Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 64 (2008) 204–218
Tetrahedron
www.elsevier.com/locate/tet

Synthesis of *N*-heterocyclic compounds via ene–yne metathesis reactions

Elisabetta Groaz [a], Donatella Banti [a,b,*], Michael North [a,c]

[a] *Department of Chemistry, King's College, Strand, London, WC2R 2LS, UK*
[b] *School of Pharmacy and Chemistry, Kingston University, Penrhyn Road, Kingston-upon-Thames, Surrey KT1 2EE, UK*
[c] *School of Natural Sciences, Bedson Building, Newcastle University, Newcastle upon Tyne, NE1 7RU, UK*

Received 4 July 2007; received in revised form 28 September 2007; accepted 18 October 2007
Available online 23 October 2007

Abstract

Propargylamino and allylamino derivatives of cyclohexene and norbornene were subjected to tandem metathesis reactions with first and second generation Grubbs' catalysts **1** and **2**. Results show that the method is compatible with suitably protected nitrogen-containing compounds. Cyclohexenes gave intriguing results in terms of the possibility to perform ring rearrangement metathesis (RRM) reactions, showing a difference with the analogous allyl and propargyl ether substrates.

Keywords: Nitrogen heterocycles; Ring closing; Enyne; Metathesis; Ruthenium

1. Introduction

Metathesis reactions are a powerful tool in the hand of organic chemists for the synthesis of C–C bonds. The range of their application in synthetic chemistry has expanded rapidly in the last 15 years[1] and enyne metatheses in particular have become popular very recently.[2] These phenomena can be attributed to growing efforts and research into new catalyst design and applications. Amongst these, relatively stable and user-friendly ruthenium–carbene catalysts have been widely used.[3] First[4] and second[5] generation Grubbs' catalysts **1** and **2** (Fig. 1) are probably the most general for synthetic purposes. Our group has worked extensively on the use of both catalysts

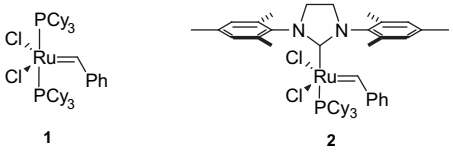


Figure 1. First, **1** and second, **2** generation Grubbs' catalysts.

1 and **2** for the synthesis of highly functionalized polycyclic oxygenated heterocycles through cascade metathesis processes or tandem metathesis/Diels–Alder reactions of norbornene derivatives,[6] our focus being the definition of scope and limitations for Cross Enyne Metathesis (CEYM) and Ring Closing Enyne Metathesis (RCEYM).

Recently, we have also reported similar chemistry with 4,5-diallyloxy and -dipropargyloxy derivatives of cyclohexane and cyclohexene. The major difference between the two substrate classes being that the unstrained, disubstituted alkene unit within the cyclohexene ring does not participate in these metathesis cascades.[7]

Nitrogen-containing heterocycles are widely represented amongst naturally occurring products and biologically active molecules in the form of isolated or fused ring systems. Therefore, it was of interest to demonstrate whether the substitution of oxygen by a nitrogen atom at the propargylic positions would also provide good candidates for domino processes upon treatment with ruthenium initiators.

Nevertheless, it is important to be aware of issues around the presence of amino groups in metathesis reactions as it is commonly accepted that amino groups can coordinate to the transition metal and deactivate it. Successful methodologies to react amine containing substrates in metathesis reactions

* Corresponding author. Tel.: +44 208 547 7554; fax: +44 208 547 7497.
E-mail address: d.banti@kingston.ac.uk (D. Banti).

0040-4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.10.076

with catalysts **1** and **2**,[8] have mainly involved the use of amines bearing strongly electron-withdrawing groups.[9] The use of ammonium salts,[10] or the addition of Lewis acids to coordinate to the amine,[11] has also proved effective, though there are examples in the literature that prove that these prerequisites are not always essential.[12]

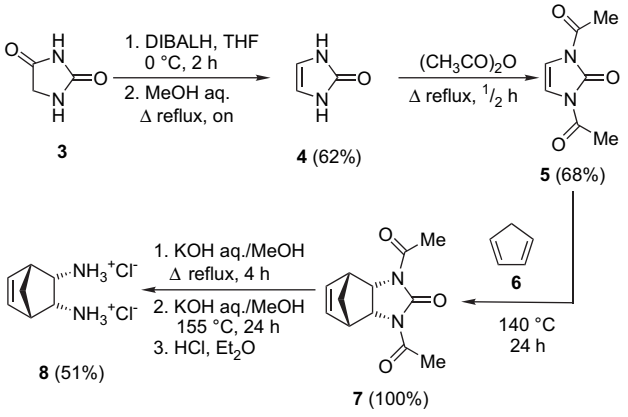
In this paper we describe the synthesis and metathesis of the allylamino and propargylamino derivatives of norbornene and cyclohexene[13] analogous to the allyl and propargyl ether derivatives used previously.[6,7] In the case of the cyclohexenes we show that the cyclohexene unit of these compounds can participate in metathesis cascade sequences, leading to 2,2′-bis-(tetrahydropyridine) derivatives.[14]

2. Results and discussion

2.1. Norbornene derivatives

By analogy with previous studies on oxygen-containing derivatives, it was decided to synthesize 2,3-diamino-*endo,cis*-norborn-5-ene dihydrochloride as the first substrate.

2,3-Diamino-*endo,cis*-norborn-5-ene dihydrochloride **8**, was obtained by a modified literature procedure using a Diels–Alder reaction between cyclopentadiene **6** and imidazolyl derivative **5** as the key step.[15] The overall strategy for preparing compound **8** is shown in Scheme 1.



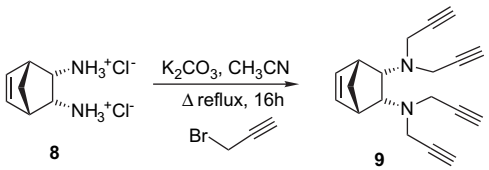
Scheme 1.

Dienophile **5** was accessed in two steps via a modified literature procedure from commercially available hydantoin **3**.[16] Addition of diisobutylaluminium hydride (DIBALH) to compound **3** was followed by hydrolysis with aqueous methanol. The so-generated reduction product underwent elimination after overnight reflux affording 1,3-dihydro-imidazol-2-one **4** in 62% yield. The subsequent acetylation of compound **4** to bisamide **5** was easily achieved by refluxing 1,3-dihydro-imidazol-2-one **4** for 30 min with an excess of acetic anhydride and yielded 68% of the desired 1,3-diacetyl-1,3-dihydro-imidazol-2-one **5**.

Compound **5** was then heated with an excess of freshly distilled cyclopentadiene **6** in a sealed tube at 140 °C for 24 h to provide Diels–Alder adduct **7**. Rather than using the reported conditions, which included the use of xylene and higher temperatures (180 °C),[15,16] we chose to perform the reaction in the absence of solvent. Under these conditions, conversion of **5** to **7** was quantitative and yields were consistently higher than those reported in the literature.

Exhaustive base hydrolysis of **7** required a two steps procedure.[15] Upon heating with aqueous KOH in refluxing methanol for 4 h, hydrolysis of Diels–Alder adduct **7** progressed only to removal of the acetyl groups. In order to fully unmask the targeted diamine, a further treatment was needed. Thus, the intermediate was heated with an alkaline aqueous solution in a sealed tube at 155 °C for 24 h. The free diamine thus generated was immediately converted to the dihydrochloride salt **8** for storage, by treatment with a 1 M solution of hydrogen chloride in diethyl ether.

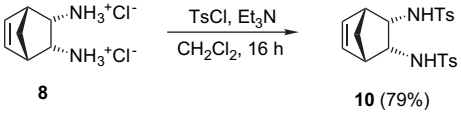
The first substrate to be tested for metathesis was the tetrapropargylamine **9**, obtained by reacting the bis-ammonium salt **8** with propargyl bromide in the presence of potassium carbonate as a base (Scheme 2).[17] Product **9** could only be isolated in a 28% yield due to its difficult purification by either chromatography or distillation.



Scheme 2.

Attempted metathesis reactions on compound **9** did not give any results with catalyst **1** or **2** when using the standard conditions of dry dichloromethane as solvent under an ethene atmosphere, either at room temperature or reflux. Substrate **9** has two amino groups that could chelate the metal centre in the catalyst deactivating it. In order to try to break a possible chelate formation a Lewis acid ($Ti(O^iPr)_4$) was added with catalyst **1**, but this strategy did not prove to be effective.

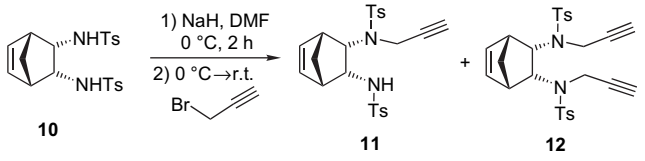
It was then decided to decrease the nucleophilicity of the amino group by converting it into a sulfonamide. The decision to use tosyl was due to a compromise between the desired steric and electronic properties. The formation of ditosyl diamine **10** essentially followed the literature procedure for similar transformations (Scheme 3).[18] Thus, the addition of triethylamine followed by *p*-toluenesulfonyl chloride in dichloromethane at room temperature turned out to be optimal in terms of isolated yield.



Scheme 3.

For the final stage of the synthesis, compound **10** was intended to be converted into the corresponding *endo*-bispropargylamino metathesis precursor **12** via nucleophilic substitution with propargyl bromide. However, under our standard

alkylation conditions (NaH in DMF, excess of propargyl bromide, room temperature, 24 h) a mixture of mono-alkylated product **11** and unreacted starting material **10** was obtained along with the desired dialkylated product **12** (Scheme 4). Attempts to force the reaction to 100% conversion of the starting material under different conditions such as higher temperatures (50 °C or refluxing in DMF), longer reaction times (48, 72 and 96 h) and addition of sodium iodide were unsuccessful as the ratio of bis to mono-alkylated products was never increased from the initial 2:1 value, as revealed by ^{1}H NMR analysis of the crude mixture.



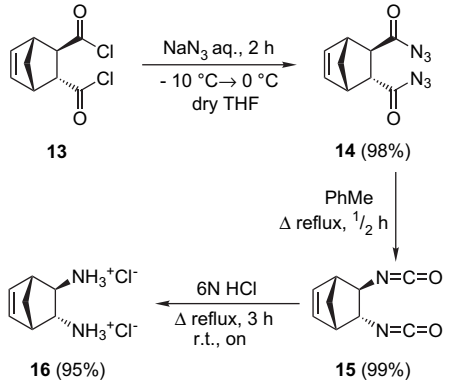
Scheme 4.

Complete separation of compounds **11** and **12** by column chromatography or recrystallization was not possible due to their very similar retention times and solubilities in a wide range of solvent mixtures. Moreover, reaction of a mixture of compound **12** containing minor amounts of **11** as impurity and with 5 mol % of catalyst **1** in dichloromethane at room temperature under an ethene atmosphere was unsuccessful since the ruthenium catalyst could not tolerate the presence of mono-alkylated compound **11** even as a minor impurity.

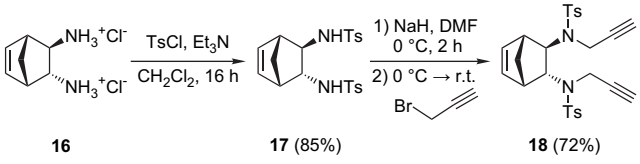
As a consequence, the screening of other possible base/solvent combinations that might affect the desired deprotonation under sufficiently mild conditions was carried out. None of the conditions examined were entirely satisfactory. Interestingly it was found that the use of a stronger base, for instance potassium hydride, avoided the formation of the mono-substituted species **11**; nevertheless only 43% of **10** was converted into bis-propargylated diamine **12** after refluxing for 3 days in THF as proven by inspection of the ^{1}H NMR spectrum. Addition of catalytic amounts of 18-crown-6 was not advantageous in encouraging the reaction to completion and the chromatographic separation of the two compounds proved very difficult. The non-nucleophilic base potassium hexamethyldisilazide (KHMDS), failed to give the desired deprotonation probably due to steric factors. At this point it was decided to discontinue this route to the bis-*endo* substituted compound **12**.

Nevertheless, we were encouraged to continue our research into amino substituted norbornene rings by a recent report on the straightforward Ring Rearrangement Metathesis (RRM) of a mono-*endo*-propargylamino norbornene.[9o] An opportunity to test our protocol on *N*,*N*′-bis-amino substituted norbornenes was available by using the analogous *trans*-substrates.

