Ring-Closing Metathesis of Allylic *O,O*- and *N,O*-Acetals

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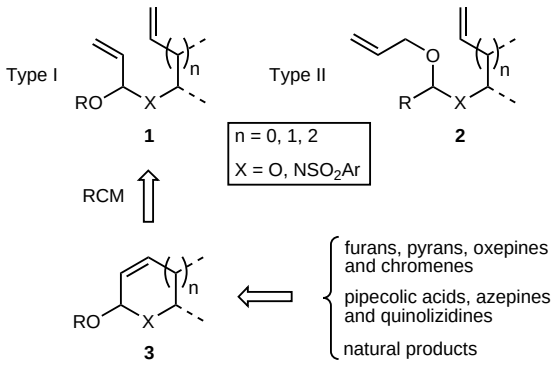
Abstract: A variety of allylic *O,O*- and *N,O*-acetals were synthesized using a mild palladium-catalyzed coupling of an alcohol or sulfonamide with an alkyl or aryl 1,2-propadienyl ether. The resulting linear acetals were used for the synthesis of unsaturated rings *via* ring-closing metathesis, in which the acetal carbon – a precursor for oxycarbenium or *N*-sulfonyliminium ions, respectively – served as a reactive center for further introduction of functional groups. The products – unsaturated oxygen and nitrogen heterocyclic scaffolds – offer multiple opportunities for derivatization as illustrated with the synthesis of substituted dihydropyrans, chromenes, enantiopure tetrahydropyridines and an enantiomerically pure quinolizidine amino acid.

Keywords: allylic *N,O*-acetals; allylic *O,O*-acetals; amidopalladation; oxypalladation; ring-closing metathesis

Introduction

Ring-closing metathesis has emerged over the past decade or so as a mild an general method for the construction of small to large sized unsaturated heterocyclic systems.[1] The mild, neutral conditions under which these reactions are conducted in combination with the broad tolerance of the Ru- and Mo-catalysts towards virtually any functional group render this method especially valuable for the synthesis of acid, base, and/or thermally labile heterocyclic molecules. In recent years, with the emergence of improved and highly active metathesis catalysts the usefulness of this method has even been further extended due to the fact that high reaction temperatures are often no longer required.[2] Cyclic *O,O*-, and *N,O*-acetals represent compound classes that are rather sensitive and would be especially well suited for construction via a ring-closing metathesis process. Interestingly, examples of ring-closing metathesis of linear acetals are scarce in literature; in fact, only a handful of such transformations has been described.[3] In contrast with the occurrence of these few examples, the resulting products are highly desirable, functionalized, multipurpose heterocyclic compounds,[4] which may serve as precursors for the synthesis of natural products and other potentially biologically relevant substances (Scheme 1).[5]

In principle, one can distinguish two types of allylic *O,O*- and *N,O*-acetal precursors, both of which are displayed in Scheme 1. In the type I precursors, only one of the two olefinic moieties is part of the acetal function, while in the type II precursors the acetal is built up from two olefinic side chains. Although ring-closing metathesis of class II precursors is also highly valuable and examples have been described in the literature,[6] this paper focuses on the ring-closing metathesis of class I type precursors. We anticipated that the latter approach, where olefin-containing alcohols and sulfonamides were used to produce the required acetals, first of all would upon cyclization give rise to a double bond that can be used for additional transformations, but that



Scheme 1. Allylic *O,O*- and *N,O*-acetal ring-closing metathesis.

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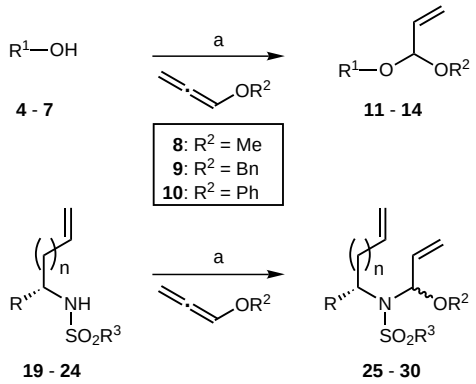
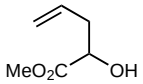
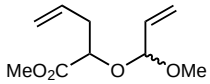
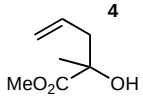
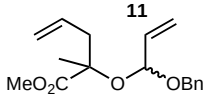
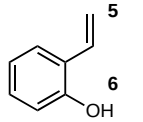
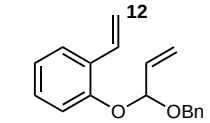
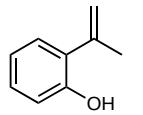
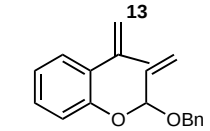


Scheme 2. Amido- and oxypalladation of alkoxyallenes. *Reagents and conditions*: (a) Method A: propadienyl ether **8** (3 equiv.), $Pd(OAc)_2$ (5 mol %), dppp (5 mol %), Et_3N (1.5 equiv.), MeCN, sealed tube, reflux, 3–6 h. Method B: propadienyl ether **9** or **10** (1.1 equiv.), $Pd(OAc)_2$ (5 mol %), dppp (5 mol %), Et_3N (1.5 equiv.), MeCN, rt, 16 h.

Table 1. Oxypalladation of alkoxyallenes.

Entry	Alcohol	Allene (method)	Product	Yield [%]
1	 **4**	**8** (A)	 **11**	98
2	 **5**	**9** (B)	 **12**	97
3	 **6**	**9** (B)	 **13**	62[a]
4	 **7**	**9** (B)	 **14**	63[a]

[a] Reaction time less than 60 sec.

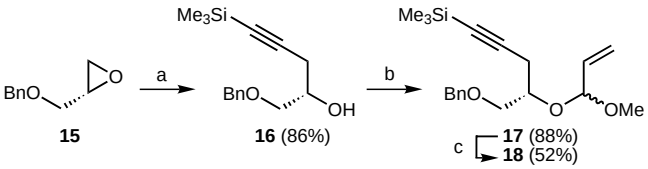
especially the presence of the alkoxy group adjacent to the ring heteroatom would give access to the corresponding highly reactive oxycarbenium and *N*-sulfonyliminium cations[7] and hence ample opportunities for derivatization at this position. In this paper, we will underline the viability of this approach by describing an efficient synthesis of members of several heterocyclic compound classes such as amongst others pyrans, chromenes, azepines, and pipecolic acids.

