of *cis*) as monitored by ^{1}H-NMR in CD_2Cl_2 at 25 °C. Upper plot: *x* axis, time in h after addition of 3 mol-% **2**; *y* axis, mol fractions of unchanged **1b**, RCM product **5b** and cross-metathesis product **7b** (whose mol fraction is plotted as half the mol fraction of 'monomer' **1b** incorporated).
Lower plot: same as upper plot but for reaction of **1c**.

with styrene or *cis*-**1b**.[20] Only occasionally does *trans*-**3b** undergo cross-metathesis with reversed ('*endo*') regioselectivity to generate 'dimeric' **7b**

Although the reaction profile of **1c** (Figure 4, lower plot) at first glance appears quite similar to that of **1b**, the effect that the RCM and cross-metathesis reactions have on the *cis*/*trans* ratio of **1c** is quite different. This was initially surprising since there is more *cis* isomer of **1c** present to start with (relative to **1b**) and we expected there to be a greater proportion of RCM relative to cross-metathesis (to give 'dimeric' **7c**). However, because the relative rate of consumption of *cis*- versus *trans*- isomers of **1c** is almost identical to that observed with **1b** (*ca.* 2.2/1) and turnover effectively ceases after ca. 50% conversion, the increase in the *trans*/*cis* ratio of **1c** (R=Me) is much less dramatic than that of **1b** (Figure 5).

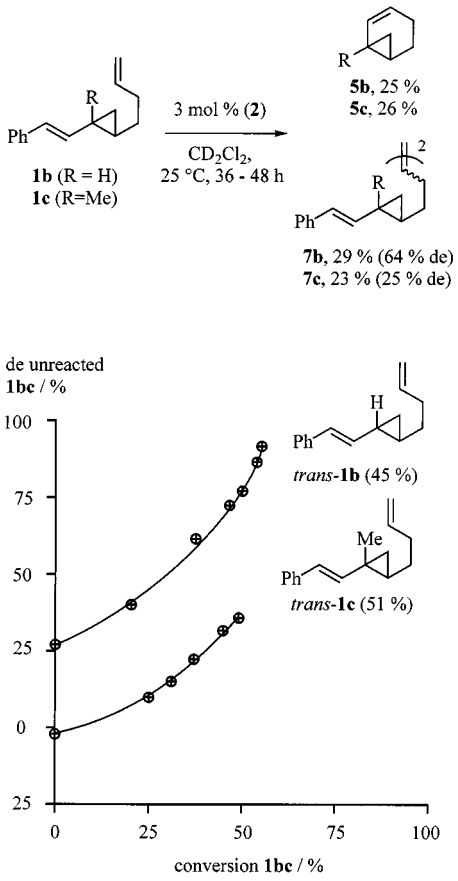


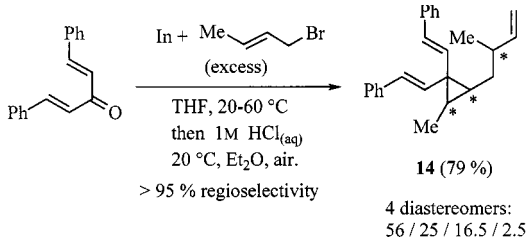
Figure 5. The relationship of diastereomeric excess (*de*/%) of unchanged *trans*-**1b** and *trans*-**1c** (*y* axis) with conversion of **1b** and **1c** (*x* axis) for RCM reaction in CD_2Cl_2 at ambient temperature and catalysed by Ru-carbene complex **2**.

After a total of ca. 36 h at 25 °C, during which there was less than 2% conversion of **1b**, the volatiles were stripped into a liquid nitrogen trap. The reaction of **1c** was worked-up analogously. ^{1}H NMR analysis of the condensates showed they were essentially pure solutions of styrene and **5b** (or styrene and **5c**) in CD_2Cl_2. Analysis of the residue from reaction of **1b** by ^{1}H-NMR confirmed that unchanged **1b** was >96% the *trans*-isomer and cross-metathesis product **7b** was 82% *trans* at C(1)[21] as a 2/1 ratio of double-bond isomers.[22] Analysis of **1c** (67% *trans*) and **7c** (63% *trans*) indicated a less dramatic enhancement.

In an attempt to solve the problem of competing cross-metathesis, we performed RCM reactions of **1b** and **1c** under a static atmosphere of ethylene (*ca.* 1 atm.) so that metathesis of the ethylene with *trans*-**3bc** would regenerate *trans*-**1bc**. However, the ethylene appeared to inhibit or terminate the RCM reaction and after 24 h unchanged **1b** and **1c** were recovered with little or no change in diastereomer ratio and no evidence for **7b** or **7c**. The effect may possibly be due to rapid cross-metathesis of ethylene with *cis*-**3bc** competing too effectively with slow intramolecular cyclisation.

Crotylindium Reagents – Assignment of Relative Configuration Based on NOE and Reactivity

We have also reported on the reaction of dibenzylidene acetone with more substituted allylindium species and whilst this proceeded well with crotylindium species (to give triene **14a** in 79% yield), with prenylindium species reaction diverted to give a different set of products. The HAC reaction of dibenzylidene acetone with crotyl bromide/indium could give 4 possible regioisomeric products but the regioselectivity is excellent, giving only **14a** (Scheme 3). However, the presence of 3 stereogenic centers in triene **14a** leads to 4 possible (racemic) diastereoisomers.



Scheme 3. The indium-mediated homoallyl cyclopropanation reaction of dibenzylidene acetone with crotyl bromide which generates triene **14a** with near perfect regioselectivity (>95% – other regioisomers not detected by ^{13}C-NMR – see ref. [8]). The presence of three stereogenic centres (marked with *) in **14a** results in four diastereomers which are present in a ratio 56/25/16.4/2.5.