There was no precedent in the literature for the preparation of *trans*-2,3-diamino-norborn-5-ene dihydrochloride **16**. The synthesis, illustrated in Scheme 5, started with the addition of an aqueous solution of sodium azide to commercially available (+/−)-*trans*-5-norbornene-2,3-dicarbonyl chloride **13** to form the corresponding diacyl azide **14** in excellent yield (98%). Compound **14** was then subjected to thermal rearrangement without further purification. Curtius rearrangement of the crude azide in toluene formed bis-isocyanate **15**, which was immediately hydrolysed to the dihydrochloride salt of *trans*-diamine **16** in 95% yield. Standard tosylation conditions were applied to **16** to give the bis-tosylated *trans*-norbornene diamine **17** in high yield (85%) after work-up and purification by column chromatography (Scheme 6). We were pleased to find that bis-propargylation of **17** could be achieved effortlessly under standard conditions. The crude compound was purified by recrystallization from ethyl acetate/hexane, thus providing the *trans*-diamine **18** in 72% yield.

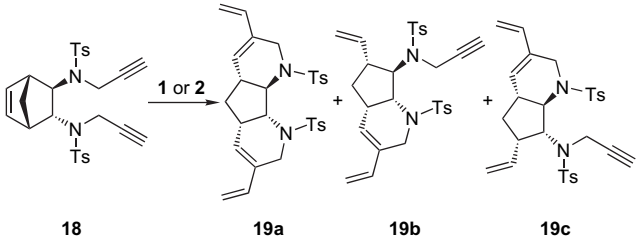


Scheme 5.



Scheme 6.

Three possible RRM products could be obtained by treating substrate **18** with either catalyst **1** or **2** (Scheme 7). First, the metathesis of **18** was attempted with 5 mol % of **1** in dry dichloromethane at room temperature. As expected, by working under a nitrogen atmosphere and in the absence of an additional olefin, no conversion was observed after 48 h.



Scheme 7.

Therefore, the experiment was repeated in the presence of an ethene atmosphere. Results are presented in Table 1. Reaction with 5 mol % of **1** in dichloromethane at room temperature in the presence of ethene resulted in complete consumption of starting material over a period of 6 h (Table 1,

Table 1
Metathesis of diyne **18** with catalysts **1** and **2** in the presence of ethene

Entry	Cat (mol %)	Solvent	T (°C)	t (h)	Conv[a]	**19a** (%)[b]
1	**1** (5)	CH_2Cl_2	25	6	100	41
2	**1** (5)	CH_2Cl_2	25	16	100	43
3	**1** (5)+**2** (5)	CH_2Cl_2	25	24	100	37
4	**2** (5)	Toluene	60	24	0	0

[a] Percentage conversion was estimated from the ^{1}H NMR spectrum of the crude mixture.
[b] This column reports the percentage yield calculated on the product recovered after chromatographic purification.

entry 1). Inspection of the ^{1}H NMR spectrum of the crude residue obtained after removal of all the volatiles and TLC analysis showed that the reaction yielded multiple products, the identification of which was complicated by the lack of symmetry in compounds **18** and **19**.

In attempts to purify the products by flash chromatography, different solvent mixtures were employed but none was particularly successful. However, using dichloromethane as eluent it was possible to isolate the tricyclic compound **19a** incorporating two azacyclohexene substructures in 41% yield. Evidence of two additional products: *cis*- and *trans*-mono-cyclized compounds **19b** and **19c**, was observed by NMR spectroscopy, but they were only present in mixed fractions. Given the difficulties in obtaining analytically pure samples of these compounds by conventional separation techniques; the impure samples were submitted to GC–MS analysis, which showed the presence of the expected molecular ion peaks. The exact relative ratio of the two mono-cyclized products could not be established, however, a cis preference of ring closure (forming **19b**) for the ring opened carbene could be postulated due to the shape of the substrate.

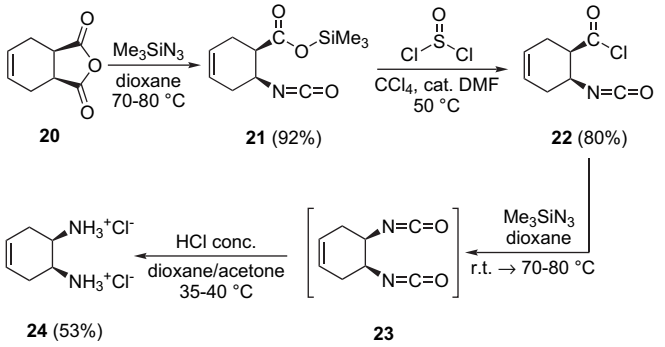
Longer reaction times did not produce a significant change in the chemoselectivity of the process and compound **19a** was still formed in 43% yield (Table 1, entry 2). An additional attempt to drive the reaction towards the selective formation of tricycle **19a** was carried out by adding 5 mol % of **1** followed by 5 mol % of **2**. This approach, which was found to be useful in previous examples,[6] in this case did not lead to any improvement in the yield of **19a** (Table 1, entry 3). The use of catalyst **2** alone in toluene at 60 °C did not give any positive results (Table 1, entry 4).

2.2. Cyclohexyl derivatives

2.2.1. Alkene metathesis

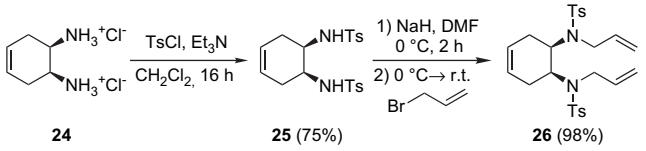
As mentioned in Section 1, cyclohexene derivatives bearing analogous propargyl and allyl tosyldiamino groups were also synthesized and tested for metathesis reactions with catalysts **1** and **2**.

The synthesis of *cis*-1,2-diamino-cyclohex-4-ene dihydrochloride **24** (Scheme 8) has been previously reported.[19] Commercially available 1,2,3,6-tetrahydrophthalic anhydride **20** was purified by heating under reflux for 3 h with acetic anhydride and petroleum ether before being treated with trimethylsilylazide in dioxane. Trimethylsilyl ester product **21** was purified by Kugelröhr distillation prior to use in the subsequent chlorination reaction, which was carried out with thionyl chloride in CCl_4 upon addition of a catalytic amount of DMF. The so-formed acyl chloride **22** underwent a second Curtius rearrangement, followed by hydrolysis of bis-isocyanate **23** to afford *cis*-diamine **24** in the form of a dihydrochloride salt. Diamine **24** was thus prepared in a comparable yield to that reported in the literature (53%).[19]



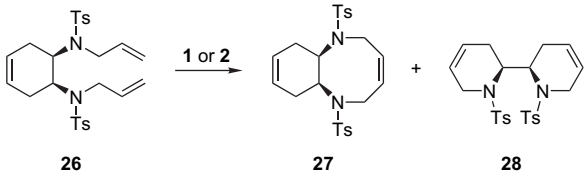
Scheme 8.

Compound **24** was converted into the corresponding *N*,*N*′-bis-tosylate **25** in 75% yield after purification by flash chromatography (Scheme 9). This core structure was then used in alkylation reactions for the synthesis of different substrates for metathesis reactions. Once again, the first substrate to be tested for metathesis activity was a simple olefinic substrate **26**. *N*,*N*′-Bis-allylation of bis-tosyl *cis*-diamine **25** was carried out with NaH as base in DMF as solvent following a general literature procedure (Scheme 9).[20] The reaction was quenched with saturated aqueous NH_4Cl and after work-up readily yielded substrate **26** in excellent yield (98%).



Scheme 9.

Substrate **26** was subjected to metathesis reaction in the presence of either catalyst **1** or **2**. The possible products that could result follow the rationale previously illustrated for the ether analogues[7] of **26** (Scheme 10). Reaction conditions and results are presented in Table 2. As was the case for bis-allyl ethers,[7] ring-closing metathesis at the exocyclic double bonds was found to prevail over the alternative tandem ROM/RCM route.



Scheme 10.

Table 2
Metathesis of diene **26** with catalysts **1** and **2**

Entry[a]	Cat (mol %)	Atm	Yield[b] (%)		
			27	**28**	**26**[c]
1	**1** (5)	N_2	100	0	0
2	**1** (5)	$H_2C{=}CH_2$	83	0	17
3	**2** (5)	N_2	71	29	0
4	**2** (5)	$H_2C{=}CH_2$	21	9	70

[a] All the reactions were carried out at 25 °C in dry dichloromethane.
[b] Yields were calculated on the product recovered after chromatographic purification.
[c] Recovered starting material.

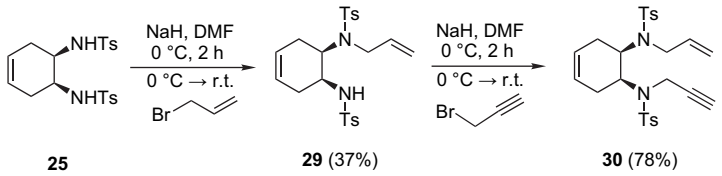
When *cis*-*N*,*N*′-bis-allyl-*N*,*N*′-bis-(*p*-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene **26** was treated with 5 mol % of **1** in dichloromethane at room temperature for 20 h under a nitrogen atmosphere (Table 2, entry 1), intramolecular alkene metathesis proceeded quantitatively leading exclusively to 6,8-fused bicycle **27**. Notably, no oligomerization was observed in the metathesis of **26**, in contrast to our results with structurally similar compounds. Indeed under exactly the same experimental conditions, the reaction of 1,2-bis-allyloxy-*cis*-cyclohex-4-ene[7] did not proceed to completion and products resulting from oligomerization were also present. This could be related to the presence of an element of constraint in the substrate represented by the tosyl groups on the nitrogens. It has been suggested for similar substrates that pre-organized conformational constraints facilitate RCM by enhancing the rates of the reaction relative to the rates of competing intermolecular metathesis leading to oligomers.[21]

Performing the reaction under an ethene atmosphere (Table 2, entry 2) did not prevent the RCM reaction from taking place and product **27** could still be obtained in an appreciable yield (83%). This is quite surprising considering that ethene is released as a by-product upon ring-closing and that the oxo-analogues did not react under the same conditions.[7] By conducting the reaction in the presence of **2** (5 mol %) (Table 2, entries 3 and 4) it was observed that the rates of alkene RCM metathesis leading to product **27** decreased relative to the competing formation of bis-dihydropyrrolidine product **28** via the anticipated tandem ROM/RCM reaction. After consumption of the starting diene **26** over a period of 20 h at room temperature under nitrogen, the two products were formed in an approximate ratio of 2.5:1 in favour of product **27** (Table 2, entry 3). Under an ethene atmosphere, complete consumption of the starting material did not occur, but **27** and **28** were still formed with the same ratio in an overall 30% yield (Table 2, entry 4).

2.2.2. Enyne metathesis

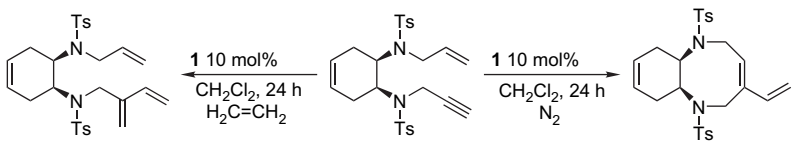
In view of the successful metathesis of bis-allyl amine **26**, related enyne metatheses were investigated. Substrate **30**, having an allyl and a propargyl substituent was synthesized, following the procedure shown in Scheme 11. The mono-allylated precursor **29** was obtained by reacting diamine **25** with allylbromide under standard alkylation conditions. Compound **29** was easily isolated by column chromatography from a mixture of bis-alkylated product **26** (43%) and unreacted ditosylamine **25** (3%). Compound **29** was then treated with propargyl bromide to give the enyne metathesis precursor **30** in 78% yield after purification by column chromatography.

When compound **30** was treated with catalyst **1**, two different products were obtained depending on the reaction conditions (Scheme 12). The reaction was first attempted using standard reaction condition of 5 mol % catalyst **1**, in dichloromethane at room temperature under a nitrogen atmosphere. Product **32** was obtained in 32% yield along with 51% of recovered starting material **30**. For subsequent reactions, the amount of catalyst **1** was increased to 10 mol %. Results are presented in Table 3. By carrying out the reaction in dichloromethane under an inert atmosphere using 10 mol % of catalyst **1** (Table 3, entries 1 and 2), the only isolable product after column chromatography was 6,8-fused bicyclic butadiene **32**. In analogous RCM of dienes, Mori et al. associated an accelerating effect on the rate of eight-membered ring formation via ring-closing enyne metathesis to the steric bulk of the tosyl



25 **29** (37%) **30** (78%)

Scheme 11.



31 **30** **32**

Scheme 12.

Table 3
Metathesis of substrate **30** with 10 mol % catalyst **1**

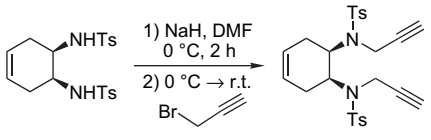
Entry[a]	T (°C)	Atm	Yield[b] (%)		
			32	**31**	**30**[c]
1	25	N_2	44	0	26
2	35	N_2	56	0	13
3	25	$H_2C{=}CH_2$	0	68	—
4	35	$H_2C{=}CH_2$	0	79	—

[a] All the reactions were carried out in dry dichloromethane using 10 mol % of catalyst **1**.
[b] Yields were calculated on the product recovered after chromatographic purification.
[c] Recovered starting material.

group.[22,23] It was therefore expected for **30** to display increased metathesis reactivity compared to *cis*-*O*-enyne.[7] The yields of these reactions were, however, uncharacteristically moderate.