Results and Discussion

The synthesis of the ring-closing metathesis precursors was performed using a palladium-catalyzed coupling between an alcohol or a sulfonamide and an alkyl 1,2-propadienyl ether (Scheme 2). These metal-catalyzed reaction conditions were especially developed to serve this purpose, since in most cases commonly used combinations of reagents involving protic acids did not or only to a very small extent provide the required acid labile *O,O*- and *N,O*-allylic acetals. Generally, two methods were used for the acetal formation, which differ only in reaction temperature: with method A methyl 1,2-propadienyl ether (**8**) was used in refluxing acetonitrile (sealed tube), while with method B allenes **9** and **10** were used in the same solvent at room temperature.[8] The usefulness of this palladium-mediated coupling method for the construction of such acetals has already been illustrated in publications from our group[3a, g,h] and from others.[3c]

Subjecting the secondary, tertiary and phenolic alcohols **4**–**7** to one of the electron-rich alkoxy-substituted allenes **8**–**10** in the presence of a catalytic amount of $Pd(OAc)_2$/dppp under basic conditions in dry acetonitrile led to the desired ring-closing metathesis precursors in reasonable to excellent yields (Table 1). Reaction of the α-hydroxy ester **4** with methyl 1,2-propadienyl ether (**8**) in refluxing acetonitrile catalyzed by $Pd(OAc)_2$ gave the desired acetal **11** in 97% yield (entry 1). Not surprisingly, the product was obtained as a *ca.* 1:1 mixture of diastereoisomers, which was the case in all of these acetalization reactions. The related tertiary alcohol **5** also gave in nearly quantitative yield the corresponding acetal (**12**) using milder reaction conditions (room temperature instead of 80 °C, thus preventing decomposition of the product) using benzyl 1,2-propadienyl ether (**9**) as the allene source (entry 2). This new example once again demonstrates the usefulness of this type of acetal synthesis, since even very hindered tertiary alcohols react to provide the desired acetals. The same mild reaction conditions appeared extremely useful in the case of the substituted phenols **6** and **7**. Subjection of these alcohols to similar conditions led to almost instantaneous product formation at room temperature (5 mol % of catalyst), affording the acetals **13** and **14** in 62 and 63% yield, respectively (entries 3 and 4). Despite the fact that TLC indicated a clean conversion, the somewhat disappointing yields after isolation and purification by column chromatography were probably the result of the labile nature of the phenolic acetals. Due to the good leaving group ability of the phenol substituent, these acetals are more prone to acid-catalyzed hydrolysis or isomerization reactions.

In addition to the racemic olefinic substrates, an enantiomerically pure acetylenic substrate was prepared, which might serve as a substrate for enyne ring-closing metathesis. The synthesis commenced with the readily available benzyl-protected (*R*)-glycidol **15** (Scheme 3). Regioselective epoxide ring-opening with trimethylsilyl-protected ethynyllithium as the alkylating agent in the presence of $BF_3 \cdot OEt_2$ proceeded smoothly, giving the protected acetylenic alcohol **16** in 86% yield. The product was then coupled to methyl 1,2-propadien-



Scheme 3. Enyne acetal synthesis. *Reagents and conditions*: (a) $BF_3 \cdot OEt_2$ (1.5 equiv.), 1-trimethylsilylethynyllithium (1.5 equiv.), THF, −78 °C. (b) Methyl propadienyl ether, $Pd(OAc)_2$/dppp 5 mol %, Et_3N (1.5 equiv.), MeCN, sealed tube, reflux, 4 h. (c) K_2CO_3 (5 equiv.), MeOH, rt, 16 h.

Table 2. Amidopalladation of alkoxyallenes.

Entry	Amide	n	R	Allene	Method	Product (R^3)	Yield [%]
1	**19**	0	H	**8**	A	**25** ($C_6H_4CH_3$)	64
2	**20**	1	H	**9**	B	**26** ($C_6H_4CH_3$)	82
3	**21**	0	CH_2OBn	**9**	B	**27** ($pC_6H_4NO_2$)	96
4	**22**	1	CO_2Me	**9**	B	**28** ($pC_6H_4NO_2$)	84
5	**23**	1	CO_2Me	**10**	B	**29** ($C_6H_4CH_3$)	62
6	**24**	2	CO_2Me	**9**	B	**30** ($pC_6H_4NO_2$)	90

yl ether in refluxing acetonitrile using 5 mol % of $Pd(OAc)_2$/dppp as the catalyst affording the acetal **17** in a yield of 88%. This compound could serve as a substrate for enyne metathesis, but also the corresponding desilylated compound **18** which was obtained upon treatment of **17** with K_2CO_3 in MeOH.

The linear *N*,*O*-acetals were all prepared via the same method and are displayed in Table 2. Reaction of *N*-tosylallylamine (**19**) with methyl 1,2-propadienyl ether at reflux temperature in acetonitrile afforded the product **25** in a reasonable yield of 64% (entry 1). Analogously, but under milder conditions (allene **9**, room temperature) its homologue **20** was converted into the *N*,*O*-acetal **26** in 82% yield. The racemic vinylglycinol-derived[9] sulfonamide **21** (Ns = 4-nitrobenzenesulfonyl), and the enantiomerically pure sulfonylated unsaturated amino acids **22** and **24**[10] were successfully reacted with benzyl propadienyl ether (**9**) at room temperature to give the desired products (**27**, **28**, and **30**, respectively) in very good yields (entries 3, 4, and 6). The conversion of the allylglycine-derived sulfonamide **23** with phenyl 1,2-propadienyl ether (**10**) proceeded smoothly at room temperature, albeit that the yield of the resulting *N*,*O*-acetal **29** was somewhat lower (62%) presumably due to the better leaving group ability of the phenoxy moiety (entry 5). In the cases of the enantiomerically pure precursors, it was demonstrated with chiral HPLC that the coupling reaction proceeded without loss of stereochemical integrity at the amino acid stereocenter (at the acetal center, a 1:1 mixture of diastereoisomers was formed). Considering these examples, it should be emphasized that this Pd-catalyzed condensation of sulfonamides with alkoxyallenes represents a new method for the formation of *N*-sulfonyl-protected *N*,*O*-acetals, which are not readily accessible via other pathways.[11]

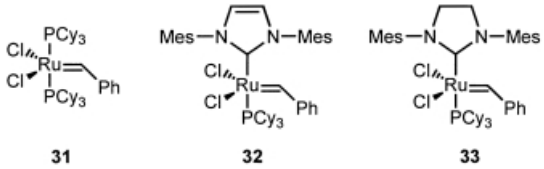
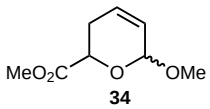
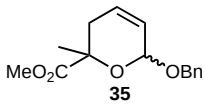
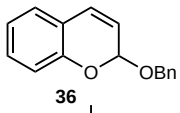
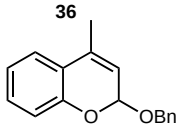
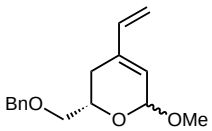


Figure 1. Ruthenium catalysts.

Table 3. Allylic *O*,*O*-acetal ring-closing metathesis.

Entry	Precursor	Conditions[a]	Product	Yield [%]
1	**11**	**31**, rt, 4 h	 **34**	74
2	**12**	**33**, rt, 6 h	 **35**	77
3	**13**	**32**, 80 °C, 4 h	 **36**	78
4	**14**	**31**, rt, 8 h	 **37**	87
5	**17**	**31**, 40 °C, 16 h	-	-
6	**18**	**31**, rt, 2 h	 **38**	36

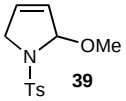
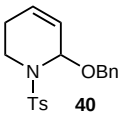
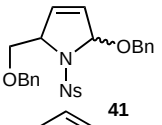
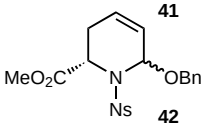
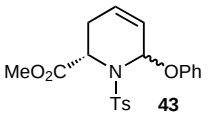
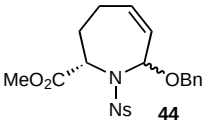
[a] Catalyst **31** was used in CH_2Cl_2, catalysts **32** and **33** were used in toluene.