Despite many attempts, we were unable to separate out any diastereoisomeric forms of **14a** by chromatography on silica-gel that had been impregnated with Ag^+.[23] However, after screening a range of NMR solvents, we found that in [D_6]acetone we could confirm that all four diastereomers had indeed been obtained in a ratio of *ca.* 56/25/16.5/2.5%. Using 2D NOESY at 500 MHz and spectral simulation, we were able to identify that the two major diastereomers had a *cis* stereochemistry at the cyclopropane ring [at C(2) and C(3)] and thus the overall diastereoselectivity at the cyclopropane centre is 81% *cis*. However, due to free rotation about the allylic-homoallylic C–C bond, the NOESY data was ambiguous regarding the relative stereochemistry at the allylic stereogenic centre (C(2′′)). The RCM reaction therefore appeared an ideal method since this would generate cyclic triene **15a** (potentially as a diastereomeric mixture) in which the conformational mobility of the allylic carbon was restricted by annelation (Figure 6). The test reactions performed with triene **1a** had indicated that RCM of **14a** should proceed smoothly, provided that the extra two methyl groups did not interfere.

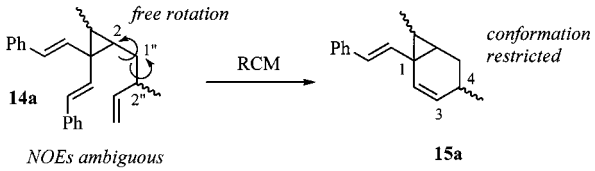


Figure 6. Free rotation about C(2)–C(1′′) and C(1′′)–C(2′′) results in ambiguous NOE experiments regarding the relative configuration at C(2′′)–Me in **14a**. This problem was overcome by RCM reaction to generate **15a** in which the bonds surrounding the stereogenic centre of interest [now (C4)] are restricted in conformation by annelation.

Using the conditions we had employed for **1a**, we observed, by TLC, smooth partial conversion of the mixture of four diastereomers (56/25/16.5/2.5 *cis, cis, trans, trans* isomers) of **14a** over a period of ca. 24 h. However, even after 2 days at ambient temperature there was still **14a** remaining (by TLC analysis) and a further 3 mol-% catalyst was added. However, over a further 2 days this had no effect and the reaction was worked up to afford the 4,7-dimethylbicyclo[4.1.0]hept-2-ene **15a** in 64% yield (Figure 7).

A range of deuterated solvents were screened and eventually ([D_6]benzene) was found to allow sufficient shift dispersion for ^{1}H NMR analysis of diastereomer ratios of **15a**. This indicated that **15a** had been obtained as one major isomer (90%) and two minor isomers (8% and 2%). Furthermore, analysis of recovered **14a** (22%) by ^{1}H NMR ([D_6]acetone) demonstrated that this consisted essentially of a single diastereomer – whose identity was confirmed by comparison with that of the original sample of **14a** as the minor *cis* isomer (25% of original mixture). Material balance indicates that the major isomer of the RCM product **15a** must be derived from the major *cis* isomer of **14a** (56% of original mixture). Clearly a powerful kinetic diastereoselection had occurred in which the major isomer of **14a** underwent complete RCM and the second most abundant isomer (*cis*) of **14a** (25%) is unreactive. The whole process allows isolation of the unreactive minor *cis* isomer of **14a** in 88% yield as a single diastereomer (>95%), and the RCM product **15a** from the reactive major *cis* isomer of **14a** in essentially quantitative yield and reasonable purity.

After chemical shift assignments (PECSY), careful analysis of close contacts (PNOSY) and $^nJ_{HH}$ (n = 1–4) coupling constants in the 500 MHz ^{1}H NMR spectrum of the major (90%) isomer of **15a** gave conclusive information not only regarding its relative configuration (±-1*R**4*S**6*R**7*S**) but also the dominant conformer (Figure 7).

The relative configuration was deduced from the following key observations. A characteristically *cis* ^3J coupling of 8.9 Hz between C(6)–H and C(7)–H and a moderate NOE contact between C(7)–CH_3 and C(3)–H confirmed that, as expected, the methyl group on C(7) is *syn* with respect to the cyclohexenyl ring. Analysis of the coupling constants gave some information about the conformation of the cyclohexenyl ring. In particular, the ^3J coupling of C(4)–H with C(3)–H (1.9 Hz) is smaller than its ^4J coupling with C(2)–H (3 Hz) indicative that C(4)–H is perpendicular to the alkene π-system. The cyclopropyl C(6)–H proton couples more strongly with C(5)–H_{anti} (8.6 Hz) than with C(5)–H_{syn} (5.3 Hz) indicative that C(6)–H and C(5)–H_{anti} are eclipsed. Furthermore, C(4)–H couples strongly with C(5)$_{syn}$ (11.3 Hz) and less so with C(5)–H_{anti} (5.6 Hz). These couplings suggest eclipsing around C(4)–C(5) and C(5)–C(6) bonds and thus the dominant conformer in solution is a flattened form of the boat conformer (**B**) observed with parent compound **5a** which lacks the extra two methyl groups. The flattening is presumably a result of the increased transannular interaction of the *syn*-methyl group at C(7) in **15a** relative to a proton at C(7) (**5a**). However, despite the transannular interaction, conformation **A** is not