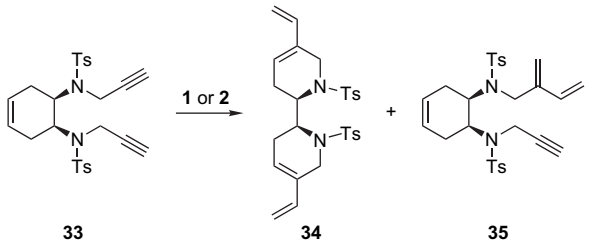
In contrast with earlier results, we found that the reaction also proceeded when performed under an ethene atmosphere, though through a different pathway. Substrate **30** underwent cross metathesis with ethene at the alkyne moiety, yielding compound **31** as the sole reaction product in good yield after purification by column chromatography (Table 3, entries 3 and 4). This is in accordance with literature reports[24] for enyne cross metathesis under 1 atm of ethene using catalyst **1**, according to which the bulkiness of the substituent at the propargylic position has a profound influence on the product yield while at the same time oxygen functionalities impede enyne metathesis by chelation. The structure of products **31** and **32** could be deduced from their spectroscopic data. In the case of compound **32**, the NOESY spectrum was particularly diagnostic as it demonstrated that the cyclohexene ring was still intact.

The next substrate to be investigated was bis-propargylamine **33**, which was prepared by a standard procedure as illustrated in Scheme 13. The metathesis reactivity of compound **33** catalysed by complex **1** was investigated first. As previously observed for related compounds, changing the steric and electronic requirement of the substituents on the cyclohexene resulted in a dramatic change in reactivity. Indeed, compound **33** did not behave similarly to the analogous dipropargyl ether described in earlier papers.[7] Compound, **33** reacted readily with catalyst **1**, giving monocross-metathesised derivative **35** as the major product, together with smaller quantities of bis-azacycle **34** (Scheme 14). In the light of this result, it can be concluded that compound **33** is a useful probe of the mechanistic diversity available by metathesis of differently substituted cyclohexene derivatives.



25 **33** (96%)

Scheme 13.



33 **34** **35**

Scheme 14.

Table 4
Metathesis of diyne **33** with **1** and **2** under an ethene atmosphere

Entry[a]	Cat (mol %)	Solvent	T (°C)	Yield[b] (%)		
				34	**35**	**33**[c]
1	**1** (5)	CH_2Cl_2	25	10	53	37
2	**1** (10)	CH_2Cl_2	25	16	63	20
3	**1** (10)	CH_2Cl_2	50	17	44	39
4	**2** (10)	Toluene	60	22	59	18

[a] All the reactions were carried out in dry dichloromethane using an ethene atmosphere.
[b] Yields were calculated on the product recovered after chromatographic purification.
[c] Recovered starting material.

Several conditions for the metathesis of substrate **33** were systematically examined. It was generally observed that no reaction was observed under a nitrogen atmosphere with either catalyst **1** or **2**. Table 4 reports the results obtained with catalysts **1** and **2** under an ethene atmosphere with different reaction conditions.

It was observed that when the reaction was carried out at room temperature, increasing the amount of catalyst from 5 mol % to 10 mol % increased the overall conversion of the starting diyne into ring rearranged product **34** and cross metathesis product **35** after overnight stirring, without significantly changing the ratio of products **35** and **34** (Table 4, entries 1 and 2). Based on literature precedent,[25] the reaction was performed at 50 °C in a sealed system in order to increase the chemoselectivity towards bis-aza-cycle **34**. Although leading to a lower overall conversion, the higher temperature produced a decrease in the **35**/**34** ratio (2.5:1) (Table 4, entry 3). The same effect was observed with the use of catalyst **2** in toluene at 60 °C (Table 4, entry 5). We were able to elucidate the structure of the products from this reaction only after detailed examination of 2D NMR experiments including HMQC, HMBC, long-range $^1H-^1H$ correlations and NOESY spectra. Although Ring Rearrangement Metathesis (RRM) reaction of diyne **33** occurs slowly, and the major compound formed from the metathesis of **33** is monocross-metathesised product **35**, this result is interesting as it proves that the metathesis catalysts can react via ring opening for 1,2-disubstituted cyclohexenes.

3. Conclusions

In conclusion, attempts to extend the cascade enyne metathesis process promoted by ruthenium based metathesis

initiators **1** and **2** to allyl- and propargyl-amino-substituted norbornene and cyclohexene derivatives gave some intriguing results, highlighting the different catalytic reactivities of the two complexes.[13] The study also illustrated once again that the usual generalization that complex **2** is more reactive than complex **1** is not always valid.

This study also led to the discovery of an interesting dichotomy occurring between the chemistry of oxygen and nitrogen-containing systems. In addressing the possibility of applying this chemistry to nitrogen-containing derivatives, it is clear that the method is compatible with amino compounds if they are suitably protected.

In the norbornene systems a *trans*-disposition of the precursor does not prevent the reaction from taking place. With regards to the cyclohexene derivatives, apart from its preparative utility, this study raises several mechanistically relevant issues. A contrast in reactivity between ether and amino compounds with metathesis catalysts has been suggested before throughout the literature[24,26,27] although an accurate rationale for this occurrence was not provided.

It has been previously observed[7] that treatment of *cis*- and *trans*-cyclohexene systems bearing *O*-propargylic side chains with second generation Grubbs' catalyst **2** in the presence of ethene generates intermediates possessing the functionality to undergo ring-closing diene–yne metathesis, allowing unusual fused 6,8-bicyclic triene heterocycles to be formed (the first generation Grubbs' catalyst **1** was found to be completely inactive in this reaction). The same reaction conditions, in the presence of either catalyst **1** or **2** applied to the analogous *N*-tosyl derivative **33** led to a monocross-metathesised product as the major compound, but RRM (namely tandem ROM/RCEYM) was also observed rather than ring closing at the side chain.

It is possible to speculate that for amino derivatives, the required conformations for RRM might be more energetically accessible than those of the related ether compounds. In this context, it is possible to assume that a step in the catalytic cycle serves as a kinetic barrier for formation of rearranged products and the presence of sterically demanding tosyl functions at the nitrogen atoms in compound **33** could bias the equilibrium amongst the possible rotamers towards the production of a rotamer, which is energetically and conformationally disposed towards ROM/RCEYM.

A similar analysis can be carried out for diallyl substrate **26** giving the RRM (ROM/RCM) product **28** as a minor product and in the presence of catalyst **2** only. The formation of RCM product **27** as a major product shows that when an alternative RCM path is available, the formation of metathesis products seems to be kinetically governed, as the thermodynamically favourable route is indeed less favoured. These are intriguing results as no conditions were found under which the analogous oxygenated cyclohexene compounds would undergo RRM reactions.[7]

To summarise this parallel analysis of oxygen- and nitrogen-containing analogues it is possible to say that for oxygen-containing derivatives the presence of strain in the six-membered ring of norbornene drives the metathesis reaction towards the RRM pathway while the six-membered ring of cyclohexene derivatives does not participate and they undergo mainly RCM or RCEYM.[7] For the nitrogen-containing derivatives, however, it is possible to obtain RRM products (that is, tandem ROM/RCM) for both cyclohexene and norbornene substrates. This evidences that for nitrogen-containing derivatives it is possible to achieve enough stabilization by forming cyclic products such as **19a–c** and bicyclic products such as **28** and **34** to drive the equilibrium towards the ring opening of either a strained or an unstrained six-membered ring.

4. Experimental section

4.1. General

Dichloromethane was dried by distillation over calcium hydride. Toluene was dried by distillation from metallic sodium prior to use. All reactions were carried out under a nitrogen atmosphere. Chromatographic separations were performed using silica gel 60 (230–400 mesh) supplied by Merck. Analytical thin layer chromatography (TLC) was carried out on Merck polyester backed sheets coated with silica gel 60 F254, using short wavelength (254 nm) ultraviolet light, or basic potassium permanganate ($KMnO_4$) stains to visualise components.

Melting points were determined on a Gallenkemp melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer Paragon 1000 Fourier transform IR spectrometer using sodium chloride plates. Characteristic absorptions are reported in wavenumbers (cm^{-1}) with the following abbreviations: strong (s), medium (m) or weak (w).

^{1}H and ^{13}C NMR spectra were recorded using Bruker Avance digital NMR spectrometers operating at 360, 400 or 500 MHz for protons and 90, 100 or 125 MHz for carbons. All spectra were recorded at room temperature in $CDCl_3$ (unless otherwise stated) and referenced to tetramethylsilane. Chemical shifts are expressed in parts per million. Coupling constants are given in Hertz. The multiplicity of signals is reported as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad (br) or a combination of any of these. The proton or carbon attributed to the peak is sometime italicised for clarity and a * or a ** indicates that assignment for the corresponding nuclei could be interchanged. Determination of structures was achieved with the aid of DEPT spectra and 2D NMR techniques including COSY, long-range COSY, NOESY, one-bond heteronuclear correlation and multiple bond heteronuclear correlation as appropriate.

Low and high resolution mass spectra were recorded at the EPSRC national service at the University of Wales, Swansea, or on a Bruker Apex III FTMS or Jeol AX505W spectrometer within the chemistry department at King's College London. The sample was ionized by electron ionization (EI), chemical ionization (CI) or positive electrospray ionization (ESI). The major fragment ions are reported and only the molecular ions are assigned. GC–MS was performed on the Jeol AX505W spectrometer using a 0.25 μm BP1 column (25 m×0.25 mm) with helium as the carrier gas at 12 psi.

The temperature was held at 60 °C for 2 min, and then increased at 8 °C/min to 280 °C.

All metathesis products were purified by flash chromatography so that the concentration of residual ruthenium species and/or phosphine was below the detection limits of ^{1}H and ^{13}C NMR spectroscopy.

4.2. 1,3-Dihydro-imidazol-2-one (**4**)[16]

Compound **4** was prepared by the following modification of a literature procedure. Hydantoin **3** (3.00 g, 30.0 mmol) was suspended in dry tetrahydrofuran (30 ml) and cooled to 0 °C under a nitrogen atmosphere. DIBALH (53 ml, 1.5 M, 25% in toluene) was added dropwise with stirring over a period of 30 min and the solution was stirred for 2 h at 0 °C. Aqueous methanol (90%, 225 ml) was carefully added, then the solution was heated at reflux overnight, filtered and evaporated to dryness to give 1,3-dihydro-imidazol-2-one **4** (1.56 g, 18.6 mmol, 62%) as a white solid. Mp 240–243 °C (lit.[28] 250–251 °C); ^{1}H NMR (δ, DMSO): 9.70 (br s, 2H, 2×NH), 6.24 (s, 2H, 2×CH).

4.3. 1,3-Diacetyl-1,3-dihydro-imidazol-2-one (**5**)[16]

Compound **5** was prepared by the following modification of a literature procedure. 1,3-dihydro-imidazol-2-one[16] **4** (4.00 g, 47.6 mmol) was stirred with acetic anhydride (30.1 g, 27.8 ml, 295.2 mmol) at reflux for 30 min. The reaction was then cooled to room temperature and evaporated to dryness to leave a yellow solid. The residue was recrystallized from diethyl ether to give pure 1,3-diacetyl-1,3-dihydro-imidazol-2-one **5** (5.44 g, 32.4 mmol, 68%) as a white solid. Mp 103–105 °C (lit.[28] 105–106 °C); ^{1}H NMR (δ, DMSO): 7.15 (s, 2H, CH=CH), 2.53 (s, 6H, 2×CH_3).

4.4. 2,3-Diacetyl-1,3,3a,4,7,7a-hexahydro-4,7-methano-2H-benzimidazol-2-one (**7**)[16]

Compound **7** was prepared by the following modification of a literature procedure. 1,3-Diacetyl-1,3-dihydro-imidazol-2-one[16] **5** (1.00 g, 5.95 mmol) and an excess of freshly distilled cyclopentadiene **6** (3.93 g, 4.90 ml, 59.5 mmol) were stirred in a sealed tube at 140 °C for 24 h. The mixture was then cooled to room temperature and evaporated in vacuo. The residue was purified by column chromatography (first dichloromethane, then diethyl ether) to give diacetyl adduct **7** (1.39 g, 5.94 mmol, 100%) as a white solid. Mp 120–123 °C (lit.[16] 119–120 °C); ^{1}H NMR (δ, $CDCl_3$): 5.96 (t, *J* 1.8 Hz, 2H, CH=CH), 4.34 (t, *J* 1.6 Hz, 2H, 2×CHN), 3.44 (t, *J* 1.6 Hz, 2H, 2×CHCH=), 2.37 (s, 6H, 2×CH_3), 1.61 (dt, *J* 9.8, 1.7 Hz, 1H, CH_2), 1.32 (d, *J* 9.7 Hz, 1H, CH_2).