Having these precursors in hand, we set out to explore both the ring-closing and the enyne metathesis reactions. Whenever possible we used the mildest conditions to complete the metathesis process: in most cases the ruthenium-based Grubbs catalyst **31** (Figure 1) was used (5 mol %), either at room temperature or at reflux temperature in dichloromethane.

In reactions where this catalyst gave an unsatisfactory rate or yield, we turned to the more active, dihydroimidazolidene-substituted ruthenium catalyst **33** (5 mol %), with which reactions were performed in toluene at elevated temperatures. The metathesis results of the *O*,*O*-acetal precursors are listed in Table 3.

In these oxygen series, acetal **11** gave the dihydropyran product **34** (1:1 mixture of *cis*/*trans* isomers) in a good yield of 74% (entry 1).[3a] A comparable result was obtained with the α-methyl-substituted analogue **12**, which upon treatment with catalyst **33** gave the corresponding product **35** in 77% yield as a 1:1 mixture of *cis*/*trans*-isomers that could be separated by column chromatography (entry 2). The phenolic acetal precursors **13**

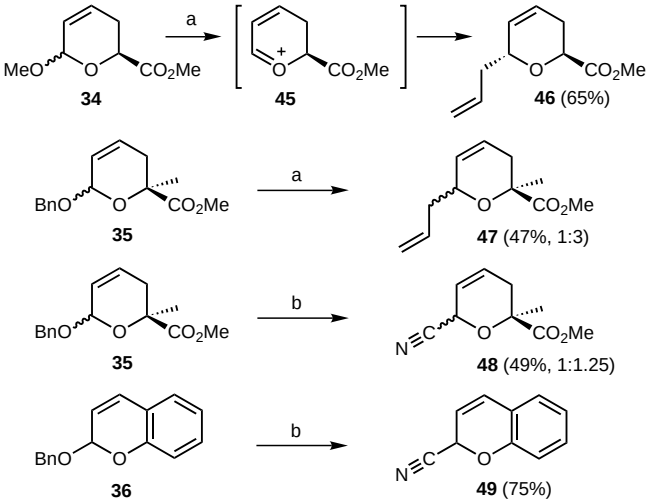
Table 4. Allylic *N,O*-acetal ring-closing metathesis.

Entry	Precursor	Conditions[a]	Product	Yield [%]
1	**25**	**31**, rt, 2 h	 **39**	95
2	**26**	**31**, rt, 4 h	 **40**	68
3	**27**	**31**, 60 °C[b], 16 h	 **41**	42
4	**28**	**31**, rt, 16 h	 **42**	89
5	**29**	**31**, 40 °C, 16 h	 **43**	60
6	**30**	**31**, rt, 16 h	 **44**	70

[a] Catalyst **31** was used in CH_2Cl_2.
[b] Toluene was used as the solvent.

and **14** could both be ring-closed in a satisfactory yield (78 and 87%, respectively); we observed that in the former case use of catalyst **32** (4 mol %) at higher temperature was preferred, since with catalyst **31**, more than 10 mol % of catalyst had to be added portionwise over a period of several hours in order to reach the same conversion. (entries 3 and 4). The enyne ring-closing metathesis reactions were studied using catalyst **31** (5 mol %) in dichloromethane at room temperature or at 40 °C. Enyne metathesis of such acetal precursors would yield interesting multifunctionalized acetal-diene systems, which may be used in a variety of ways for further derivatization. While the trimethylsilyl-protected acetylenic precursor **17** appeared unreactive under these reaction conditions (entry 5), the corresponding deprotected acetylene **18** gave the desired diene in a reasonable 36% yield. Application of this series of reactions onto the corresponding homologous acetal (obtained starting from addition of trimethylsilyl-protected propargyllithium onto **15**) unfortunately did only result in trace amounts of the seven-membered ring diene.

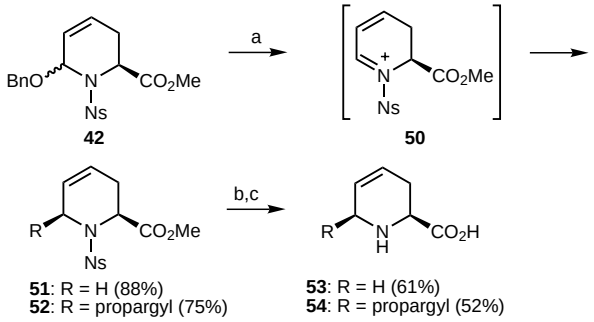
The first example in the nitrogen series was the formation of the acid-sensitive five-membered 2,5-dihydropyrrole system **39** from precursor **25** in 95% isolated yield (Table 4, entry 1). This five-membered ring was rapidly formed in 2 hours at room temperature, but the product had to be purified with great care to



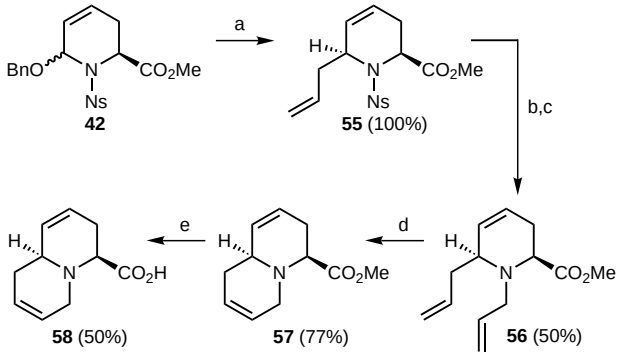
Scheme 4. Oxycarbenium ion chemistry. *Reagents and conditions*: (a) $BF_3 \cdot OEt_2$ (2 equiv.), allyltrimethylsilane (2 equiv.), CH_2Cl_2, 0 °C to rt, 1 h. (b) $BF_3 \cdot OEt_2$ (2 equiv.), trimethylsilyl cyanide (2 equiv.), CH_2Cl_2, 0 °C to rt, 1 h.

prevent aromatization to the corresponding pyrrole. The successful construction of this labile system demonstrates once more the mildness of the metathesis process. A similar level of instability was encountered in ring-closing precursor **27** (entry 3). This time, a higher temperature was required to obtain the desired product **41** in 42% yield. The use of more active catalysts such as **32** or **33** did not improve the yield, but instead led to more extensive decomposition. The product was formed as an approximately 1:1 mixture of *cis*/*trans*-isomers, indicating that both precursor diastereoisomers cyclized at a comparable rate. The six-membered ring precursors **26**, **28**, and **29** all gave products (**40**, **42**, and **43**) of a significantly higher stability and yields ranging from 60–89% (entries 2, 4, and 5). Interestingly, the ester functionality of **28** had a positive effect on the cyclization process, resulting in a clear increase of the yield of **42** compared to **40**. In contrast, partial hydrolysis upon silica gel purification of the more labile phenol-substituted *N,O*-acetal **43** was probably the reason for the somewhat lower yield in this case. Furthermore, we were pleased that the seven-membered ring **44** in this series was smoothly formed at room temperature in a good yield of 70% (entry 6).