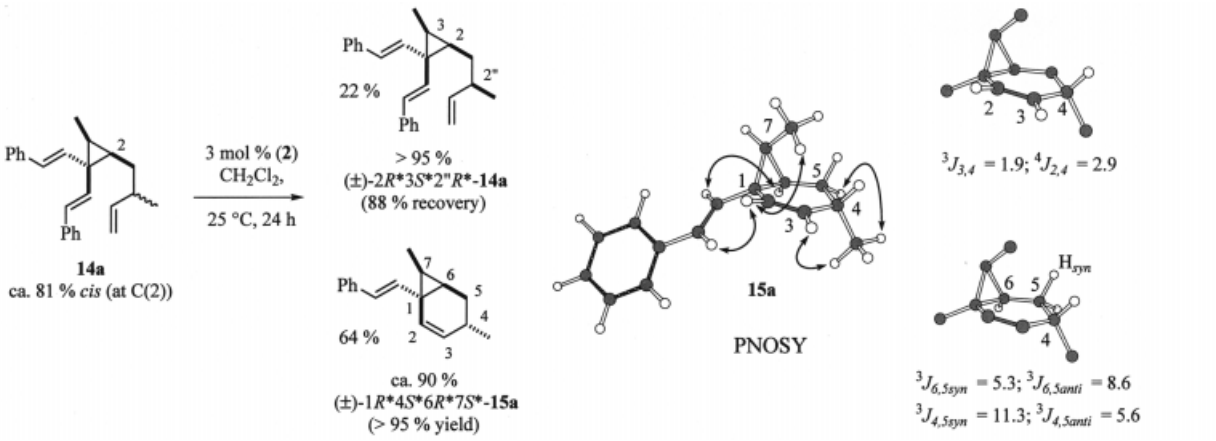


Figure 7. The RCM reaction of **14a** (81% *cis*) which occurs with very high kinetic diastereoselectivity results in complete conversion of one diastereomer to **15a** and recovery of the other isomer of **14a** in > 90% *de* with little or no competing cross-metathesis. The 19% *trans*-isomers of **14a** are not recovered and account for less than 10% of product **15a**. Right-hand side: selected PNOSY contacts and ^{1}H coupling constants that allow the complete assignment of relative stereochemistry in the major (90%) isomer of **15a**. This also allows complete assignment of relative stereochemistry in the two major (81%) diastereomers of **14a**.

dominant since this would result in the two ^3J couplings of C(4)–H with C(5)–H_2 being similar. Conformation **A** is presumably disfavoured by a second transannular interaction on the opposite face of the ring due to the C(4)–Me group which would be pseudoaxial. Having ascertained that the cyclohexenyl ring geometry is approximately flat, the NOE contact between C(4)–Me and C(5)$_{anti}$ indicates that the relative configuration at C(4) is such that the methyl group is on the opposite face of the cyclohexenyl (i.e. *anti*) to the cyclopropane. This then allows assignment of the relative stereochemistry of the precursor to **15a**, which is the major isomer (56%) of **14a**. This, in turn allows complete assignment of the relative configuration of the diastereomerically pure recovered **14a** (the minor *cis* isomer of **14a**) which is epimeric at C(2′′) (Figure 7). The two minor *trans*-isomers of the pre-RCM sample of **14a** (16.5% and 2.5%) were not present in recovered **14a** and only account for <10% of RCM-product **15a**. Presumably, they do undergo RCM (vide infra) but then undergo a subsequent polymerisation (e.g. by ROMP). However, the small quantities that remain (<10% of **15a**) were insufficient for conclusive NOE contacts to be observed to establish their relative configuration at C(4).

Whilst the diastereoselectivity can be rationalised (vide infra) the clean recovery of unchanged diastereomerically pure **14a** is very surprising for the following reasons. As with the diasteromers of **1b** and **1c**, the reactivity of the terminal vinyl group of **14a** (where the Ru-carbene catalyst **2** will effect metathesis first) should be near identical between diastereomers. Thus although three of the now Ru-carbene bearing intermediates (**16**) can undergo intermolecular [2+2] then retro [2+2] to generate **15a**, one (that generated from the minor *cis* isomer of **14a**) cannot. However, this latter intermediate must be able to cross metathesise to regenerate **14a** since the catalyst is not terminated. Thus in contrast to the problematic reactions with **1bc**, there was little or no trace of any dimeric material (**17a**) with **14a** as substrate. Clearly the extra methyl group at C(2′′), strongly inhibits dimerisation.

This may crudely be rationalised by considering a pseudo-A^{1,3}-strain based model. Thus, A^{1,3}-strain with a nonspecified Ru-ligand ('L') will place L in plane with the allylic proton (C(2′′)H in the rutheniumcarbene intermediate **16** – as illustrated in the upper section of Figure 8Now approach from both the upper and lower faces is hindered by methyl or methylene groups and thus metathesis will always occur in the '*exo*' mode resulting in regeneration of **14a**.

The kinetic diastereoselection process can also be explained in a qualitative manner by consideration of the intermediates **16** which must undergo [2+2] cycloaddition (lower section of Figure 8). Examination of Dreiding models indicates that for a parallel co-planar arrangement of the styrene and the Ru=CHR unit, a twist boat geometry must be attained (conformation **B** in Figure 3). Ignoring for a moment the methyl group on the cyclopropane, the methyl group at the allylic carbon results in two epimeric configurations **16**-eq and **16**-ax (where eq. and ax. refer to the geometric placement of the allylic methyl group upon RCM). In the [2+2] cycloaddition involving **16**-ax, both A^{1,3}-strain and transannular interaction of the pseudoaxial methyl group with the cyclopropane make this process highly disfavoured.

In contrast, A^{1,3}-strain in **16**-eq places the Ru-carbene in the correct orientation for [2+2] cycloaddition and also places the allylic methyl group in a pseudoequatorial position (see inset at bottom of Figure 8). Thus although the major diastereomer of **14a** (56%) has a *'cis'*-disposed methyl group and one might anticipate this would strongly disfavour RCM through transannular interaction, in fact this diastereomer is cyclised quantitatively. Of course, in the nonreacting diastereomer of **14a** (25%) this interaction augments the selectivity induced by the allylic methyl group since the transannular interaction is now 'Me/Me'.