4.5. 2,3-Diamino-endo,cis-norborn-5-ene dihydrochloride (**8**)[15]

A slurry of diacetyl adduct[16] **7** (3.00 g, 12.8 mmol) in methanol (10 ml) and 50% aq KOH (40 ml) was heated at reflux for 4 h. The resulting slurry was filtered and the solid washed several times with water and dried in a vacuum oven for 24 h at 60 °C to provide crude product (1.62 g). The filtrate was partially concentrated (30 ml), extracted with chloroform (3×20 ml), neutralized with 6 N HCl and extracted again with chloroform (3×20 ml). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo to give additional crude product (2.30 g). The combined crude material (3.92 g) was suspended in 50% aq KOH (35 ml) and methanol (14 ml) and the mixture was then heated in a pressure tube at 155 °C for 24 h. After cooling to room temperature, the reaction mixture was extracted with chloroform (6×20 ml). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give a brown oil. The oil was dissolved in diethyl ether and filtered to remove solid brown impurities. The filtrate was cooled to 0 °C and treated with ethereal HCl to provide the bis-ammonium chloride salt **8** (1.28 g, 6.53 mmol, 51%) as a pale brown solid. Mp>280 °C dec (lit.[15] 275 °C dec); ^{1}H NMR (δ, DMSO): 8.33 (br s, 6H, 2×NH_3^+), 6.33 (s, 2H, CH=CH), 3.93 (br s, 2H, 2×CHN), 3.15 (br s, 2H, CHC=), 1.55 (d, *J* 9.8 Hz, 1H, CH_2), 1.53 (d, *J* 9.8 Hz, 1H, CH_2).

4.6. N,N,N′,N′-Tetra-(prop-2-ynyl)-2,3-diamino-endo,cis-norborn-5-ene (**9**)

To a solution of bis-ammonium chloride salt **8** (0.10 g, 0.51 mmol) in CH_3CN (2 ml) were added propargyl bromide (0.38 g, 80% toluene soln, 2.54 mmol) and potassium carbonate (0.70 g, 5.08 mmol). The mixture was heated to reflux for 16 h, then cooled to room temperature and evaporated to give a brown oil (0.16 g), which was purified by column chromatography to give product **9** (0.04 g; 28%) as an off white viscous liquid. IR (ν_{max}, cm^{-1}): 3299 (s), 3062 (w), 2966 (s), 2872 (s), 2817 (s), 2361 (w), 2247 (w), 2120 (w); ^{1}H NMR (δ, $CDCl_3$): 6.08 (t, *J* 1.7 Hz 2H, CH=CH), 3.65 (dd, *J* 16.7, 2.3 Hz, 4H, 4×NCH_2), 3.59 (dd, *J* 16.7, 2.3 Hz, 4H, 4×NCH_2), 3.29–3.28 (m, 2H, CHN), 3.07 (br s, 2H, CHC=), 2.12 (t, *J* 2.3 Hz, 4H, 4×≡CH), 1.39 (dt, *J* 8.9, 2.2 Hz, 1H, CH_2), 1.15–1.18 (m, 1H, CH_2); ^{13}C NMR (δ,$CDCl_3$): 133.6 (C=C), 79.6 (C≡), 71.3 (≡CH), 63.0 (CHN), 45.9 (CH_2N), 44.6 (CHC=), 40.7 (CH_2); *m/z* (CI, %): 277 (MH^+, 100); found (ESI) 277.1713 (MH^+), $C_{19}H_{21}N_2$ requires: 277.1704.

4.7. N,N′-Bis-(p-toluenesulfonyl)-2,3-diamino-endo,cis-norborn-5-ene (**10**)

To a suspension of 2,3-diamino-*endo*,*cis*-norborn-5-ene dihydrochloride[15] **8** (0.38 g, 1.90 mmol) in dry dichloromethane (15 ml) was added freshly distilled triethylamine (0.77 g, 1.06 ml, 7.61 mmol), followed by a solution of *p*-toluenesulfonyl chloride (0.73 g, 3.81 mmol) in dry dichloromethane (8 ml). The mixture was stirred for 16 h at room temperature under a nitrogen atmosphere. The solution was then acidified with 2 M aq HCl and extracted with

dichloromethane (3×10 ml). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and evaporated in vacuo. The residue was purified by column chromatography (hexane/ethyl acetate 60:40) to leave the title compound **10** (0.65 g, 1.50 mmol, 79%) as a white solid. Mp 185–187 °C; IR (ν_{max}, KBr): 3294 (s), 2977 (w), 1599 (m), 1497 (w), 1438 (s) and 1328 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.68 (d, *J* 8.3 Hz, 4H, CH_{Ar}), 7.26 (d, *J* 8.0 Hz, 4H, CH_{Ar}), 6.04–6.03 (m, 2H, CH=CH), 4.73–4.67 (m, 2H, 2×NH), 3.61–3.54 (m, 2H, 2×CH), 2.69 (br s, 2H, 2×CHC=), 2.37 (s, 6H, 2×CH_3), 1.30 (dt, *J* 9.6, 2.0 Hz, 1H, CH_2), 1.03 (d, *J* 9.6 Hz, 1H, CH_2); ^{13}C NMR (δ, $CDCl_3$): 144.2 (C_{Ar}), 137.1 (C_{Ar}), 136.6 (CH=), 130.3 (CH_{Ar}), 127.6 (CH_{Ar}), 55.4 (CHN), 46.7 (CHC=), 44.9 (CH_2), 22.0 (CH_3); *m/z* (EI, %): 433 (MH^+, 3), 366 (35), 277 (13), 211 (100); found (ESI) 455.1082 ($M+Na^+$), $C_{21}H_{24}N_2O_4S_2Na$ requires 455.1075.

4.8. trans-Norborn-5-ene-2,3-dicarbonyl azide (*14*)

A concentrated aqueous solution of sodium azide (7.42 g, 114.1 mmol) was added dropwise to a stirring solution of *trans*-norborn-5-ene-2,3-dicarbonyl chloride **13** (5.00 g, 3.71 ml, 22.8 mmol) in dry THF (50 ml) under an argon atmosphere at −10 °C. The solution was allowed to warm slowly to room temperature over 1 h and then left for a further hour at room temperature. The solution was then diluted with water (50 ml) and extracted with ethyl acetate (3×50 ml). The combined organic phases were then washed with saturated aq Na_2CO_3 (2×50 ml), saturated aq NaCl (2×50 ml), dried over anhydrous $MgSO_4$, filtered and evaporated in vacuo to give product **14** (4.39 g, 18.9 mmol, 98%) as a pale yellow oil. IR (ν_{max}, neat): 2988 (m), 2263 (m), 2142 (s) and 1701 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 6.23 (dd, *J* 5.6, 3.2 Hz, 1H, CH=), 6.07 (dd, *J* 5.6, 2.8 Hz, 1H, CH=), 3.35 (t, *J* 4.0 Hz, 1H, CHCO), 3.21 (br s, 1H, CHC=), 3.11 (br s, 1H, CHC=), 2.63 (dd, *J* 4.5, 1.6 Hz, 1H, CHCO), 1.53 (d, *J* 9.0 Hz, 1H, CH_2), 1.43 (dq, *J* 9.0, 1.7 Hz, 1H, CH_2); ^{13}C NMR (δ, $CDCl_3$): 181.3 (CO), 180.1 (CO), 138.1 (C=), 135.5 (C=), 50.7 (CHCO), 49.9 (CHCO), 48.5 (CHC=), 47.6 (CH_2), 46.5 (CHC=); *m/z* (CI, %): 250 ($M+NH_4^+$, 100).

4.9. trans-Norborn-5-ene-2,3-diisocyanate (*15*)

A stirring solution of *trans*-norborn-5-ene-2,3-dicarbonyl azide **14** (4.30 g, 18.5 mmol) in dry toluene (40 ml) was heated to gentle reflux (85–90 °C). The reaction was followed by IR spectroscopy (~2140–2260 cm^{-1}), and after 30 min the solvent was removed in vacuo to yield product **15** (3.13 g, 17.8 mmol, 96%) as a pale golden oil. IR (ν_{max}, neat): 2983 (m), 2253 (s) and 1685 cm^{-1} (m); ^1H NMR (δ, $CDCl_3$): 6.27 (dd, *J* 5.7, 3.3 Hz, 1H, CH=), 6.21 (dd, *J* 5.8, 2.8 Hz, 1H, CH=), 3.61 (dd, *J* 3.5, 2.4 Hz, 1H, CHCO), 3.19 (s, 1H, CHCO), 3.00 (br s, 1H, CHC=), 2.86 (br s, 1H, CHC=), 1.73 (d, *J* 1.1 Hz, 1H, CH_2), 1.72 (d, *J* 1.3 Hz, 1H, CH_2); ^{13}C NMR (δ, $CDCl_3$): 135.8 (C=), 134.6 (C=), 121.6 (NCO), 61.9 (CHN), 50.1 (CHN), 46.9 (CHC), 42.3 (CH_2); *m/z* (EI, %): 176 (M^+, 6), 147 (6), 134 (11), 120 (56).

4.10. trans-2,3-Diamino-norborn-5-ene dihydrochloride (*16*)

A stirring solution of *trans*-norborn-5-ene-2,3-diisocyanate **15** (3.00 g, 17.0 mmol) in 6 N HCl (60 ml) was gently refluxed for 3 h. The reaction mixture was then allowed to cool to room temperature overnight. The solvent was removed in vacuo by azeotroping with ethanol to yield product **16** (3.31 g, 16.8 mmol, 99%) as a light brown solid. Mp>260 °C dec; IR (ν_{max}, Nujol): 3470 (w), 2923 (s) and 1564 cm^{-1} (m); ^1H NMR (δ, DMSO): 8.30 (br s, 6H, 2×NH_3^+), 6.42 (dd, *J* 5.5, 3.3 Hz, 1H, CH=), 6.19 (dd, *J* 5.7, 2.7 Hz, 1H, CH=), 3.59 (d, *J* 3.2 Hz, 1H, CHN), 3.09 (s, 1H, CHC=), 2.98 (s, 1H, CHC=), 2.87 (br s, 1H, CHN), 2.02 (d, *J* 10.1 Hz, 1H, CH_2), 1.59 (d, *J* 10.1 Hz, 1H, CH_2); ^{13}C NMR (δ, DMSO): 138.0 (CH=), 134.1 (CH=), 55.4 (CHN), 55.1 (CHN), 45.7 (CHC=), 44.8 (CH_2), 44.6 (CHC=); *m/z* (EI, %): 125 ($M-HCl_2^+$, 100), 108 (39); found (ESI) 125.1080 (MH^+), $C_7H_{13}N_2$ requires 125.1079.

4.11. trans-N,N′-Bis-(p-toluenesulfonyl)-2,3-diamino-norborn-5-ene (*17*)

To a suspension of *trans*-2,3-diamino-norborn-5-ene dihydrochloride **16** (1.00 g, 5.08 mmol) in dry dichloromethane (40 ml) was added freshly distilled triethylamine (2.05 g, 2.83 ml, 20.3 mmol), followed by a solution of *p*-toluenesulfonyl chloride (1.93 g, 10.1 mmol) in dry dichloromethane (20 ml). The mixture was stirred for 16 h at room temperature under a nitrogen atmosphere. The solution was then acidified with 2 M aq HCl and extracted with dichloromethane (3×15 ml). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and evaporated in vacuo. The residue was purified by column chromatography (hexane/ethyl acetate 60:40) to leave the title compound **17** (1.87 g, 4.33 mmol, 85%) as a white solid. Mp 171–175 °C; IR (ν_{max}, CH_2Cl_2): 3522 (w), 3262 (s), 2980 (w), 1652 (w), 1597 (m), 1495 (w), 1436 (s) and 1327 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.74 (d, *J* 8.3 Hz, 4H, CH_{Ar}), 7.34 (d, *J* 8.3 Hz, 2H, CH_{Ar}), 7.35 (d, *J* 8.3 Hz, 2H, CH_{Ar}), 6.18 (dd, *J* 5.7, 3.3 Hz, 1H, CH=), 6.03 (dd, *J* 5.7, 2.8 Hz, 1H, CH=), 4.88 (br s, 1H, NH), 4.39 (br s, 1H, NH), 3.32 (t, *J* 2.7 Hz, 1H, CHN), 2.89 (br s, 1H, CHC=), 2.75 (br s, 1H, CHC=), 2.64 (br s, 1H, CHN), 2.46 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 1.61 (s, 1H, CH_2), 1.62 (s, 1H, CH_2); ^{13}C NMR (δ, $CDCl_3$): 143.8 (C_{Ar}), 137.3 (CH=), 136.3 (C_{Ar}), 134.8 (CH=), 129.9 (CH_{Ar}), 129.8 (CH_{Ar}), 127.2 (CH_{Ar}), 127.1 (CH_{Ar}), 62.7 (CHN), 62.5 (CHN), 47.4 (CHC=), 45.3 (CHC=), 44.9 (CH_2), 21.5 (CH_3); *m/z* (EI, %): 433 (MH^+, 4), 366 (33), 277 (14), 211 (100); found (ESI) 455.1072 ($M+Na^+$), $C_{21}H_{24}N_2O_4S_2Na$ requires 455.1075.