The products resulting from the ring-closing metathesis reactions proved to be useful building blocks for further derivatization. This was illustrated with the synthesis of substituted dihydropyrans[3a,12] and chromenes[3h,13] in the cyclic, unsaturated oxygen-acetal series. Lewis acid treatment of these cyclic acetals will lead to conjugated oxycarbenium ion intermediates (*viz*. **45**), which in principle, can undergo 1,2- and 1,4-type additions of suitable nucleophiles. The reactivity of these allylic acetals was studied, of which some examples are shown in Scheme 4.



Scheme 5. Substituted pipecolic acid synthesis. *Reagents and conditions*: (a) $BF_3 \cdot OEt_2$ (3 equiv.), triethylsilane (3 equiv.) or allenyltributyltin (3 equiv.), CH_2Cl_2, −78 °C to rt, 4 h. (b) PhSH (3 equiv.), K_2CO_3 (4 equiv.), MeCN, rt, 24 h. (d) LiOH (1.1 equiv), MeOH/H_2O (1:1), rt, 24 h.



Scheme 6. Quinolizidine amino acid synthesis. *Reagents and conditions*: (a) $BF_3 \cdot OEt_2$ (3 equiv.), allyltributyltin (3 equiv.), CH_2Cl_2, −78 °C to rt, 4 h. (b) PhSH (3 equiv.), K_2CO_3 (4 equiv.), MeCN, rt, 24 h. (c) allyl bromide (2 equiv.), K_2CO_3 (2 equiv.), MeCN, 60 °C, 30 h. (d) **32**, toluene, 80 °C, 6 h. (e) LiOH (1.1 equiv), MeOH/H_2O (3:1), rt, 24 h.

The acetals were treated with the Lewis acid $BF_3 \cdot OEt_2$ at 0 °C and in spite of the use of different nucleophiles, in all cases solely 1,2-substitution was observed. In the first example, allyltrimethylsilane addition onto acetal **34** provided the allyl-substituted dihydropyran **46** as a single *trans*-diastereoisomer in 65% yield. Most likely, the ester substituent on the planar intermediate **45** forces the nucleophile to come in from the opposite site. Inversely, the comparable α-methyl-substituted acetal **35** showed much lower diastereoselectivity upon reaction with allyltrimethylsilane and trimethylsilyl cyanide giving products **47** and **48** in 47 and 49% yield. The low to virtually non-existing selectivity clearly reflects the difference in size between a proton and a methyl substituent on the side of the electrophile, but also the difference in bulk between the allylsilane and the cyanide on the side of the nucleophile. Moreover, in the aromatic series the benzopyran acetal **36** gave under the same reaction conditions the 2-cyano-2*H*-chromene **49** in 75% isolated yield.

The unsaturated sulfonamide-derived acetals proved to be good precursors for the synthesis of enantiomerically pure substituted pipecolic acids via *N*-sulfonyliminium ion chemistry (Scheme 5).

Therefore, precursor **42** was treated at −78 °C with $BF_3 \cdot OEt_2$ and the resulting intermediate *N*-sulfonyliminium ion species **50** was reacted *in situ* with the nucleophiles triethylsilane and allenyltributylstannane.[14] This approach afforded the protected pipecolic acids **51** and **52** in 88 and 75% yield, respectively, in a completely regioselective fashion without any detectable formation of the corresponding 1,4-adducts. In the latter case, the product was proven to consist only of the *cis*-adduct after deprotection to the corresponding free amino acid and comparison with deprotected **55** (*vide infra*).[3g] The *cis*-relation between the allyl and the ester group is most probably a result of so-called chirality relay:[15] the ester substituent forces the arylsulfonamide moiety to point downwards, thus preventing the nucleophile to attack from the bottom face of the planar intermediate. Deprotection of both cyclic amino esters using standard reaction conditions (thiophenolate-mediated sulfonamide cleavage, followed by lithium hydroxide-induced saponification and subsequent purification via ion exchange chromatography) yielded the free pipecolic amino acids **53** and **54** without detectable racemization and epimerization, respectively. Thus compound **53**, which is identical to the natural product baikiain, was obtained {$[\alpha]_D$: −182.6 (*c* 0.3, H_2O; lit.[16] −201.6 (*c* 1, H_2O)}, representing a novel pathway towards its synthesis.[16]

In addition, a novel enantiomerically pure quinolizidine amino acid was synthesized using similar *N*-sulfonyliminium ion chemistry and a second ring-closing metathesis step (Scheme 6). Treatment of the *N*,*O*-acetal **42** with $BF_3 \cdot OEt_2$ at −78 °C *in situ* gave the conjugated *N*-sulfonyliminium ion **50**, which was trapped in this case by the allyltributylstannane as the nucleophile to give the addition product. In spite of the fact that four possible isomers can be formed in this reaction (1,2- and 1,4-addition, *cis* and *trans* with respect to the ester group), a single diastereoisomer (**55**) was obtained. The selectivity was strongly influenced by the nature of the nucleophile (allyltrimethylsilane instead of the more reactive allyltributylstannane gave a *ca*. 3:1 mixture of 1,2- and 1,4-regioisomers) and the reaction temperature (at higher temperatures, lower selectivities were obtained). The *cis*-stereochemistry of the adduct was assigned on the basis of ^1H NMR NOE studies after deprotection to the free amino acid, which showed a 10% enhancement of H6 upon irradiation of H2 and *vice versa*.[17] Successive sulfonamide cleavage by the thiophenolate anion, followed by allylation using standard conditions afforded the diallyl compound **56** in 50% over these two steps. Remarkably, subjection of this triolefin to the ruthenium catalyst **31** in dichloromethane gave almost no product formation. In contrast, the more active catalyst **32** showed a good reactivity in

toluene at 80 °C and afforded the unsaturated, bicyclic quinolizidine skeleton **57** in 77%. Strikingly, use of only 1% of catalyst **32** was sufficient to complete the reaction in six hours, compared to virtually no reactivity of catalyst **31** at all at 40 °C. Finally, the ester was saponified to give the free, conformationally restricted quinolizidine amino acid **58**. Beside the fact that this compound represents a new tertiary amino acid, it may also be applied as an enantiopure building block for alkaloid synthesis.

Conclusions

In this paper, we demonstrated the efficient transformation of various alcohols and sulfonamides into allylic *O,O*-acetals or *N,O*-acetals under mild palladium-catalyzed conditions. The sensitive allylic acetals appeared to be suitable substrates for ring-closing and enyne metathesis as shown by many examples. The usefulness of these cyclic acetals was illustrated with the synthesis of substituted dihydropyran derivatives and the synthesis of a substituted chromene derivative. Their usefulness was further underlined by application in the synthesis of several novel unsaturated pipecolic acid derivatives and a new quinolizidine-type amino acid, which may be used as an enantiopure building block in alkaloid synthesis. In conclusion, the combination of allylic acetal formation, ring-closing metathesis and acid-mediated functionalization constitutes straightforward and efficient methodology that may be widely used in the synthesis of strongly functionalized building blocks, potentially biologically active compounds, and natural products.