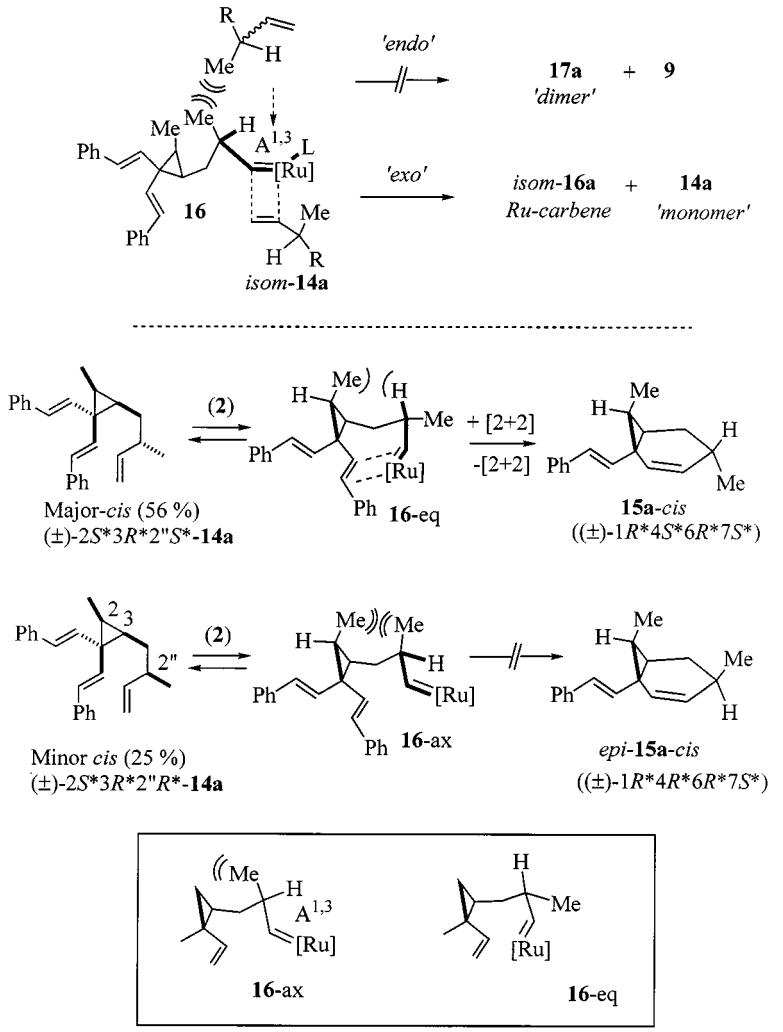


Figure 8. Upper section: A possible rationalisation, based on a pseudo-$A^{1,3}$-strain model, for the observation that Ru-carbene intermediates **16** do not undergo '*endo*' cross-metathesis to generate dimer **17a** (in stark contrast to **3bc**, generated from **1bc**, which readily generate **7bc**). The recovery of a single diastereomer of **14a** indicates that **16** can undergo *exo*-cross-metathesis to regenerate **14a**. Middle section: Possible origin of the powerful kinetic diastereoselectivity in the Ru-catalysed RCM of *cis*-**14a**. Lower section: The combination of $A^{1,3}$-strain and developing transannular interaction that disfavours [2+2]-cycloaddition in **16**-ax (where the C(2′′) methyl group is pseudoaxial on approach to the transition state.

Conclusions

The ring closing metathesis (RCM) reaction of a range of 2-alk-*n*-enyl-1-styrylcyclopropanes (**1a–c, 14a** and **11a**) have been investigated. In some examples, the RCM reactions proceed very efficiently under mild conditions using commercially available and easily handled Grubbs catalyst (**2**). In other examples there are problems involving competing cross-metathesis. No problems of reactivity of the cyclopropyl unit towards the Ru intermediates, e.g. VCP rearrangements, were observed.

The RCM reaction generates structures **5a–c** which are reminiscent of the core bicyclo[4.1.0]hept-2-ene ring structure of the terpenoid chenopodene.[11] Furthermore, by analogy with a double bond, the cyclopropane geometry controls the reactivity of the substrates and thus the RCM reactions of diastereomeric **1b** and **1c** can proceed only in the *cis* isomers. One might consider using this to substantially enrich these compounds in their unreactive *trans*-isomers. Indeed, the RCM of **1b** does increases the *de* from 27% to 92% *trans*, at the expense of ca. 55% conversion. However, as was elucidated by ^{1}H-NMR studies, although the RCM of *cis*-**1bc** occurs selectively, the enrichment suffers from a competing side reaction to generate 'dimeric' **7bc**. We are currently investigating the use of selective cross-metathesis reagents (e.g. allytrimethylsilane) to control this process. In contrast to the problems encountered with **1bc**, the dimethyl analogue (**14a**) of **1a** generated by HAC reaction with crotylindium reagents, undergoes smooth RCM reaction. The resulting product (**15a**) has the desired restriction of conformational mobility of the allylic carbon and this allowed nonambiguous NOE experiments to be performed. This has allowed complete assignment of the relative stereochemistry in the two major (81% *cis*) isomers of **14a** and major diastereomer (90%) of **15a** to be determined. Furthermore, the reaction proceeds with powerful kinetic diastereoselection which can be rationalised on the basis of a simple model involving a combination of pseudo-$A^{1,3}$-strain

and developing transannular interaction in the transition state leading to [2+2] *intramolecular* cycloaddition. The homologue (**11a**) of **1a** does not undergo RCM to generate a bicyclo[5.1.0]oct-2-ene (**12a**) under the conditions described. Although this may be ascribed to ring strain in the [2+2] cycloaddition, further work is required to fully address the distinct difference between the RCM of trienes **1a** and **11a**.

Future work will concentrate on further exploiting kinetic diastereoselection in RCM reactions involving dienes tethered through a cyclopropane ring and on the total synthesis of one of the terpenoid bicyclo[*n*.1.0]alk-2-ene family.