4.12. trans-N,N′-Bis-(prop-2-ynyl)-N,N′-bis-(p-toluenesulfonyl)-2,3-diamino-norborn-5-ene (*18*)

To a stirring solution of *trans*-N,N′-bis-(*p*-toluenesulfonyl)-2,3-diamino-norborn-5-ene **17** (1.00 g, 2.31 mmol) in

dimethylformamide (20 ml) at 0 °C was slowly added sodium hydride (0.28 g, 6.94 mmol, 60% in mineral oil). After stirring for 1 h at 0 °C, propargyl bromide (1.72 g, 1.3 ml, 11.6 mmol, 80% in toluene) was added and the reaction mixture was allowed to warm to room temperature. The mixture was then stirred overnight. To the reaction mixture was added saturated aq NH_4Cl, and the aqueous layer was extracted with ethyl acetate (4×15 ml). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and evaporated in vacuo to leave a yellow solid, which was recrystallized from ethyl acetate/hexane to give product **18** (0.85 g, 1.67 mmol, 72%) as a white solid. Mp 138–140 °C; IR (ν_{max}, CH_2Cl_2): 3274 (m), 2979 (w), 2120 (w), 1597 (m), 1494 (w), 1438 (w) and 1335 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.73 (d, *J* 8.1 Hz, 2H, CH_{Ar}), 7.67 (d, *J* 8.1 Hz, 2H, CH_{Ar}), 7.23 (d, *J* 6.0 Hz, 4H, CH_{Ar}), 6.16 (s, 2H, CH=CH), 4.25–4.20 (m, 2H, CHN, CH_2N), 4.07 (dd, *J* 18.7, 1.8 Hz, 1H, CH_2N), 3.82 (dd, *J* 19.0, 1.9 Hz, 1H, CH_2N), 3.71 (dd, *J* 18.7, 1.9 Hz, 1H, CH_2N), 3.60 (d, *J* 4.6 Hz, 1H, CHN), 2.81 (br s, 1H, CHC=), 2.41 (br s, 1H, CHC=), 2.36 (s, 6H, CH_3), 2.08 (t, *J* 2.1 Hz, 1H, ≡CH), 2.05 (t, *J* 2.2 Hz, 1H, ≡CH), 1.75 (d, *J* 9.5 Hz, 1H, CH_2), 1.52 (d, *J* 8.9 Hz, 1H, CH_2); ^{13}C NMR (δ, $CDCl_3$): 143.8 (C_{Ar}), 143.7 (C_{Ar}), 137.3 (CH=), 136.6 (C_{Ar}), 135.3 (CH=), 129.6 (CH_{Ar}), 129.5 (CH_{Ar}), 128.0 (CH_{Ar}), 127.8 (CH_{Ar}), 79.5 (C≡), 79.0 (C≡), 73.3 (≡CH), 72.7 (≡CH), 61.2 (CHN), 57.7 (CHN), 47.2 (CH_2), 45.3 (CHC=), 44.7 (CHC=), 33.7 (CH_2N), 33.3 (CH_2N), 21.6 (CH_3); *m/z* (CI, %): 526 ($M+NH_4^+$, 30), 355 (12), 227 (6), 174 (100); found (ESI) 509.1565 (MH^+), $C_{27}H_{29}N_2O_4S_2$ requires 509.1563.

4.13. Racemic (4aS,5aR,9aR,9bR)-1,9-bis-(toluene-4-sulfonyl)-3,7-divinyl-2,4a,5,5a,8,9,9a,9b-octahydro-1H-cyclopenta[2,1-b;3,4-b′]dipyridine (*19a*)

Diyne **18** (0.100 g, 0.197 mmol) was dissolved in dry dichloromethane (17 ml) and ethene was passed through the stirred solution for 20 min. A solution of first generation Grubbs' catalyst **1** (0.008 g, 0.010 mmol, 5 mol %) in dry dichloromethane (3 ml) was then added and the reaction mixture was stirred at room temperature for 20 h under an ethene atmosphere until all the starting material had been consumed. The solvent was then removed in vacuo to leave a residue, which was subjected to column chromatography (dichloromethane/ethyl acetate 95:5) to give tricyclic product **19a** (0.045 g, 0.085 mmol, 43%) as a colourless oil. IR (ν_{max}, CH_2Cl_2): 2980 (w), 1652 (w), 1596 (w), 1494 (w), 1436 (m) and 1334 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.86 (d, *J* 8.3 Hz, 2H, CH_{Ar}), 7.66 (d, *J* 8.2 Hz, 2H, CH_{Ar}), 7.24 (d, *J* 8.1 Hz, 2H, CH_{Ar}), 7.13 (d, *J* 8.1 Hz, 2H, CH_{Ar}), 6.13 (dd, *J* 17.8, 11.0 Hz, 1H, $CH=CH_2$), 5.96 (dd, *J* 17.8, 11.0 Hz, 1H, $CH=CH_2$), 5.72 (s, 1H, CH=C), 5.22 (s, 1H, CH=C), 5.10–4.91 (m, 5H, 2×$=CH_2$, CHN), 4.34 (d, *J* 18.3 Hz, 1H, CH_2N), 4.15 (d, *J* 17.1 Hz, 1H, CH_2N), 3.84 (d, *J* 17.1 Hz, 1H, CH_2N), 3.57 (d, *J* 18.3 Hz, 1H, CH_2N), 3.13 (t, *J* 11.2 Hz, 1H, CHN), 2.55–2.49 (m, 2H, CHCH=), 2.36 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.17–2.09 (m, 1H, CH_2), 0.92–0.83 (m, 1H, CH_2); ^{13}C NMR (δ, $CDCl_3$): 143.3 (C_{Ar}), 143.1 (C_{Ar}), 137.9 (C_{Ar}), 137.3 (C_{Ar}), 136.6 ($CH=CH_2$), 135.7 ($CH=CH_2$), 135.2 (C=), 131.3 (CH=C), 130.5 (CH=C), 130.0 (C=), 129.5 (CH_{Ar}), 129.3 (CH_{Ar}), 127.9 (CH_{Ar}), 127.6 (CH_{Ar}), 112.8 ($=CH_2$), 112.1 ($=CH_2$), 62.3 (CHN), 55.5 (CHN), 48.1 (CH_2N), 38.9 (CH_2N), 37.4 (CHC=), 31.7 (CHC=), 31.6 (CH_2), 21.6 (CH_3), 21.5 (CH_3); *m/z* (ESI, %): 559 ($M+Na^+$, 100), 537 (MH^+, 8), 227 (6), 174 (100); found (ESI) 559.1691 ($M+Na^+$), $C_{29}H_{32}N_2O_4S_2Na$ requires 559.1696.

4.14. Trimethylsilyl cis-2-isocyanatocyclohex-4-ene-1-carboxylate (*21*)[19,29]

Commercial 1,2,3,6-tetrahydrophthalic anhydride **20** (40.00 g, 263.2 mmol) was purified by being heated under reflux for 3 h with acetic anhydride (72.00 g, 66.5 ml, 705.3 mmol) and light petroleum ether (210 ml). The mixture was allowed to cool over 12 h. The white needles, which crystallized were filtered, washed with dry diethyl ether and dried, affording pure 1,2,3,6-tetrahydrophthalic anhydride **20** (28.94 g, 190.1 mmol). Mp 101–102 °C (lit.[29] 101–102 °C).

Freshly recrystallized 1,2,3,6-tetrahydrophthalic anhydride[29] **20** (5.00 g, 32.9 mmol) was dissolved in dry dioxane (30 ml) under an argon atmosphere. Trimethylsilyl azide (5.31 g, 6.1 ml, 46.0 mmol) was then added slowly to the solution at room temperature. The gently stirred solution was immersed in an oil bath preheated to 70–80 °C. A vigorous reaction occurred and was controlled by occasional cooling. After nitrogen evolution had subsided (30–45 min), the reaction mixture was boiled for 30 min. The solution was then cooled to 35–40 °C and concentrated in vacuo (bath temperature <35 °C) to a slightly yellow oil, which was purified by distillation under reduced pressure to yield trimethylsilyl ester **21** (7.27 g, 30.4 mmol, 92%) as a colourless oil. IR (ν_{max}, neat): 3032 (w), 2946 (w), 2265 (m) and 1720 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 5.73–5.70 (m, 1H, CH=), 5.55–5.52 (m, 1H, CH=), 4.22–4.21 (m, 1H, CHN), 2.61–2.57 (m, 1H, CHCO), 2.41–2.22 (m, 4H, 2×CH_2), 0.25 (s, 9H, 3×CH_3).

4.15. cis-2-Isocyanatocyclohex-4-ene-1-carbonyl chloride (*22*)[19]

Trimethylsilyl ester[19,29] **21** (7.27 g, 30.4 mmol) was dissolved in carbon tetrachloride (15 ml). Dimethylformamide (3 drops) was then added followed by freshly distilled thionyl chloride (5.07 g, 3.1 ml, 42.6 mmol). The reaction mixture was heated to 40–50 °C in an oil bath. Gas evolution began within 5–10 min. The temperature of the reaction mixture was maintained at ~50 °C and the progress of the reaction was followed by infrared spectroscopy. Upon disappearance of the ester group absorption at 1720 cm^{-1} (30–45 min), the solution was cooled to room temperature and concentrated in vacuo to leave a viscous yellow oil, which was distilled under reduced pressure to afford the desired product **22** (4.52 g, 24.4 mmol, 80%) as a colourless oil. The compound was used

immediately in the next reaction. IR (ν_{max}, neat): 3032 (w), 2945 (w), 2250 (m) and 1790 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 5.82–5.79 (m, 1H, CH=), 5.69–5.66 (m, 1H, CH=), 4.47 (br s, 1H, CHN), 3.10 (ddd, *J* 10.6, 6.0, 2.0 Hz, 1H, CHCO), 2.64–2.41 (m, 4H, 2×CH_2).

4.16. *cis*-1,2-Diamino-cyclohex-4-ene dihydrochloride (**24**)[19]

Acid chloride[19] **22** (4.52 g, 24.4 mmol) was dissolved in dry dioxane (14 ml) under an argon atmosphere. Trimethylsilyl azide (3.93 g, 4.5 ml, 34.1 mmol) was added dropwise at room temperature to the stirring solution, which was subsequently heated to 70–80 °C in an oil bath. Vigorous nitrogen evolution began within 5–10 min and continued for 20–30 min. The reaction was then cooled to 35–40 °C and diluted with acetone. Concentrated hydrochloric acid (7 ml) was added cautiously through the top of the condenser. Stirring was continued until CO_2 formation ceased (~30 min). The resulting precipitate was filtered and washed with acetone and diethyl ether, providing the bis-ammonium chloride salt **24** (2.40 g, 13.0 mmol, 53%) as a white powder. Mp 285–290 °C (lit.[19] 255–265 °C); ^1H NMR (δ, DMSO): 8.56 (br s, 6H, 2×NH_3), 5.65 (s, 2H, CH=CH), 3.70 (br s, 2H, 2×CH), 2.54–2.50 (m, 2H, CH_2), 2.29 (dd, *J* 17.2, 6.7 Hz, 2H, CH_2).

4.17. *cis*-*N*,*N*′-Bis-(*p*-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene (**25**)

To a suspension of *cis*-1,2-diamino-cyclohex-4-ene dihydrochloride[19] **24** (2.00 g, 10.8 mmol) in dry dichloromethane (80 ml) was added freshly distilled triethylamine (4.38 g, 6.0 ml, 43.2 mmol), followed by a solution of *p*-toluenesulfonyl chloride (4.53 g, 23.8 mmol) in dry dichloromethane (30 ml). The reaction mixture was stirred for 16 h at room temperature under a nitrogen atmosphere. The solution was then acidified with 2 M aq HCl and extracted with dichloromethane (3×20 ml). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and evaporated in vacuo. The residue was purified by column chromatography (first hexane/ethyl acetate 60:40 and then dichloromethane/ethyl acetate 90:10) to afford ditosylate **25** (3.38 g, 8.05 mmol, 75%) as a white solid. Mp 180–182 °C; IR (ν_{max}, CH_2Cl_2): 3271 (s), 3034 (w), 2923 (w), 1597 (m), 1437 (s) and 1328 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.71 (d, *J* 8.3 Hz, 4H, CH_{Ar}), 7.33 (d, *J* 8.1 Hz, 4H, CH_{Ar}), 5.50 (s, 2H, CH=CH), 4.97 (d, *J* 9.1 Hz, 2H, 2×NH), 3.30–3.56 (m, 2H, 2×CHN), 2.47 (s, 6H, 2×CH_3), 2.25 (dd, *J* 16.9, 4.8 Hz, 2H, 2×CH_2), 1.84 (dd, *J* 17.3, 6.5 Hz, 2H, 2×CH_2); ^{13}C NMR (δ, $CDCl_3$): 144.1 (C_{Ar}), 137.9 (C_{Ar}), 130.2 (CH_{Ar}), 127.6 (CH_{Ar}), 124.7 (CH=CH), 51.3 (CHN), 31.0 (CH_2), 22.0 (CH_3); *m/z* (CI, %): 438 ($M+NH_4^+$, 100), 353 (8), 267 (21); found (ESI) 443.1072 ($M+Na^+$), $C_{20}H_{24}N_2O_4S_2Na$ requires 443.1070.