Experimental Section

General information

Unless otherwise noted, materials were purchased from commercial suppliers and used without purification. Toluene, dichloromethane and acetonitrile were freshly distilled from calcium hydride. Tetrahydrofuran and diethyl ether were freshly distilled from sodium with benzophenone as indicator. Triethylamine was stored over potassium hydroxide pellets and used as such. All air and moisture sensitive reactions were carried out under an inert atmosphere of dry nitrogen, except for the ring-closing metathesis reactions, which were stirred under a dry argon atmosphere. Column chromatography was performed using Aldrich silica gel (70–230 mesh, 60 Å). R_f values were obtained by using thin layer chromatography (TLC) on silica gel-coated plastic sheets (Merck silica gel 60 F_{254}) with the indicated solvents. Infrared spectra were recorded on a Bruker IFS 28 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were obtained on a Bruker ARX 400 or a Varian Inova-500. Spectra are reported in units of ppm on the δ scale, relative to chloroform (7.26 ppm for ^{1}H NMR and 77.0 ppm for ^{13}C NMR). Mass spectra were measured using a JEOL JMS SX/SX102A four-sector mass spectrometer, coupled to a JEOL MS-MP7000 data system. Melting and boiling points are uncorrected. Melting points were determined with Büchi melting point B-545. Methyl 1,2-propadienyl ether **8**,[18] benzyl 1,2-propadienyl ether **9**, and phenyl 1,2-propadienyl ether **10** were prepared following the procedure described by Brandsma et al.[14,19]

General Methods for the Oxy- and Amidopalladation

Method A: In a sealed tube was added to a solution of the sulfonamide or alcohol (0.3 M) in dry acetonitrile under a nitrogen atmosphere Et_3N (1.5 equiv.), $Pd(OAc)_2$ (5 mol %), dppp (5 mol %), and the alkyl 1,2-propadienyl ether (3 equiv.). The mixture was heated at 100 °C for the indicated time. The crude mixture was cooled and quenched with H_2O, and the product was extracted with diethyl ether. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated under vacuum. The crude oil was purified by column chromatography as indicated.

Method B: To a solution of the sulfonamide or alcohol (0.1 M) in dry acetonitrile under a nitrogen atmosphere was added Et_3N (1.5 equiv.), $Pd(OAc)_2$ (5 mol %), dppp (5 mol %), and the alkyl 1,2-propadienyl ether (1.1 equiv). The reaction mixture was stirred at room temperature for the indicated time and worked up identical to method A.

Methyl 2-(1-Methoxyallyloxy)pent-4-enoate (11)

2-Hydroxypent-4-enoic acid methyl ester **4** (2.00 g, 15.4 mmol) was reacted with methyl 1,2-propadienyl ether according to method A. Column chromatography (petroleum ether/diethyl ether, 1:1) afforded **11** as a colorless oil; yield: 3.01 g (98%); IR (film): $\nu = 1068, 1129, 1205, 1754, 2834, 2935, 3079\ cm^{-1}$; ^{1}H NMR (400 MHz, $CDCl_3$): isomer 1: $\delta = 5.84-5.73$ (m, 2H), 5.47–5.29 (m, 2H), 5.14–5.06 (m, 2H), 4.93 (d, $J = 4.5$ Hz, 1H), 4.27 (d, $J = 6.3$ Hz, 1H), 3.71 (s, 3H), 3.30 (s, 3H), 2.50 (q, $J = 5.9$ Hz, 2H); isomer 2: $\delta = 5.84-5.73$ (m, 2H), 5.47–5.29 (m, 2H), 5.14–5.06 (m, 2H), 4.86 (d, $J = 5.1$ Hz, 1H), 4.10 (t, $J = 6.3$ Hz, 1H), 3.71 (s, 3H), 3.36 (s, 3H), 2.50 (q, $J = 5.9$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): both diastereoisomers: δ = 134.0, 133.8, 132.8, 132.6, 119.3, 119.2, 118.1, 117.9, 102.7, 101.5, 73.9, 72.9, 53.5, 52.8, 51.6, 37.3; HRMS (EI^+): calcd. for $(M-OMe)^+$: 169.0865; found: 169.0850.

Methyl 2-(1-Benzyloxyallyloxy)-2-methylpent-4-enoate (12)

2-Hydroxy-2-methylpent-4-enoic acid methyl ester **5** (0.29 g, 2.0 mmol) was reacted with benzyl 1,2-propadienyl ether according to method B. Column chromatography (heptane/ethyl acetate 3:1) gave the **12** as a slightly yellow oil; yield: 0.58 g (97%); ^{1}H NMR (300 MHz, $CDCl_3$): both diastereoisomers: $\delta = 7.35-7.21$ (m, 5H), 6.00–5.69 (m, 2H), 5.50–5.24 (m, 3H), 5.12–5.06 (m, 2H), 4.68–4.45 (m, 2H), 3.62 and 3.55 (s, 3H), 2.56 (m, 2H), 1.52 and 1.44 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): both diastereoisomers: δ = 175.1, 139.8, 139.6, 137.0, 136.8, 134.1, 133.9, 129.8, 129.2, 119.6, 119.3, 119.2, 98.5, 98.2, 80.7, 79.6, 67.7, 67.0, 66.0, 52.5, 44.4, 44.1, 23.1, 21.2.

1-(1-Benzyloxyallyloxy)-2-vinylbenzene (13)

According to general procedure B, phenol **6** (0.50 g, 4.19 mmol) was reacted with benzyl 1,2-propadienyl ether. Column chromatography (petroleum ether/ethyl acetate, 40:1) afforded **13** as a colorless oil; yield: 0.69 g (2.60 mmol, 62%); IR (film): $\nu = 3029$, 1230, 985 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz): $\delta = 7.45$ (dd, $J = 1.6$, 7.7 Hz, 1H), 7.36 (dd, $J = 11.2$, 17.8 Hz, 1H), 7.20 – 7.18 (m, 2H), 7.12 – 7.03 (m, 4H), 7.00 (dt, $J = 1.6$, 7.3 Hz, 1H), 6.84 (dt, $J = 0.7$, 8.2 Hz, 1H), 5.91 (ddd, $J = 4.3$, 10.7, 17.3 Hz, 1H), 5.73 (dd, $J = 1.4$, 17.8 Hz, 1H), 5.56 (d, $J = 4.3$ Hz, 1H), 5.41 (td, $J = 1.3$, 17.4 Hz, 1H), 5.21 (dd, $J = 1.4$, 11.1 Hz, 1H), 5.07 (td, $J = 1.2$, 10.7 Hz, 1), 4.64 (d, $J = 11.8$ Hz, 1H), 4.43 (d, $J = 11.8$ Hz, 1H); ^{13}C NMR (C_6D_6, 50 MHz): $\delta = 155.3$, 138.9, 135.6, 132.9, 129.7, 129.3, 129.2 (2′), 128.7 (2′), 128.4, 127.4, 123.1, 119.7, 117.6, 115.3, 101.7, 68.3; HRMS (FAB): calcd. for $C_{18}H_{18}O_2$: 266.1307; found: 266.1306.