Experimental Section

General: Solvents and reagents were purified by standard procedures. Anhydrous solvents were purchased from Fluka or Aldrich and used as received. All manipulations and reactions were carried out under an argon atmosphere using standard Schlenk techniques. – NMR experiments were performed on JEOL Delta 270, Lambda 300, JEOL GX400 and JEOL Alpha 500 instruments. Chemical shift, multiplicities, assignments and coupling constants are based on a combination of some or all of the following: $^1H^1H$ COSY, PECSY, DEPT, $^{13}C^1H$ COSY (long and short range), PNOSY, $^1J_{CC}$ and $^1J_{CH}$ coupling. In cases where spectra were significantly second order, overlapping or complicated, iterative simulations (*g*-NMR) were performed until a satisfactory fit was obtained (in these cases chemical shifts and coupling constants are denoted "*simul.*"). – Mass spectra were obtained using both CI and EI sources on a Fisons Micromass Autospec mass spectrometer. – Elemental analysis of the compounds were performed by the analytical service of the School of Chemistry, University of Bristol. Some of the reaction products, whilst homogeneous by ^1H and ^{13}C NMR, gave slightly unsatisfactory elemental analyses – even after kugelrohr distillation. However, in all cases high-resolution mass spectra (HRMS) were satisfactory. – IR spectra: Perkin–Elmer 1600 FT, samples were prepared as thin films on NaCl or as KBr discs, absorptions are reported in cm^{-1} as strong (*s*), medium (m) or weak (w). – Flash column chromatography: Merck silica gel 60 eluting with a constant gravity head of ca. 15 cm solvent. – TLC: 0.25 mm, Merck silica gel 60 F254 visualising at 254 nm or with acidic (H_2SO_4) aq. $KMnO_4$ solution (ca. 2%).

Ring Closing Metathesis (RCM) Reactions

(±)-1-[(*E*)-2′-[Phenylethenyl]bicyclo[4.1.0]hept-2-ene (5a): (±)-2-(3′′-butenyl)-1,1-bis[(*E*)-2′-phenylethenyl]cyclopropane (**1a**) 110 mg (0.37 mmol) was dissolved in dry degassed dichloromethane (9 mL) and to the solution (0.041 M in **1a**) was added 9 mg of Grubbs catalyst (**2**) (0.011 mmol, 3 mol-%). The resulting orange solution was monitored by TLC. After 3 h 15 min no **1a** could be detected. The volatiles were removed in vacuo, the residue applied directly to pre-solvated silica-gel column and **5a** (55 mg, 73%) collected by fractional elution with hexanes. – IR (NaCl): $\tilde{\nu}$ = 3058 (m), 3025 (s), 2997 (m), 2924 (s), 2848 (m), 2360 (w), 1942 (w), 1867 (w), 1800 (w), 1648 (m), 1601 (w), 1493 (m), 1446 (m), 1344 (w), 1265 (w), 1214 (w), 1188 (w), 1087 (w), 1072 (w), 1052 (w), 1026 (w), 957 (s), 908 (m), 825 (w), 769 (s), 742 (s), 720 (m), 692 (s). – ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.04 [*dd*, 1H, ^2J(H,H) = 4.4 Hz, ^3J(H,H) = 8.6 Hz, C(7)H_{exo}]; 1.13 [*dd*, 1H, ^2J(H,H) = 4.4 Hz, ^3J(H,H) = 6.4 Hz, C(7)H_{endo}]; 1.50 [*simul*. *ddddd*, 1H, ^3J(H,H) = 8.6, 6.4, 3.3, 2.1 Hz; ^4J(H,H) = 1.9 Hz, C(6)H]; 1.67 [*simul*. *dddd*, 1H, ^2J(H,H) = 13.1 Hz, ^3J(H,H) = 12.2, 5.4, 3.3 Hz, C(5)H_{anti}]; 1.80 [*simul*. *ddddd*, 1H, ^2J(H,H) = 16.6 Hz, ^3J(H,H) = 12.2, 7.1, 2.6 Hz, ^4J(H,H) = 2.9 Hz, C(4)H_{syn}]; 1.98 [*simul*. *dddd*, 1H, ^2J(H,H) = 13.1 Hz, ^3J(H,H) = 7.1, 2.1, 1.5 Hz, C(5)H_{syn}]; 2.04 [*simul*. *dddddd*, 1H, ^2J(H,H) = 16.6, ^3J(H,H) = 6.4, 5.4, 1.5, ^4J(H,H) = 1.9, 1.0 C(4)H_{anti}]; 5.60 [*simul. ddd*, 1H, ^3J(H,H) = 10.1, 6.4, 2.6 Hz, C(3)H]; 5.95 [*d*, 1H, ^3J(H,H) = 16.0 Hz, C(1′)H]; 6.30 [*ddd*, 1H, ^3J(H,H) = 10.1, ^4J(H,H) = 2.9, 1.0 Hz, C(2)H]; 6.38 [*d*, 1H, ^3J(H,H) = 16.0 Hz, C(2′)H]; 7.15 (m, 1H, *p*-CH_{arom}); 7.27 (m, 2H, *m*-CH_{arom}); 7.32 (m, 2H, *o*-CH_{arom}). – $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ = 18.4 [C(5)H_2]; 20.6 [C(4)H_2]; 21.1 [C(7)H_2]; 21.3 [C(1)]; 25.1 [C(6)H]; 123.3 [C(3)H]; 125.56 [C(1′)H]; 125.61 (*o*-CH_{arom}); 126.5 (*p*-CH_{arom}); 128.5 (*m*-CH_{arom}); 129.1 [C(2)H]; 136.9 [C(2′)H]; 137.8 (*i*-C_{arom}). – HRMS(CI): $[M + H]^+$, $C_{15}H_{17}$ calcd. 197.1330; found 197.1325. – MS(CI); *m*/*z* (%): 197 $[M + H]^+$ (24), 196 $[M]^+$ (72), 181 (23), 168 (25), 155 (17), 141 (14), 129 (16), 117 (22), 105 (19), 93 (30), 91 (40). – TLC: *Rf* = 0.52 (hexane/EtOAc, 19:1).