4.18. *cis*-*N*,*N*′-Bis-allyl-*N*,*N*′-bis-(*p*-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene (**26**)

To a stirring solution of *cis*-*N*,*N*′-bis-(*p*-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene **25** (0.50 g, 1.19 mmol) in dimethylformamide (15 ml) at 0 °C was slowly added sodium hydride (0.14 g, 3.57 mmol, 60% in mineral oil). After stirring for 2 h at 0 °C, allyl bromide (0.72 g, 0.52 ml, 5.95 mmol) was added and the reaction mixture was allowed to warm to room temperature. The mixture was then stirred overnight. To the reaction mixture was added saturated aq NH_4Cl, and the aqueous layer was extracted with diethyl ether (4×20 ml). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and evaporated in vacuo to leave a residue, which was purified by column chromatography (dichloromethane/ethyl acetate 95:5) to give the desired compound **26** (0.58 g, 1.16 mmol, 98%) as a white solid. Mp 175–177 °C; IR (ν_{max}, CH_2Cl_2): 3076 (m), 3037 (m), 2977 (m), 2922 (s), 1639 (m), 1596 (s), 1495 (m), 1432 (s) and 1335 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.61 (d, *J* 8.2 Hz, 4H, CH_{Ar}), 7.22 (d, *J* 8.1 Hz, 4H, CH_{Ar}), 5.92 (ddt, *J* 16.5, 10.3, 6.2 Hz, 2H, C*H*=CH_2), 5.51 (s, 2H, CH=CH), 5.06 (dd, *J* 17.3, 1.7 Hz, 2H, 2×=CH_2), 5.02 (dd, *J* 10.3, 1.0 Hz, 2H, 2×=CH_2), 4.04 (t, *J* 5.5 Hz, 2H, 2×CHN), 3.95 (d, *J* 5.8 Hz, 4H, 2×CH_2N), 2.37 (s, 6H, 2×CH_3), 2.09 (dd, *J* 16.9, 5.1 Hz, 2H, 2×CH_2C=), 1.8–1.9 (m, 2H, 2×CH_2C=); ^{13}C NMR (δ, $CDCl_3$): 143.6 (C_{Ar}), 137.8 (C_{Ar}), 137.2 (*C*H=CH_2), 130.0 (CH_{Ar}), 128.0 (CH_{Ar}), 126.5 (CH=CH), 117.3 (=CH_2), 55.9 (CHN), 48.7 (NCH_2), 28.9 (−*C*HCH_2), 21.9 (CH_3); *m/z* (CI, %): 518 ($M+NH_4^+$, 100), 345 (14), 283 (13), 191 (66), 174 (70); found (ESI) 501.1879 (MH^+), $C_{26}H_{33}N_2O_4S_2$ requires 501.1876.

4.19. Metathesis products racemic (3*Z*,6a*R*,10a*S*)-1,2,5,6,6a,7,10,10a-octahydro-1,6-ditosyl-benzo[b][1,4]diazocine (**27**) and racemic (*R*)-1,2,3,6-tetrahydro-2-((*S*)-1,2,3,6-tetrahydro-1-tosyl-pyridin-2-yl)-1-tosylpyridine (**28**)

4.19.1. Procedure A

To a stirring solution of compound **26** (0.050 g, 0.100 mmol) in dry dichloromethane (8 ml) was added a solution of first generation Grubbs' catalyst **1** (0.004 g, 0.005 mmol, 5 mol %) in dry dichloromethane (2 ml). The reaction mixture was stirred for 20 h at room temperature under a nitrogen atmosphere. After the solvent was removed in vacuo, the residue was purified by column chromatography (dichloromethane/ethyl acetate 96:4) to afford 6,8-fused bicyclic product **27** (0.047 g, 0.100 mmol, 100%) as a white solid.

4.19.2. Procedure B

To a stirring solution of compound **26** (0.060 g, 0.120 mmol) in dry dichloromethane (10 ml) was added a solution of second generation Grubbs' catalyst **2** (0.005 g, 0.006 mmol, 5 mol %) in dry dichloromethane (2 ml). The reaction mixture was stirred for 20 h at room temperature under a nitrogen atmosphere. After the solvent was removed in

vacuo, the residue was subjected to column chromatography (dichloromethane/ethyl acetate 98:2) to give RCM product **27** (0.040 g, 0.085 mmol, 71%) together with ROM/RCM product **28** (0.016 g, 0.034 mmol, 29%) as white solids.

*4.19.3. Data for **27***

Mp 166–169 °C; IR (ν_{max}, CH_2Cl_2): 3028 (w), 2920 (w), 1639 (w), 1597 (m), 1493 (w), 1334 (s) and 1157 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.56 (d, *J* 8.3 Hz, 4H, CH_{Ar}), 7.23 (d, *J* 8.2 Hz, 4H, CH_{Ar}), 5.69 (t, *J* 3.3 Hz, 2H, 2×=C*H*CH_2N), 5.47 (s, 2H, 2×=C*H*CH_2CH), 4.30 (dd, *J* 16.7, 2.7 Hz, 2H, 2×NCH_2), 4.15 (t, *J* 4.9 Hz, 2H, 2×CHN), 3.91 (dd, *J* 17.3, 3.3 Hz, 2H, 2×NCH_2), 2.43–2.34 (m, 2H, 2×CH_2CHN), 2.37 (s, 6H, 2×CH_3), 2.22 (dd, *J* 17.4, 5.7 Hz, 2H, 2×CH_2CHN); ^{13}C NMR (δ, $CDCl_3$): 143.4 (C_{Ar}), 137.5 (C_{Ar}), 129.8 (CH_{Ar}), 128.7 (=*C*HCH_2N), 126.8 (CH_{Ar}), 125.2 (=*C*HCH_2CH), 53.9 (CHN), 43.5 (NCH_2), 30.2 (*C*H_2CH), 21.6 (CH_3); *m/z* (CI, %): 490 ($M+NH_4^+$, 100), 317 (10), 255 (7), 163 (43); found (ESI) 490.1822 ($M+NH_4^+$), $C_{24}H_{32}N_3O_4S_2$ requires 490.1829.

*4.19.4. Data for **28***

Mp 172–174 °C; IR (ν_{max}, CH_2Cl_2): 2921 (w), 1648 (w), 1596 (w), 1496 (m), 1334 (s) and 1159 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.56 (d, *J* 8.2 Hz, 4H, CH_{Ar}), 7.23 (d, *J* 8.1 Hz, 4H, CH_{Ar}), 5.54–5.51 (m, 4H, 2×CH=CH), 4.14–4.13 (m, 2H, 2×CH_2N), 4.07 (br s, 2H, 2×CHN), 3.58–3.57 (m, 1H, CH_2N), 3.52–3.51 (m, 1H, CH_2N), 2.33 (s, 6H, 2×CH_3), 2.18 (d, *J* 17.6 Hz, 2H, CHCH_2C=), 1.77 (d, *J* 16.8 Hz, 2H, CHCH_2C=); ^{13}C NMR (δ, $CDCl_3$): 143.8 (C_{Ar}), 137.9 (C_{Ar}), 130.1 (CH_{Ar}), 127.2 (CH_{Ar}), 124.6 (CH=), 122.0 (CH=), 49.6 (CHN), 41.0 (CH_2N), 23.2 (CH_2CH), 22.0 (CH_3); *m/z* (CI, %): 490 ($M+NH_4^+$, 100), 317 (10); found (ESI) 495.1379 ($M+Na^+$), $C_{24}H_{28}N_2O_4S_2Na$ requires 495.1383.

*4.20. cis-N-Allyl-N,N′-bis-(p-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene (**29**)*

To a stirring solution of *cis-N,N′*-bis-(*p*-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene **25** (0.60 g, 1.43 mmol) in dimethylformamide (15 ml) at 0 °C was slowly added sodium hydride (0.07 g, 1.71 mmol, 60% in mineral oil). After stirring for 2 h at 0 °C, allyl bromide (0.17 g, 0.12 ml, 1.43 mmol) was added and the reaction mixture was allowed to warm to room temperature. The mixture was then stirred overnight. To the reaction mixture was added saturated aq NH_4Cl, and the aqueous layer was extracted with diethyl ether (4×20 ml). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and evaporated in vacuo to leave a crude product. The residue was subjected to column chromatography (hexane/dichloromethane/ethyl acetate 50:50:10) to give the title compound **29** (0.24 g, 0.53 mmol, 37%) as a white solid. *cis-N,N′*-Bis-allyl-*N,N′*-bis-(*p*-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene **26** (0.30 g, 0.61 mmol, 43%) and *cis-N,N′*-bis-(*p*-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene **25** (0.02 g, 0.04 mmol, 3%) were also obtained. Mp 170–172 °C; IR (ν_{max}, CH_2Cl_2): 3268 (m), 3033 (w), 2923 (w), 1645 (w), 1597 (m), 1494 (w), 1436 (m), 1332 (s) and 1160 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.7–7.5 (m, 4H, CH_{Ar}), 7.3–7.1 (m, 4H, CH_{Ar}), 5.71 (ddt, *J* 16.1, 10.3, 5.8 Hz, 1H, C*H*=CH_2), 5.52 (d, *J* 9.9 Hz, 1H, C*H*=CH), 5.36 (dd, *J* 10.1, 1.7 Hz, 1H, CH=C*H*), 5.08 (dd, *J* 17.2, 1.3 Hz, 1H, =CH_2), 5.01 (dd, *J* 10.2, 1.2 Hz, 1H, =CH_2), 4.89 (d, *J* 8.8 Hz, 1H, NH), 4.01 (ddt, *J* 17.2, 5.8, 1.4 Hz, 1H, NCH_2), 3.85 (dd, *J* 17.1, 5.8 Hz, 1H, NCH_2), 3.82–3.79 (m, 1H, CHN), 3.41–3.35 (m, 1H, C*H*NH), 2.38 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.16–2.01 (m, 3H, CH_2CHN), 1.65 (br d, *J* 16.7 Hz, 1H, CH_2CHN); ^{13}C NMR (δ, $CDCl_3$): 143.6 (C_{Ar}), 143.4 (C_{Ar}), 137.7 (C_{Ar}), 137.4 (C_{Ar}), 136.4 (*C*H=CH_2), 129.7 (CH_{Ar}), 127.3 (CH_{Ar}), 127.1 (CH_{Ar}), 126.0 (*C*H=CH), 123.7 (CH=*C*H), 116.7 (=CH_2), 54.5 (CHN), 51.2 (CHNH), 47.8 (CH_2NH), 32.2 (*C*H_2CH), 26.9 (*C*H_2CH), 21.6 (CH_3); *m/z* (CI, %): 478 ($M+NH_4^+$, 100), 307 (34), 267 (11), 174 (41); found (ESI) 483.1376 ($M+Na^+$), $C_{23}H_{28}N_2S_2O_4Na$ requires 483.1383.

*4.21. cis-N-Allyl-N′-prop-2-ynyl-N,N′-bis-(p-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene (**30**)*

To a stirring solution of *cis-N*-allyl-*N,N′*-bis-(*p*-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene **29** (0.20 g, 0.44 mmol) in dimethylformamide (8 ml) at 0 °C was slowly added sodium hydride (0.05 g, 1.30 mmol, 60% in mineral oil). After stirring for 2 h at 0 °C, propargyl bromide (0.13 g, 0.10 ml, 1.30 mmol) was added and the reaction mixture was allowed to warm to room temperature. The mixture was then stirred overnight. To the reaction mixture was added saturated aq NH_4Cl, and the aqueous layer was extracted with diethyl ether (4×10 ml). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and evaporated in vacuo to leave a residue, which was purified by column chromatography (dichloromethane/ethyl acetate 95:5) to give the desired compound **30** (0.17 g, 0.34 mmol, 78%) as a white solid. Mp 162–164 °C; IR (ν_{max}, CH_2Cl_2): 3273 (m), 3032 (w), 2923 (m), 2118 (w), 1639 (m), 1598 (s), 1497 (m), 1432 (s), 1332 (s) and 1161 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.69 (d, *J* 8.3, Hz, 2H, CH_{Ar}), 7.65 (d, *J* 8.2 Hz, 2H, CH_{Ar}), 7.21 (d, *J* 8.4 Hz, 4H, CH_{Ar}), 6.00–5.89 (m, 1H, C*H*=CH_2), 5.53 (s, 2H, CH=CH), 5.09 (dd, *J* 17.5, 1.8 Hz, 1H, =CH_2), 5.05 (dd, *J* 10.4, 1.1 Hz, 1H, =CH_2), 4.36 (dd, *J* 18.9, 2.2 Hz, 1H, $CH_2C{\equiv}$), 4.20–4.13 (m, 2H, $CH_2C{\equiv}$, CHN), 4.02–3.83 (m, 3H, CH_2C=, CHN), 2.37 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.23–2.16 (m, 3H, CH_2CHN), 2.11 (t, *J* 2.4 Hz, 1H, ≡CH), 1.89 (br d, *J* 18.2 Hz, 1H, CH_2CHN); ^{13}C NMR (δ, $CDCl_3$): 143.4 (C_{Ar}), 143.3 (C_{Ar}), 137.1 (C_{Ar}), 136.6 (C*H*=CH_2), 129.6 (CH_{Ar}), 129.4 (CH_{Ar}), 127.7 (CH_{Ar}), 127.5 (CH_{Ar}), 126.0 (*C*H=CH), 125.8 (CH=*C*H), 117.2 (=CH_2), 80.5 (C≡), 72.6 (≡CH), 55.8 (CHN), 55.0 (CHN), 48.1 (NCH_2), 34.7 ($CH_2C{\equiv}$), 28.5 (*C*H_2CH), 27.4 (*C*H_2CH), 21.6 (CH_3); *m/z* (CI, %): 516 ($M+NH_4^+$, 100), 345 (10), 174 (32); found (ESI) 516.1982 ($M+NH_4^+$), $C_{26}H_{34}N_3O_4S_2$ requires 516.1985.