1-Isopropenyl-2-(1-benzyloxyallyloxy)benzene (14)

According to general procedure B, phenol **7** (346 mg, 2.58 mmol) was reacted with benzyl 1,2-propadienyl ether. Column chromatography (petroleum ether/ethyl acetate, 20:1) afforded acetal **14** as a colorless oil; yield: 447 mg (63%); IR (film): $\nu = 3075$, 3029, 2917, 1219, 979 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz): $\delta = 7.24 – 7.20$ (m, 3H), 7.16 – 7.01 (m, 5H), 6.86 (dt, $J = 1.2$, 7.4 Hz, 1H), 5.93 (ddd, $J = 4.3$, 10.7, 17.4 Hz, 1H), 5.60 (td, $J = 1.1$, 4.3 Hz, 1H), 5.44 (td, $J = 1.4$, 17.4 Hz, 1H), 5.16 (m, 2H), 5.10 (td, $J = 1.3$, 10.7 Hz, 1H), 4.65 (d, $J = 11.8$ Hz, 1H), 4.47 (d, $J = 11.8$ Hz, 1H), 2.20 (s, 3H); ^{13}C NMR (C_6D_6, 50 MHz): $\delta = 153.8$, 144.2, 137.8, 134.5, 134.2, 129.4 (2′), 128.0 (2′), 127.5, 127.4, 127.2, 121.9, 118.4, 116.3, 115.0, 100.2, 66.7, 23.2; HRMS (FAB): calcd. for $C_{19}H_{20}O_2$: 280.1463; found: 280.1465.

(*S*)-1-Benzyloxy-5-trimethylsilylpent-4-yn-2-ol (16)

To a solution of trimethylsilylacetylene (2.7 g, 27.5 mmol) in dry THF (35 mL) at −78 °C was slowly added *n*-butyllithium (17.5 mL, 27.9 mmol). The solution was allowed to warm to −30 °C in 30 min. The reaction mixture was again cooled to −78 °C and $BF_3 \cdot OEt_2$ (3.75 mL, 30.5 mmol) was added, followed by stirring at this temperature for 30 min. A solution of benzyl glycidol **15** (3.0 g, 18.3 mmol) in THF (15 mL) was added and the mixture was stirred at −78 °C for 2 h. The reaction was quenched by adding saturated aqueous NH_4Cl (50 mL) and allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. Column chromatography (petroleum ether/ethyl acetate 4:1) afforded **16** as a slightly yellow oil; yield: 4.1 g (86%); $[\alpha]_D = +10.5$ (*c* 10, CH_2Cl_2); IR (film): $\nu = 3417$, 2126, 1249, 840 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.38 – 7.26$ (m, 5H), 4.57 (s, 2H), 3.98 – 3.93 (m, 1H), 3.61 (dd, $J = 9.6$, 3.9 Hz, 1H), 3.50 (dd, $J = 9.6$, 6.5 Hz, 1H), 2.50 (dd, $J = 6.1$, 3.8 Hz, 2H), 2.43 (br, 1H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 137.7$, 128.3, 127.7, 102.4, 87.2, 73.3, 72.7, 68.7, 24.9, −0.09.

5-Benzyloxy-4-(1-methoxyallyloxy)pent-1-ynyl]trimethylsilane (17)

According to method A, alcohol **16** was reacted with methyl 1,2-propadienyl ether. Column chromatography (petroleum ether/diethyl ether, 20:1) afforded **17** as slightly yellow colored oil; yield: 0.79 g (88%); $[\alpha]_D$: +9.1 (*c* 1, CH_2Cl_2); IR (film): $\nu = 2957$, 2176, 1250, 840 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): both diastereoisomers: $\delta = 7.35 – 7.26$ (m, 5H), 5.84 (m, 1H), 5.39 (m, 1H), 5.30 and 5.29 (s, 1H), 5.05 (m, 1H), 4.60 and 4.55 (s, 2H), 3.96 (m, 1H), 3.64-3.57 (m, 2H), 3.36 and 3.33 (s, 3H), 2.58-2.51 (m, 2H), 0.13 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): both diastereoisomers: $\delta = 138.1$, 134.9, 128.3, 128.2, 118.6, 103.4, 103.3, 102.3, 102.1, 86.3, 86.2, 73.5, 73.4, 73.3, 52.6, 52.4, 23.7, −0.1; HRMS (FAB): calcd. for $C_{19}H_{29}O_3Si$ (MH^+): 333.1886; found: 333.1886.

[2-(1-Methoxyallyloxy)pent-4-ynyloxymethyl]benzene (18)

To a solution of **17** (0.67 g, 2.55 mmol) in methanol (5 mL) was added K_2CO_3 (35 mg, 10.3 mmol). After stirring for 16 h, the reaction mixture was poured into saturated aqueous NH_4Cl (5 mL). After layer separation, the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. Column chromatography (petroleum ether/diethyl ether, 20:1) afforded **18** as a yellowish oil; yield: 0.25 g (52%); IR (film): $\nu = 3296$, 2936 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): both diastereoisomers: $\delta = 7.34 – 7.26$ (m, 5H), 5.79 (m, 1H), 5.44 (m, 1H), 5.30 and 5.29 (s, 1H), 5.02 (m, 1H), 4.57 and 4.55 (s, 2H), 3.96 (m, 1H), 3.64 – 3.57 (m, 2H), 3.35 and 3.34 (s, 3H), 2.57-2.48 (m, 2H), 1.98 and 1.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): both diastereoisomers: $\delta = 138.0$, 134.7, 128.3, 127.4, 118.6, 102.3, 102.0, 88.9, 72.9, 73.2, 73.3, 68.6, 52.6, 52.5, 23.2; HRMS (FAB): calcd. for $C_{16}H_{21}O_3$ (MH^+): 261.1491; found: 261.1491.

N-Allyl-*N*-(1-methoxy-allyl)-4-methylbenzenesulfonamide (25)

N-Tosylallylamine (**19**, 1.0 g, 4.8 mmol) and methyl 1,2-propadienyl ether were reacted according to method A. Column chromatography (petroleum ether/diethyl ether, 9:1) afforded **25** as a yellowish oil; yield: 0.86 g (64%); IR (film): $\nu = 2833$, 1345 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.70$ (d, $J = 8.3$ Hz, 2H), 7.27 (d, $J = 8.0$ Hz, 2H), 5.74 (m, 1H), 5.57 (m, 1H), 5.46 (dt, $J = 4.3$, 1.3 Hz, 1H), 5.33 (dt, $J = 17.2$, 1.5 Hz, 1H), 5.21 (dt, $J = 10.5$, 1.5 Hz, 1H), 5.11 (dq, $J = 17.2$, 1.4 Hz, 1H), 5.02 (dq, $J = 10.1$, 1.3 Hz, 1H), 3.75 (m, 2H), 3.31 (s, 3H), 2.4 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 143.2$, 137.8, 135.0, 133.8, 129.5, 127.1, 118.5, 117.1, 88.3, 55.4, 45.3, 22.0; HRMS (FAB): calcd. for $C_{14}H_{20}NO_3S$ (MH^+): 282.1164; found: 282.1164.

N-(1-Benzyloxyallyl)-*N*-but-3-enyl-4-methylbenzenesulfonamide (26)

N-Tosyl-3-butenylamine (**20**, 1.0 g, 4.43 mmol) was reacted with benzyl 1,2-propadienyl ether according to method B. Column chromatography (pentane/diethyl ether, 4:1 – 1:1)

afforded **26** as a colorless oil; yield: 1.34 g (82%); IR (film): ν = 2930, 1341, 1163 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 7.3 Hz, 2H), 7.28 – 7.38 (m, 7H), 5.70 – 5.75 (m, 1H), 5.68 (s, 1H), 5.43 – 5.52 (m, 2H), 5.26 (d, *J* = 10.3 Hz, 1H), 5.00 – 5.06 (m, 2H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 12.2 Hz, 1H), 3.25 – 3.30 (m, 1H), 3.09 – 3.15 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.4, 137.8, 137.6, 135.1, 133.8, 129.7, 128.3, 127.7, 127.6, 127.0, 119.0, 116.6, 86.4, 69.4, 43.1, 35.0, 21.5; HRMS (FAB): calcd. for $C_{21}H_{26}NO_3S$ (MH^+): 372.1633; found: 372.1637.