Bicyclo[4.1.0]hept-2-ene (5b):[24] 1-(*E*-2′-phenylethenyl)-2-(but-3′′-enyl) cyclopropane **1b** (5 mg, 0.024 mmol) was dissolved in CD_2Cl_2 (1.0 mL) under argon. After a preliminary ^1H NMR (270 MHz) spectrum had been taken, 60 μL (0.7 μmol, 3 mol-%) of a pale pink solution of **2** (2 mg, 3.5 μmol in 0.2 mL CD_2Cl_2) was added *via* microsyringe resulting in a pale orange solution. This was monitored by ^1H NMR over a period of 24 h. After a total of 30 h the volatiles were removed at < 0.1 Torr and collected in a liquid nitrogen trap. The residue was re-dissolved in CD_2Cl_2 (1.0 mL) and ^1H NMR analysis indicated the presence of **1b** (96% *trans*) and **7b** (82% *trans* at C(1) and as a 2/1 ratio double bond isomers) in a 3/1 mol ratio. Material collecting in the trap was identified at a ca. 1/1 mixture of styrene and **5b** in CD_2Cl_2. – **Material collecting in trap (5b):**[24] ^1H NMR (CD_2Cl_2, 300 MHz): δ = 0.52 [*ddd*, 1H, ^2J(H,H) = 4.4 Hz, ^3J(H,H) = 5.7, 5.7 Hz, C(7)H_{exo}]; 0.64 [*ddd*, 1H, ^2J(H,H) = 4.4 Hz, ^3J(H,H) = 8.3, 8.3 Hz, C(7)H_{endo}]; 1.15–1.25 [m, 2H, C(5)–H_{anti} and C(6)H]; 1.60–1.78 [m, 2H, C(1)–H and C(4)H_{syn}]; 1.80–1.93 [m, 2H, C(4)–H_{anti} and C(5)H_{syn}]; 5.25–5.35 [m, 1H, C(3)–H]; 5.94 [*ddd*, 1H, ^3J(H,H) = 9.5, 5.5 Hz, ^4J(H,H) = 3.1 Hz, C(2)H]. – MS(CI); *m*/*z* (%): 95 $[M + H]^+$ (10), 81 (13), 69 (30), 57 (95), 55 (100).

1-Methylbicyclo[4.1.0]hept-2-ene (5c):[25] (±)-2-(3′′-Butenyl)-1-methyl-1-[(*E*)-2′-phenylethenyl]cyclopropane **1c** (5 mg, 0.025 mmol) in CD_2Cl_2 (1.0 mL) was reacted as above with 3 mol-% (58 μL stock solution) of **2**. After > 40 removal of the volatiles and ^1H NMR analysis of the residue (in CD_2Cl_2, 1.0 mL) indicated the presence of **1c** (67% *trans*) and **7c** (63% *trans* at C(1)) in a 1.7/1 mol ratio. Material collecting in the trap was identified at a ca. 1/1 mixture of styrene and **5c** in CD_2Cl_2. – **Material collecting in trap (5c):**[25] ^1H NMR (CD_2Cl_2, 270 MHz): δ = 0.47 [*dd*, 1H, ^2J(H,H) = 4.0 Hz, ^3J(H,H) = 8.3 Hz, C(7)–H_{endo}]; 0.69 [*dd*, 1H, ^2J(H,H) = 4.0 Hz, ^3J(H,H) = 4.3 Hz, C(7)–H_{exo}]; 1.03–1.12 [m, 1H, C(6)–H]; 1.53–1.60 [m, 1H, C(5)–H_{syn}]; 1.69 [*dddd*, 1H, ^2J(H,H) = 11.6 Hz, ^3J(H,H) = 16.8, 2.6, 2.6 Hz, C(5)–H_{anti}]; 1.80–2.00 [m, 2H, C(4)H_2]; 5.39 [*ddd*, 1H, ^3J(H,H) = 9.9, 6.6, 1.3, C(3)–H]; 5.85 [*dd*, 1H, ^3J(H,H) = 9.9 Hz, ^4J(H,H) = 2.6 Hz, C(2)–H]. – HRMS(CI): $[M + H]^+$ C_8H_{13} calcd. 109.1017; found 109.1015.

(±)-1*R4*S**6*R**7*S**-4,7-Dimethyl-1-[(*E*)-2′-phenylethenyl]bicyclo-[4.1.0]hept-2-ene (15a):** (±)-2-[3′′-(2′′-methyl)butenyl)]-3-methyl-1,1-bis[(*E*)-2′-phenylethenyl]cyclopropane **14a** 153 mg (0.47 mmol) was dissolved in dry degassed dichloromethane (12 mL) and to the solution (0.04 M in **1a**) was added Grubbs catalyst (**2**) 12 mg (0.014 mmol, 3 mol-%). The resulting purple solution was stirred at ambient temperature and turned orange then brown in colour