*4.22. Metathesis products racemic (1R,2S)-N^1-allyl-N^2-(2-methylenebut-3-enyl)-N^1,N^2-ditosylcyclohex-4-ene-1,2-diamine (**31**) and racemic (3Z,6aR,10aS)-1,2,5,6,6a,7,10,10a-octahydro-1,6-ditosyl-3-vinylbenzo[b][1,4]diazocine (**32**)*

4.22.1. Procedure A

Compound **30** (0.050 g, 0.100 mmol) was dissolved in dry dichloromethane (8 ml) and ethene was passed through the stirred solution for 20 min. A solution of first generation Grubbs' catalyst **1** (0.008 g, 0.010 mmol, 10 mol %) in dry dichloromethane (2 ml) was then added and the reaction mixture was stirred at 35 °C for 20 h under an ethene atmosphere. The solvent was then removed in vacuo. The residue was subjected to column chromatography (dichloromethane/ethyl acetate 98:2) to give product **31** as a colourless oil (0.042 g, 0.080 mmol, 79%). Data for **31**. IR (ν_{max}, CH_2Cl_2): 3268 (s), 3133 (m), 2923 (m), 1732 (s), 1645 (w), 1598 (m), 1494 (w), 1436 (m), 1336 (s) and 1160 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.76 (d, *J* 8.2 Hz, 2H, CH_{Ar}), 7.33 (d *J* 8.1 Hz, 2H, CH_{Ar}), 7.29 (d, *J* 8.1 Hz, 2H, CH_{Ar}), 7.17 (d, *J* 8.1 Hz, 2H, CH_{Ar}), 6.35 (dd, *J* 17.9, 11.2 Hz, 1H, C−C*H*=CH_2), 5.92−5.85 (m, 1H, CH_2−C*H*=CH_2), 5.57−5.56 (m, 1H, C*H*=CH), 5.42−5.41 (m, 1H, CH=C*H*), 5.23 (s, 1H, C=CH_2), 5.21 (d, *J* 18.0 Hz, 1H, CH=CH_2), 5.13 (s, 1H, C=CH_2), 5.05 (d, *J* 11.2 Hz, 1H, CH=CH_2), 4.9−5.0 (m, 2H, CH=CH_2), 4.63−4.58 (m, 1H, CH_2C=), 4.45−4.40 (m, 1H, CH_2C=), 4.03−4.00 (m, 1H, CHN), 3.86−3.84 (m, 1H, CHN), 3.70−3.63 (m, 2H, NCH_2), 2.42 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.17−2.01 (m, 3H, CH_2CH), 1.23 (br d, 1H, CH_2CH); ^{13}C NMR (δ, $CDCl_3$): 143.4 (C=)*, 143.3 (C_{Ar})*, 143.0 (C_{Ar})*, 137.1 (CH=), 136.6 (CH=), 129.6 (CH_{Ar}), 129.5 (CH_{Ar}), 127.9 (CH_{Ar}), 127.2 (CH_{Ar}), 125.2 (CH=CH), 117.2 (=CH_2), 116.4 (C=*C*H_2), 113.7 (=CH_2), 55.2 (CHN), 55.1 (CHN), 48.1 (NCH_2), 46.7 (NCH_2), 29.8 (*C*H_2CH), 27.9 (*C*H_2CH), 21.6 (CH_3), 21.5 (CH_3); *m/z* (CI, %): 544 (M+NH_4^+, 72), 490 (100), 373 (29), 217 (45), 188 (25), 174 (84); found (ESI) 527.2026 (MH^+), $C_{28}H_{35}N_2O_4S_2$ requires 527.2033.

4.22.2. Procedure B

To a stirring solution of compound **30** (0.05 g, 0.100 mmol) in dry dichloromethane (8 ml) was added a solution of first generation Grubbs' catalyst **1** (0.008 g, 0.010 mmol, 10 mol %) in dry dichloromethane (2 ml). The reaction mixture was stirred for 20 h at 35 °C under a nitrogen atmosphere. After the solvent was removed in vacuo, the residue was subjected to column chromatography (dichloromethane/ethyl acetate 98:2) to afford 6,8-fused bicyclic diene **32** (0.028 g, 0.056 mmol, 56%) as a white solid. Unreacted starting material **30** (13%) was also recovered. Data for **32**. Mp 165−167 °C; IR (ν_{max}, CH_2Cl_2): 3032 (w), 2920 (w), 2849 (w), 1639 (w), 1596 (m), 1496 (w), 1432 (m), 1334 (s) and 1157 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.57 (d, *J* 8.0 Hz, 2H, CH_{Ar}), 7.55 (d, *J* 7.6 Hz, 2H, CH_{Ar}), 7.25 (d, *J* 8.0 Hz, 2H, CH_{Ar}), 7.24 (d, *J* 8.0 Hz, 2H, CH_{Ar}), 6.19 (dd, *J* 17.7, 11.2 Hz, 1H, C*H*=CH_2), 5.74 (t, *J* 6.9 Hz, 1H, CH=C), 5.50−5.41 (m, 2H, CH=CH), 5.15 (d, *J* 17.3 Hz, 1H, =CH_2), 5.01 (d, *J* 11.0 Hz, 1H, =CH_2), 4.48−4.42 (m, 2H, 2×NCH_2), 4.21−4.13 (m, 2H, 2×NCH), 4.09−4.04 (m, 2H, 2×NCH_2), 2.38 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.34−2.09 (m, 4H, 2×CH_2); ^{13}C NMR (δ, $CDCl_3$): 143.6 (C_{Ar})*, 143.4 (C_{Ar})*, 139.7 (C=)*, 138.4 (*C*H=CH_2), 137.5 (C_{Ar}), 137.3 (C_{Ar}), 129.9 (CH_{Ar}), 129.8 (CH_{Ar}), 128.2 (*C*H=C), 126.9 (CH_{Ar}), 126.8 (CH_{Ar}), 126.0 (*C*H=CH), 124.8 (*C*H=CH), 113.6 (=CH_2), 52.7 (CHN), 52.6 (CHN), 43.1 (NCH_2), 42.3 (NCH_2), 30.7 (*C*H_2CH), 30.6 (*C*H_2CH), 21.6 (CH_3); *m/z* (CI, %): 516 (M+NH_4^+, 86), 188 (79), 174 (100); found (ESI) 499.1720 (MH^+), $C_{26}H_{31}N_2O_4S_2$ requires 499.1720.

*4.23. cis-N,N′-Bis-(prop-2-ynyl)-N,N′-bis-(p-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene (**33**)*

To a stirring solution of *cis-N,N′*-bis-(*p*-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene **25** (0.50 g, 1.19 mmol) in dimethylformamide (15 ml) at 0 °C was slowly added sodium hydride (0.14 g, 3.57 mmol, 60% in mineral oil). After stirring for 2 h at 0 °C, propargyl bromide (0.89 g, 0.66 ml, 5.95 mmol, 80% in toluene) was added and the reaction mixture was allowed to warm to room temperature. The mixture was then stirred overnight. To the reaction mixture was added saturated aq NH_4Cl, and the aqueous layer was extracted with diethyl ether (4×10 ml). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and evaporated in vacuo to leave a residue, which was purified by column chromatography (dichloromethane/ethyl acetate 95:5) to afford the desired product **33** (0.54 g, 1.14 mmol, 96%) as a pale yellow solid. Mp 168−172 °C; IR (ν_{max}, CH_2Cl_2): 3275 (s), 3032 (w), 2923 (m), 2118 (w), 1598 (s), 1497 (w), 1434 (m), 1347 (s) and 1161 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.73 (d, *J* 8.3 Hz, 4H, CH_{Ar}), 7.22 (d, *J* 8.1 Hz, 4H, CH_{Ar}), 5.57 (s, 2H, CH=CH), 4.25 (d, *J* 1.9 Hz, 4H, 2×CH_2C≡), 4.10−4.04 (m, 2H, CHN), 2.36 (s, 6H, 2×CH_3), 2.22 (br s, 4H, 2×CH_2CH), 2.17 (t, *J* 2.3 Hz, 2H, ≡CH); ^{13}C NMR (δ, $CDCl_3$): 143.9 (C_{Ar}), 137.3 (C_{Ar}), 129.2 (CH_{Ar}), 128.1 (CH_{Ar}), 126.3 (CH=), 80.9 (C≡), 73.2 (≡CH), 55.7 (CHN), 35.0 (NCH_2), 28.2 (*C*H_2CH), 22.0 (CH_3); *m/z* (CI, %): 514 (M+NH_4^+, 100), 341 (8), 174 (43); found (ESI) 519.1386 (M+Na^+), $C_{26}H_{28}N_2O_4S_2Na$ requires 519.1383.

*4.24. Metathesis products racemic (R)-1,2,3,6-tetrahydro-2-((S)-1,2,3,6-tetrahydro-1-tosyl-5-vinylpyridine-2-yl)-1-tosyl-5-vinylpyridine (**34**) and racemic (1R,2S)-N^1-(2-methylenebut-3-enyl)-N^2-(prop-2-ynyl)-N^1,N^2-ditosylcyclohex-4-ene-1,2-diamine (**35**)*

cis-N,N′-Bis-(prop-2-ynyl)-*N,N′*-bis-(*p*-toluenesulfonyl)-1,2-diamino-cyclohex-4-ene **33** (0.100 g, 0.212 mmol) was dissolved in dry dichloromethane (16 ml) and ethene was passed through the stirred solution for 20 min. A solution of first generation Grubbs' catalyst **1** (0.017 g, 0.021 mmol, 10 mol %) in dry dichloromethane (5 ml) was then added and the reaction mixture was stirred at room temperature for 20 h under an

ethene atmosphere. The solvent was then removed in vacuo. The residue was subjected to column chromatography (dichloromethane/ethyl acetate 96:4) to give compound **34** (0.017 g, 0.032 mmol, 16%) as a white solid and compound **35** (0.067 g, 0.127 mmol, 63%) as a colourless oil. Unreacted starting material **33** (21%) was also recovered.

*4.24.1. Data for **34***

Mp>182 °C dec; IR (ν_{max}, CH_2Cl_2): 2923 (w), 2850 (w), 1652 (w), 1596 (w), 1496 (w), 1432 (m), 1344 (s) and 1159 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.52 (d, *J* 8.3 Hz, 4H, CH_{Ar}), 7.15 (d, *J* 8.0 Hz, 4H, CH_{Ar}), 6.16 (dd, *J* 17.9, 11.1 Hz, 2H, C*H*=CH_2), 5.48 (d, *J* 4.5 Hz, 2H, C*H*=C), 4.98 (d, *J* 18.6 Hz, 2H, =CH_2), 4.94 (d, *J* 11.7 Hz, 2H, =CH_2), 4.36 (d, *J* 18.3 Hz, 2H, 2×NCH_2), 3.96 (dd, *J* 3.5, 1.5 Hz, 2H, 2×CHN), 3.60 (d, *J* 18.3 Hz, 2H, 2×NCH_2), 2.32 (s, 6H, 2×CH_3), 2.26 (dd, *J* 18.4, 4.4 Hz, 2H, 2×CH_2CH), 1.84 (d, *J* 18.3 Hz, 2H, 2×CH_2CH); ^{13}C NMR (δ, $CDCl_3$): 143.4 (C_{Ar}), 137.3 (C_{Ar}), 136.5 (*C*H=CH_2), 130.4 (C=), 129.7 (CH_{Ar}), 126.7 (CH_{Ar}), 125.4 (*C*H=C), 111.2 (CH_2=), 49.3 (CHN), 39.8 (CH_2N), 23.3 (CH_3), 21.5 (CH_2CH); *m/z* (CI, %): 542 ($M+NH_4^+$, 89), 371 (26), 174 (100); found (ESI) 525.1883 (MH^+), $C_{28}H_{33}N_2O_4S_2$ requires 525.1876.