N-(1-Benzyloxyallyl)-*N*-(1-benzyloxymethylallyl)-4-nitrobenzenesulfonamide (27)

N-(1-Benzyloxymethylallyl)-4-nitrobenzenesulfonamide (**21**, 0.30 g, 0.81 mmol) was reacted with benzyl 1,2-propadienyl ether according to method B. Column chromatography (pentane/diethyl ether, 2:1) afforded **27** as a white, waxy solid; yield: 0.40 g (96%); IR (film): ν = 3066, 3033, 2871, 1533, 1350, 1165 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): both diastereoisomers: δ = 8.15 (m, 2H), 7.96 (m, 2H), 7.37 – 7.06 (m, 10H), 6.15 – 6.80 (m, 1H), 6.80 – 5.61 (m, 1H), 5.56 – 5.20 (m, 2H), 4.65 – 4.31 (m, 5H), 3.93 – 3.79 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): both diastereoisomers: δ = 149.5, 147.5, 137.5, 137.0, 135.2, 134.7, 134.4, 134.0, 128.6, 128.2, 128.1, 126.9, 123.7, 119.6, 119.2, 119.0, 118.4, 87.0, 73.0, 70.4, 58.9, 47.1, 15.1; HRMS (FAB): calcd. for $C_{27}H_{28}N_2O_6SNa$ (MNa^+): 531.1566; found: 531.1548.

Methyl 2-[(1-Benzyloxyallyl)-(4-nitrobenzenesulfonyl)amino]pent-4-enate (28)

Methyl (*S*)-2-(4-nitrobenzenesulfonylamino)pent-4-enoate (**22**, 2.58 g, 8.19 mmol) and benzyl 1,2-propadienyl ether were reacted following method B. Column chromatography (pentane/diethyl ether, 1:1 – 1:4) afforded **28** as a colorless oil; yield: 3.17 g (84%); IR (film): ν = 2952, 1745, 1530, 1350, 1164 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): both diastereoisomers: δ = 8.26 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 8.9 Hz, 2H), 7.35 – 7.24 (m, 5H), 5.83 – 5.63 (m, 1H), 5.54 – 5.43 (m, 2H), 5.32 – 5.27 (m, 1H), 5.15 – 4.99 (m, 2H), 4.76 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.57 – 4.52 (m, 1H), 4.24 – 4.20 (m, 1H), 3.68 and 3.6 (s, 3H), 3.05 – 2.97 (m, 1H), 2.75 – 2.69 and 2.46 – 2.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): both diastereoisomers: δ = 170.5, 149.8, 146.5, 136.7, 134.3, 128.8, 128.3, 127.5, 123.8, 119.6, 117.9, 86.4, 70.0, 57.4, 52.2, 35.8; HRMS (FAB): calcd. for $C_{22}H_{25}N_2O_7S$ (MH^+): 461.1382; found: 461.1363.

Methyl 2-[(1-Phenoxyallyl)(4-toluenesulfonyl)amino]pent-4-enoate (29)

Methyl (*S*)-2-(4-toluenesulfonylamino)pent-4-enoate (**23**, 1.00 g, 3.53 mmol) was reacted with phenyl 1,2-propadienyl ether according to method B. Column chromatography (pentane/diethyl ether, 4:1 – 2:1) afforded **29** as a colorless oil; yield: 0.90 g (62%); IR (film): ν = 3469, 1744, 1596, 1492, 1346, 1226, 1160 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) both diastereoisomers: δ = 7.68 (m, 2H), 7.18 – 7.30 (m, 4H), 7.01 (t, *J* = 7.3 Hz, 1H), 6.94 – 6.85 (m, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.35 – 6.33 (m, 1H), 6.17 – 6.08 and 5.90 – 6.00 (m, 1H), 5.85 – 5.78 (m, 1H), 5.56 – 5.46 (m, 2H), 5.10 – 5.04 (m, 2H), 4.43 – 4.48 and 4.33 – 4.30 (m, 1H), 3.72 and 3.62 (s, 3H), 3.04 – 2.99 (m, 1H), 2.58 – 2.55 (m,1H), 2.43 and 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): one diastereoisomer: δ = 170.9, 156.8, 143.6, 137.6, 134.7, 133.7, 129.3, 129.4, 127.7, 122.0, 120.0, 117.4, 115.9, 86.1, 57.9, 52.2, 35.6, 21.4; HRMS (FAB): calcd. for $C_{22}H_{26}NO_5S$ (MH^+): 416.1532; found: 416.1531.

Methyl 2-[(1-Benzyloxyallyl)-(4-nitrobenzenesulfonyl)amino]hex-5-enoate (30)

Methyl (*S*)-2-(4-nitrobenzenesulfonylamino)hex-5-enoate (**24**, 0.1 g, 0.305 mmol) was reacted with benzyl 1,2-propadienyl ether according to method B. Column chromatography (petroleum ether/diethyl ether, 4:1 – 1:1) afforded **30** as a colorless oil; yield: 0.13 g (90%); IR (film): ν = 2951, 1745, 1531, 1351, 1165 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): both diastereoisomers: δ = 8.27 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.9 Hz, 2H), 7.37 – 7.24 (m, 5H), 5.75 – 5.64 (m, 2H), 5.53 – 5.44 (m, 2H), 5.32 – 5.29 (m, 1H), 5.02 – 4.94 (m, 2H), 4.73 (d, *J* = 11.9 Hz, 1H), 4.59 – 4.54 (m, 1H), 4.23 – 4.16 (m, 1H), 3.66 and 3.60 (s, 3H), 2.40 – 2.32 (m, 1H), 2.31 – 2.13 (m, 1H), 2.07 – 1.95 and 1.78 – 1.72 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): one diastereoisomer: δ = 171.2, 147.0, 136.7, 137.0, 133.4, 129.0, 128.7, 128.3, 127.6, 123.9, 119.6, 115.8, 86.7, 70.2, 56.9, 52.2, 31.1, 30.6; HRMS (FAB): calcd. for $C_{23}H_{27}N_2O_7S$ (MH^+): 475.1539; found: 475.1535.

General Method for the Ring-Closing Metathesis Reactions

The substrate was dissolved in degassed dichloromethane or toluene in a concentration of approximately 0.01 M. Argon was bubbled through the solution for 10 min, after which the ruthenium catalyst (see: Tables, 5 mol % in most cases) was added. The reaction mixture was stirred for the indicated time (see Tables) and then stirred openly exposed to air to destroy the active catalyst. The solvent was then removed under vacuum and the crude product purified by column chromatography as indicated.