over a period of 48 h. The volatiles were removed in vacuo, the residue applied directly to pre-solvated silica-gel column and **14a** (34 mg, 22%) and **15a** (67 mg, 64%) collected by fractional elution with hexanes. – **Analytical data for 15a:** IR (NaCl): $\tilde{\nu}$ = 3058 (m), 3025 (m), 2957 (m), 2926 (m), 1638 (m), 1600 (m), 1494 (m), 1448 (m), 1098 (w), 1073 (w), 1028 (w), 964 (s), 910 (m), 745 (s), 692 (s). – ^{1}H and ^{13}C NMR assignments are given for the major (90%) diastereomer (±)-1*R**4*S**6*R**7*S**). – ^{1}H NMR (C_6D_6, 500 MHz): δ = 0.94 [*d*, 3H, ^3J(H,H) = 7.2° Hz, C(4)–CH_3]; 1.10 [*d*, 3H, ^3J(H,H) = 6.1 Hz, C(7)–CH_3]; 1.18 [*ddd*, 1H, ^2J(H,H) = 13.9 Hz, ^3J(H,H) = 11.3, 5.3 Hz, C(5)–H_{syn}]; 1.30 [*dq*, 1H, ^3J(H,H) = 8.9, 6.1 Hz, C(7)–H]; 1.34 [*dddd*, ^3J(H,H) = 8.9, 8.6, 5.3 Hz, ^4J(H,H) = 1.1 Hz, C(6)–H]; 2.00 [*ddd*, 1H, ^2J(H,H) = 13.9 Hz, ^3J(H,H) = 8.6, 5.7 Hz, C(5)–H_{anti}]; 2.32 [*dddq*, 1H, ^3J(H,H) = 11.3, 5.6, 1.9' Hz, ^4J(H,H) = 3.0 Hz, C(4)–H]; 5.83 [(*dd*, 1H, ^3J(H,H) = 9.8, 1.9 Hz, C(3)–H]; 5.90 [*ddd*, 1H, ^3J(H,H) = 9.8 Hz, ^4J(H,H) = 1.9, 1.1 Hz, C(2)–H]; 6.00 [*d*, 1H, 16.0, C(1′)–H]; 6.30 [*d*, 1H, 16.0, C(2′)–H]; 7.10 (m, 1H, *p*-$CH_{arom.}$); 7.27 (m, 2H, *m*-$CH_{arom.}$); 7.39 (m, 2H, *o*-CH_{arom}). – ^{13}C{^{1}H} NMR (C_6D_6, 75 MHz): δ = 9.1 [C(7)–CH_3]; 21.6 [C(4)–CH_3]; 22.9 [C(6)]; 26.5 [C(1)]; 28.0 [C(4)]; 28.7 [C(5)]; 29.1 [C(7)]; 126.0 [C(2)]; 126.1 [C(1')]; 126.3 [*o*-CH_{arom}]; 126.9 (*p*-CH_{arom}); 129.0 (*m*-CH_{arom}); 138.2 [C(3)]; 138.77 [C(2′)]; 138.81 (*i*-C_{arom}). – MS(CI); *m/z* (%): 225 [M + H]$^+$ (13), 224 (23), 209 (9), 195 (9), 181 (16), 169 (10), 147 (16), 131 (13), 121 (23), 109 (13), 107 (18), 105 (28), 97 (46), 91 (32), 84 (30), 79 (21), 69 (50), 57 (100), 55 (88). – HRMS(CI) [M + H]$^+$: $C_{17}H_{20}$ calcd. 224.1565; found 224.1565. – TLC: *Rf* = 0.49 (hexanes/EtOAc, 19:1).

Homologation of 1a to 11a

(±)-2-(4′′-Carboxy-3′′-butenyl)-1,1-bis[(*E*)-2′-phenylethenyl]cyclopropane (10a): To a stirred solution of oxalyl chloride (0.491 g, 2.0 mmol) in dichloromethane (25 mL) cooled to –78 °C, under argon, was added dimethylsulfoxide (0.220 mL, 3.0 mmol). After 20 min, a solution of **9a**[8](0.491 g, 1.5 mmol) in dichloromethane (3 mL) was added. After a further 90 min Et_3N (2 mL, 3.9 mmol) was added and the reaction warmed to room temp over a period of 90 min. The reaction mixture was quenched with water and extracted with dichloromethane (5 × 40 mL). The combined extracts were washed with water (2 × 50 mL), dried ($MgSO_4$) and the solvent removed in vacuo to leave a yellow oil. This was purified by flash chromatography on silica gel (hexane:EtOAc, 19:1) to give the aldehyde **11a** as a slightly yellow oil 332 mg, (68%). – IR (NaCl): $\tilde{\nu}$ = 3024 (m), 2933 (w), 2858 (w), 2720 (w), 1722 (s), 1640 (w), 1598 (w), 1493 (m), 1448 (m), 1389 (w), 1073 (w), 1028 (w), 966 (s), 910 (w), 747 (s), 693 (s). – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.96 [*dd*, 1H, ^2J(H,H) = 3.8 Hz, ^3J(H,H) = 5.1 Hz, C(3)H_{syn}]; 1.13 [m, 1H, C(3)H_{anti}]; 1.20 [m, 1H, C(2)H]; 1.44 [m, 2H, C(1′′)H_2]; 1.73 [*dddd*, ^3J(H,H) = 6.9, 6.9, 6.9, 6.9 Hz, C(2′′)H2]; 2.42 [*td*, 2H, ^3J(H,H) = 7.3, 1.8° Hz, C(3′′)H_2]; 6.17 [*d*, 1H, ^3J(H,H) = 6.0 Hz, C(2′$_{anti}$)H]; 6.36 [*d*, 1H, ^3J(H,H) = 16.0 Hz, C(1′$_{anti}$)H]; 6.37 [*d*, 1H, ^3J(H,H) = 16.0 Hz, C(1′$_{syn}$)H]; 6.47 [*d*, 1H, ^3J(H,H) = 16.0° Hz, C(2′$_{syn}$)H]; 7.14–7.42 [m, 10H, CH_{arom}); 9.71 (*t*, 1H, ^3J(H,H) = 1.8 Hz, C(4′′)H]. – ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ = 19.8 [C(3)H_2]; 22.1 [C(2′′)H_2]; 28.6 [C(2)H]; 28.7 [C(1′′)H_2]; 29.8 (C(1)]; 43.4 [C(3′′)H_2]; 125.8, 126.0 (2 × CH_{arom}); 126.8, 127.1 (2 ∞ CH_{arom}); 127.5 (C(1′$_{syn}$)H); 128.4, 128.5 (2 × CH_{arom}); 129.6 (C(1′$_{anti}$)H); 131.8 (C(2′$_{syn}$)H); 135.7 (C(2′$_{anti}$))H); 137.3, 137.4 (2 × C_{arom}); 202.3 (C(4′′)H). – MS(EI); *m/z* (%): 316 [M]$^+$ (94), 257 (52), 245 (57), 231 (21), 219 (27), 215 (50), 197 (14), 191 (12), 167 (52), 153 (50), 141 (67), 128 (56), 115 (62), 91 (100), 77 (24). – HRMS(EI): $C_{23}H_{24}O$ calcd. 316.1827; found 316.1824. – TLC: *Rf* = 0.30 (hexane/EtOAc, 9: 1).