*4.24.2. Data for **35***

IR (ν_{max}, CH_2Cl_2): 3270 (s), 3131 (m), 2924 (m), 1734 (m), 1598 (s), 1493 (m), 1436 (m), 1336 (s) and 1160 cm^{-1} (s); ^1H NMR (δ, $CDCl_3$): 7.75 (d, *J* 8.3 Hz, 2H, CH_{Ar}), 7.43 (d, *J* 8.2 Hz, 2H, CH_{Ar}), 7.28 (d, *J* 8.0 Hz, 2H, CH_{Ar}), 7.16 (d, *J* 8.0 Hz, 2H, CH_{Ar}), 6.34 (dd, *J* 17.9, 11.2 Hz, 1H, C*H*=CH_2), 5.62–5.59 (m, 1H, C*H*=CH), 5.45–5.43 (m, 1H, CH=C*H*), 5.22 (d, *J* 18.0 Hz, 1H, CH=CH_2), 5.19 (s, 1H, C=CH_2), 5.14 (s, 1H, C=CH_2), 5.03 (d, *J* 11.2 Hz, 1H, CH=CH_2), 4.60 (d, *J* 18.6 Hz, 1H, NCH_2C=), 4.40 (d, *J* 18.8 Hz, 1H, NCH_2C=), 4.17–4.09 (m, 2H, CHN, CH_2C≡), 3.98–3.87 (m, 1H, CH_2C≡), 3.87–3.84 (m, 1H, CHN), 2.42 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.27 (br s, 2H, CH_2CH), 2.13–2.07 (m, 1H, CH_2CH), 2.06 (t, *J* 2.4 Hz, 1H, ≡CH), 1.59 (br d, 1H, CH_2CH); ^{13}C NMR (δ, $CDCl_3$): 143.6 (C_{Ar})*, 143.4 (C=)*, 143.1 (C_{Ar})*, 138.2 (C_{Ar})*, 136.9 (*C*H=CH_2), 136.5 (C_{Ar})*, 129.5 (CH_{Ar}), 127.9 (CH_{Ar}), 127.5 (CH_{Ar}), 126.8 (*C*H=CH), 125.3 (*C*H=CH), 116.3 (C=*C*H_2), 114.1 (CH=*C*H_2), 80.0 (C≡), 73.1 (≡CH), 55.5 (CHN), 54.6 (CHN), 46.7 (N*C*H_2C=), 35.2 (N*C*H_2C≡), 29.2 (CHN)**, 27.9 (≡CH)**, 21.6 (CH_3), 21.5 (CH_3); *m/z* (CI, %): 542 ($M+NH_4^+$, 49), 174 (100); found (ESI) 547.1683 ($M+Na^+$), $C_{28}H_{32}N_2O_4S_2Na$ requires 547.1695.

Acknowledgements

The authors thank the EPSRC national mass spectrometry service at the University of Wales, Swansea for recording mass spectra.

References and notes

1. For reviews of metathesis reactions using ruthenium based initiators see: (a) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012–3043; (b) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29; (c) Blechert, D. S.; Connon, S. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 1900–1923; (d) McReynolds, M. D.; Dougherty, J. M.; Hanson, P. R. *Chem. Rev.* **2004**, *104*, 2239–2258; (e) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117–7140; (f) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4490–4527; (g) Wallace, D. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 1912–1915; (h) Donohoe, T. J.; Orr, A. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 2664–2670; (i) Grubbs, R. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 3760–3765; (j) Arisawa, M.; Nishida, A.; Nakagawa, M. *J. Organomet. Chem.* **2006**, *691*, 5109–5121; (k) Colacino, E.; Martinez, J.; Lamaty, F. *Coord. Chem. Rev.* **2007**, *251*, 726–764.
2. For recent reviews of enyne metathesis see: (a) Poulsen, C. S.; Madsen, R. *Synthesis* **2003**, 1–18; (b) Diver, S. T.; Giessert, A. J. *Chem. Rev.* **2004**, *104*, 1317–1382; (c) Maifeld, S. V.; Lee, D. *Chem.—Eur. J.* **2005**, *11*, 6118–6126; (d) Van de Weghe, P.; Bisseret, P.; Blanchard, N.; Eustache, J. *J. Organomet. Chem.* **2006**, *691*, 5078–5108; (e) Diver, S. T. *Coord. Chem. Rev.* **2007**, *251*, 671–701; (f) Mori, M. *Adv. Synth. Catal.* **2007**, *349*, 121–135; (g) Villar, H.; Frings, M.; Bolm, C. *Chem. Soc. Rev.* **2007**, *36*, 55–66.
3. For selected examples see: (a) Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 3887–3897; (b) Robson, D. A.; Gibson, V. C.; Davies, R. G.; North, M. *Macromolecules* **1999**, *32*, 6371–6373; (c) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J., Jr.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791–799; (d) Weskamp, T.; Kohl, F. J.; Hieringer, W.; Gleich, D.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **1999**, *38*, 2416–2419; (e) Lynn, D. M.; Mohr, B.; Grubbs, R. H.; Henling, L. M.; Day, M. W. *J. Am. Chem. Soc.* **2000**, *122*, 6601–6609; (f) Fürstner, A.; Ackermann, L.; Gabor, B.; Goddard, R.; Lehmann, C. W.; Mynott, R.; Stelzer, F.; Thiel, O. R. *Chem.—Eur. J* **2001**, *7*, 3236–3253; (g) Castarlenas, R.; Dixneuf, P. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4524–4527.
4. Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100–110.
5. Love, J. A.; Sanford, M. S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 10103–10109.
6. (a) Banti, D.; North, M. *Adv. Synth. Catal.* **2002**, *344*, 694–704; (b) Banti, D.; North, M. *Tetrahedron Lett.* **2002**, *43*, 1561–1564; (c) Banti, D.; North, M. *Tetrahedron Lett.* **2003**, *44*, 8157–8160; (d) Banti, D.; Groaz, E.; North, M. *Tetrahedron* **2004**, *60*, 8043–8052.
7. (a) Groaz, E.; Banti, D.; North, M. *Adv. Synth. Catal.* **2007**, *349*, 142–146; (b) Groaz, E.; Banti, D.; North, M. *Eur. J. Org. Chem.* **2007**, *22*, 3727–3745.
8. For a review of the synthesis of nitrogen-containing heterocycles using metathesis reactions see: Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199–2238.
9. (a) Kinoshita, A.; Mori, M. *Synlett* **1994**, 1020–1022; (b) Kinoshita, A.; Sakakibara, N.; Mori, M. *J. Am. Chem. Soc.* **1997**, *119*, 12388–12389; (c) Fürstner, A.; Thiel, O. R.; Ackermann, L.; Schanz, H.-J.; Nolan, S. P. *J. Org. Chem.* **2000**, *65*, 2204–2207; (d) Arisawa, M.; Kato, C.; Kaneko, H.; Nishida, A.; Nakagawa, M. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1873–1876; (e) Kinderman, S. S.; van Maarseveen, J. H.; Schoemaker, H. E.; Hiemstra, H.; Rutjes, F. P. J. T. *Org. Lett.* **2001**, *3*, 2045–2048; (f) Kitamura, T.; Mori, M. *Org. Lett.* **2001**, *3*, 1161–1163; (g) Sutton, A. E.; Seigal, B. A.; Finnegan, D. F.; Snapper, M. L. *J. Am. Chem. Soc.* **2002**, *124*, 13390–13391; (h) Yang, C.; Murray, W. V.; Wilson, L. J. *Tetrahedron Lett.* **2003**, *44*, 1783–1786; (i) Terada, Y.; Arisawa, M.; Nishida, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 4063–4067; (j) Brouwer, A. J.; Liskamp, R. M. J. *J. Org. Chem.* **2004**, *69*, 3662–3668; (k) Maechling, S.; Zaja, M.; Blechert, S. *Adv. Synth. Catal.* **2005**, *347*, 1413–1422; (l) Holub, N.; Neidhöfer, J.; Blechert, S. *Org. Lett.* **2005**, *7*, 1227–1229; (m) Dougherty, J. M.; Jiménez, M.; Hanson, P. R. *Tetrahedron* **2005**, *61*, 6218–6230; (n) Grigg, R.; Martin, W.; Morris, J.; Sridharan, V. *Tetrahedron* **2005**, *61*, 11380–11392; (o) Maechling, S.; Norman, S. E.; McKendrick, J. E.; Basra, S.; Koppner, K.; Blechert, S. *Tetrahedron Lett.* **2006**, *47*, 189–192.

10. (a) Fu, G. C.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9856–9857; (b) Fürstner, A.; Grabowski, J.; Lehmann, C. W. *J. Org. Chem.* **1999**, *64*, 8275–8280; (c) Fürstner, A.; Grabowski, J.; Lehmann, C. W.; Kataoka, T.; Nagai, K. *Chem. Biochem.* **2001**, *2*, 60–68; (d) Fürstner, A.; Leitner, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 308–311; (e) Scheiper, B.; Glorius, F.; Leitner, A.; Fürstner, A. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 11960–11965; (f) Guidry, E. N.; Cantrill, S. J.; Stoddart, J. F.; Grubbs, R. H. *Org. Lett.* **2005**, *7*, 2129–2132; (g) Gracias, V.; Gasiecki, A. F.; Djuric, S. W. *Tetrahedron Lett.* **2005**, *46*, 9049–9052; (h) Weihofen, R.; Tverskoy, O.; Helmchen, G. *Angew. Chem., Int. Ed.* **2006**, *45*, 5546–5549.
11. (a) Yang, Q.; Xiao, W.-J.; Yu, Z. *Org. Lett.* **2005**, *7*, 871–874; (b) Vedrenne, E.; Dupont, H.; Oualef, S.; Elkaïm, L.; Grimaud, L. *Synlett* **2005**, 670–672; (c) Bai, C.-X.; Lu, X.-B.; He, R.; Zhang, W.-Z.; Feng, X.-J. *Org. Biomol. Chem.* **2005**, *3*, 4139–4142.
12. At the time of writing we found a useful yet unpublished review on amine metathesis: Compain, P. *Adv. Synth. Catal.* **2007**, *349*, 1829–1846.
13. For preliminary results see: Groaz, E.; Banti, D.; North, M. *Tetrahedron Lett.* **2007**, *48*, 1927–1930.
14. For reviews on the synthesis and biological applications of tetrahydropyridines see: (a) Felpin, F. X.; Lebreton, J. *Curr. Org. Synth.* **2004**, *1*, 83–109; (b) Matyus, P.; Elias, O.; Tapolcsanyi, P.; Polonka-Balint, A.; Halasz-Dajka, B. *Synthesis* **2006**, 2625–2639.
15. Eissenstat, M. A.; Weaver, J. D. *J. Org. Chem.* **1993**, *58*, 3387–3390.
16. Whitney, R. A. *Tetrahedron Lett.* **1981**, *22*, 2063–2066.
17. Duckworth, D. M.; Lee-Wong, S.; Slawin, A. M. Z.; Smith, E. H.; Williams, D. J. *J. Chem. Soc., Perkin. Trans. 1* **1996**, 815–821.
18. Kinderman, S. S.; Wekking, M. M. T.; van Maarseveen, J. H.; Schoemaker, H. E.; Hiemstra, H.; Rutjes, F. P. J. T. *J. Org. Chem.* **2005**, *70*, 5519–5527.
19. Witiak, D. T.; Rotella, D. P.; Filppi, J. A.; Gallucci, J. *J. Med. Chem.* **1987**, *30*, 1327–1336.
20. Kitamura, T.; Sato, Y.; Mori, M. *Adv. Synth. Catal.* **2002**, *344*, 678–693.
21. Miller, S. J.; Kim, S. H.; Chen, Z. R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1995**, *117*, 2108–2109.
22. Mori, M.; Kitamura, T.; Sakakibara, N.; Sato, Y. *Org. Lett.* **2000**, *2*, 543–545.
23. Mori, M.; Kitamura, T.; Sato, Y. *Synthesis* **2001**, 654–664.
24. Kinoshita, A.; Sakakibara, N.; Mori, M. *Tetrahedron* **1999**, *55*, 8155–8167.
25. Ruckert, A.; Eisele, D.; Blechert, S. *Tetrahedron Lett.* **2001**, *42*, 5245–5247.
26. Randl, S.; Lucas, N.; Connon, S. J.; Blechert, S. *Adv. Synth. Catal.* **2002**, *344*, 631–633.
27. Zuercher, W. J.; Hashimoto, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 6634–6640.
28. Hilbert, G. E. *J. Am. Chem. Soc.* **1932**, *54*, 3413–3417.
29. Booth, H.; Khedhair, K. A.; Alshirayda, H. A. R. Y. *Tetrahedron* **1988**, *44*, 1465–1475.