(±)-2-(4′′-Pentenyl)-1,1-bis[(*E*)-2′-phenylethenyl]cyclopropane (11a): (±)-2-(4′′-carboxy-3′′-butenyl)-1,1-bis[(*E*)-2′-phenylethenyl]-cyclopropane **10a** (50 mg, 0.174 mmol) in THF (1 mL) was added to an orange solution of $PPh_3{=}CH_2$ (generated from 0.19 mmol [PPh_3CH_3][I], excess KH and 0.19 mmol 18-crown-6, 0 °C to room temp) in THF (2 mL) resulting in complete decolourisation (beige) after 1 h. The reaction was stirred overnight before quenching with water (3 mL) then extracting with two portions of CH_2Cl_2 (25 mL). The combined extracts were washed with water, dried ($MgSO_4$) and the solvent removed in vacuo to leave a yellow oil. Chromatography on silica-gel eluting with hexanes gave **11a** as a colourless oil 36.6 mg, (67%). – IR (NaCl): $\tilde{\nu}$ = 3059 (m), 3024 (s), 2995 (m), 2925 (s), 2854 (m), 2359 (w), 1943 (w), 1872 (w), 1800 (w), 1744 (w), 1639 (s), 1598 (m), 1576 (w), 1493 (s), 1447 (s), 1414 (w), 1202 (w), 1179 (w), 1156 (w), 1073 (w), 1028 (w), 963 (s), 910 (s), 839 (w), 746 (s), 692 (s). – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.96 [*dd*, 1H, ^2J(H,H) = 4.4 Hz, ^3J(H,H)$_{anti}$ = 5.7 Hz, C(3)H_{syn}]; 1.16 [*dd*, 1H, ^2J(H,H) = 4.4 Hz, ^3J(H,H)$_{syn}$ = 8.3 Hz, C(3)H_{anti}]; 1.22 [*dddd*, 1H, ^3J(H,H) = 8.3, 8.2, 6.3, 5.7 Hz, C(2)H]; 1.33–1.57 [m, 4H, C(1′′)H_2 and C(2′′)H_2]; 2.07 [*ddddd,* 2H, ^3J(H,H) 6.2, 6.2, 6.2 Hz, ^4J(H,H) = 1.6, 1.1 Hz, C(3′′)H_2]; 4.93 [*ddt*, 1H, ^2J(H,H) = 1.7 Hz, ^3J(H,H) = 10.3 Hz, ^4J(H,H) = 1.1 Hz, C(5′′)H_{cis}]; 5.00 [*ddt*, 1H, *2J*(H,H) = 1.7 Hz, ^3J(H,H) = 16.9 Hz, ^4J(H,H) = 1.6 Hz, C(5′′)H_{trans}]; 5.79 [*ddt*, 1H, ^3J(H,H) = 16.9, 10.3, 6.6 Hz, C(4′′)H]; 6.18 (*d,* 1H, ^3J(H,H) = 15.8 Hz, C(2'$_{anti}$)H]; 6.36 [*d*, 1H, ^3J(H,H) = 15.8 Hz, C(1′$_{anti)}$H]; 6.39 [*d*, 1H, ^3J(H,H) = 16.0 Hz, C(1′$_{syn}$)H]; 6.47 (*d*, 1H, *3J*(H,H) = 16.0 Hz, C(2′$_{syn}$)H]; 7.17 [*tt*, 1H, ^3J(H,H) = 7.2 Hz, ^4J(H,H) = 1.3 Hz, *p* -$CH_{arom.anti}$]; 7.22 [*tt*, 1H, ^3J(H,H) = 7.3 Hz, ^4J(H,H) = 1.4 Hz, *p*-$CH_{arom.syn}$]; 7.28 (m, 2H, *m*-$CH_{arom.anti}$); 7.30 (m, 2H, *m*-$CH_{arom.syn}$); 7.33 (m, 2H, *o*-$CH_{arom.anti}$); 7.39 (m, 2H, *o*-$CH_{arom.syn}$). – ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ = 20.0 [C(3)H_2]; 28.8 and 29.0 [C(1′′)H_2 and C(2′′)H_2]; 29.2 [C(2)H]; 29.9 [C(1)]; 33.5 [C(3′′)H_2]; 114.4 [C(5′′)H_2]; 125.8 (*o* -$CH_{arom.anti}$); 126.1 (*o* -$CH_{arom.syn}$); 126.8 (*p*-$CH_{arom.anti}$); 127.1 (*p* -$CH_{arom.syn}$); 127.3 [C(1')H_{syn}]; 128.5 (*m*-$CH_{arom.anti}$); 128.6 (*m*-$CH_{arom.syn}$); 130.2 (C(1')H_{anti}); 131.6 (C(2')H_{syn}); 136.3 (C(2')$_{anti}$); 137.6 (*i*-$C_{arom.syn}$); 137.7 (*i*-$C_{arom.anti}$); 138.9 [C(4′′)H]. – MS(EI); *m/z* (%): 314 [M]$^+$ (32) 271 (18), 257 (34), 245 (58), 231 (26), 219 (26), 215 (50), 202 (30), 191 (16), 181 (22), 167 (60), 153 (50), 141 (70), 128 (62), 115 (54), 91 (100). – HRMS(EI) $C_{24}H_{26}$: calcd. 314.2035; found 314.2032. – TLC: *Rf* = 0.76 (hexane/EtOAc, 9:1).

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[19] Note that generation of 10% **7b** requires conversion of 20% **1b**.
[20] Obviously, a degenerate cross-metathesis of *trans*-**3b** with *trans*-**1b** can also occur with similar propensity.
[21] The analysis of the ratio of *cis* and *trans* isomers of **7bc** was aided by the observation that the chemical shifts of the C(2')–H styryl protons were very slightly upfield of their 'monomeric' precursors.
[22] The geometric (*E*/*Z*) identities of the double bonds could not be assigned on the basis of differing second order mulitiplets in the ^{1}H-NMR signals arising from the alkenyl protons in *E*/*Z*-CH_2–CH=CH–CH_2–.
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