Methyl 6-Methoxy-3,6-dihydro-2*H*-pyran-2-carboxylate (34)

Precursor **11** (1.0 g, 5.0 mmol) was reacted following the general method. Column chromatography (petroleum ether/diethyl ether, 4:1 – 1:1) afforded **34** as a colorless oil; yield: 0.63 g (3.7 mmol, 74%); IR (film): ν = 1050, 1111, 1179, 1217, 1735, 2828, 2954 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): both diastereoisomers: δ = 6.02 – 5.98 (m, 1H), 5.77 – 5.73 (m, 0.5H), 5.66 (dd, *J* = 10.2, 2.0 Hz, 0.5H), 5.00 (t, *J* = 1.8 Hz, 0.5H), 4.97 – 4.96 (m, 0.5H), 4.49 (dd, *J* = 9.3, 6.0 Hz, 0.5H), 4.97 – 4.96 (m, 0.5H), 3.77 and 3.74 (s, 3H), 3.46 and 3.44 (s, 3H), 2.45 – 2.44 (m, 0.5H), 2.34 – 2.28 (m, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$): both diastereoisomers: δ = 171.5, 171.2, 127.5, 127.4, 126.0, 125.2, 97.0, 95.8, 69.3, 65.6, 55.5, 55.3, 52.1, 51.9, 27.3, 25.8; HRMS (EI^+): calcd. for $C_{16}H_{21}O_3$ (M^+): 172.0736; found: 172.0737.

Methyl 6-Benzyloxy-2-methyl-3,6-dihydro-2*H*-pyran-2-carboxylate (35)

Precursor **12** (137 mg, 0.47 mmol) was reacted following the general method. Column chromatography (heptane/ethyl acetate, 9:1 – 3:1) afforded **35** as two separated diastereoisomers; yield: 95 mg (0.36 mmol, 77%). Diastereoisomer 1: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.37 - 7.22$ (m, 5H), 6.08 – 5.68 (m, 1H), 5.74 – 5.68 (m, 1H), 5.09 – 5.07 (m, 1H), 4.75 (AB, $J = 12.2$, 76.0 Hz, 2H), 3.55 (s, 3H), 2.76 (m, 1H), 2.08 (dq, $J = 2.2$, 2.5, 17.6 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 183.9$, 138.7, 128.9, 128.3, 128.3, 128.1, 124.7, 94.3, 73.0, 69.8, 52.8, 32.4, 27.5. Diastereoisomer 2: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.39 - 7.24$ (m, 5H), 6.00 – 5.94 (m, 1H), 5.76 – 5.70 (m, 1H), 5.43 – 5.41 (m, 1H), 4.76 (AB, $J = 11.8$, 73.8 Hz, 2H), 3.75 (s, 3H), 2.60 (m, 1H), 2.26 (m, 1H), 1.58 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 175.0$, 138.6, 128.9, 128.5, 128.1, 127.3, 126.2, 94.9, 76.2, 69.8, 53.0, 33.1, 25.7.

2-Benzyloxy-2*H*-chromene (36)

Precursor **13** (0.20 g, 0.76 mmol) was reacted according to the general procedure. Column chromatography (petroleum ether/ethyl acetate, 40:1) afforded **36** as a slightly brown oil; yield: 0.14 g (0.59 mmol, 78%); IR (film): $\nu = 3032$, 2919, 1202, 1031 cm^{-1}; ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.20$ (m, 2H), 7.05 (m, 3H), 6.97 (m, 2H), 6.85 (br. d, $J = 7.2$ Hz, 1H), 6.77 (m, 1H), 6.36 (d, $J = 9.2$ Hz, 1H), 5.55 (m, 2H), 4.74 (d, $J = 12.1$ Hz, 1H), 4.50 (d, $J = 12.1$ Hz, 1H); ^{13}C NMR (C_6D_6, 50 MHz): $\delta = 151.7$, 137.9, 129.0, 127.8, 127.5 (2 ×), 127.1 (2 ×), 126.7, 126.1, 121.1, 120.8, 119.8, 116.4, 94.2, 68.8; HRMS (FAB): calcd. for $C_{16}H_{15}O_2$ (MH^+): 239.1072; found: 239.1060.

2-Benzyloxy-4-methyl-2*H*-chromene (37)

Precursor **14** (0.44 g, 1.58 mmol) was reacted according to the general method. Column chromatography (petroleum ether/ethyl acetate, 20:1) afforded **37** as a brown oil; yield: 0.33 g (1.31 mmol, 84%); IR (film): $\nu = 3031$, 2915, 1215, 1037 cm^{-1}; ^{1}H NMR (C_6D_6, 400 MHz) $\delta = 7.23 - 7.20$ (m, 2H), 7.12 – 7.04 (m, 6H), 6.85 – 6.81 (m, 1H), 5.58 (d, $J = 3.8$ Hz, 1H), 5.42 (m, 1H), 4.78 (d, $J = 12.1$ Hz, 1H), 4.53 (d, $J = 12.1$ Hz, 1H), 1.76 (s, 3H); ^{13}C NMR (C_6D_6, 50 MHz): $\delta = 151.3$, 138.6, 132.1, 128.9, 127.9 (2 ×), 127.5 (2 ×), 127.1, 123.6, 121.0, 118.6, 117.3, 116.5, 94.4, 68.8, 17.3; HRMS (FAB): calcd. for $C_{17}H_{16}O_2$ (MH^+): 252.1150; found: 252.1158.

2-Benzyloxymethyl-6-methoxy-4-vinyl-3,6-dihydro-2*H*-pyran (38)

Precursor **18** (0.24 g, 0.92 mmol) was reacted as indicated in the general procedure. Column chromatography (petroleum ether/diethyl ether, 20:1) afforded the dihydropyran **38** as a colorless oil; yield: 85.0 mg (0.33 mmol, 36%); IR (film): $\nu =$ 3088, 3030, 2825, 1652 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): both diastereoisomers: $\delta = 7.39 - 7.26$ (m, 5H), 6.37 (dd, $J = 17.5$, 10.7 Hz, 1H), 5.70 and 5.63 (s, 1H), 5.29 and 5.24 (d, $J = 6.8$ Hz, 1H), 5.14 (s, 1H), 5.11 and 5.03 (s, 1H), 4.62 (m, 2H), 4.18 – 4.04 (m, 1H), 3.72 – 3.58 (m, 2H), 3.49 and 3.46 (s, 3H), 2.22 – 2.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): both diastereoisomers: $\delta = 138.2$, 137.5, 128.0, 127.0, 125.8, 124.3, 114.1, 114.0, 97.8, 96.1, 73.3, 72.4, 70.9, 65.7, 55.1, 25.9, 25.8; HRMS (FAB): calcd. for $C_{16}H_{21}O_3$ (MH^+): 261.1491; found: 261.1491.

2-Methoxy-1-(4-toluenesulfonyl)-2,5-dihydro-1*H*-pyrrole (39)

Precursor **25** (0.5 g, 1.78 mmol) was reacted according to the general procedure. Column chromatography (petroleum ether/diethyl ether, 9:1) gave **39** as a brown oil; yield: 0.43 g (1.69 mmol, 95%); IR (film): $\nu = 2934$, 1339 cm^{-1}; ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.76$ (d, $J = 8.3$ Hz, 2H), 6.78 (d, $J =$ 8.0 Hz, 2H), 5.97 (d, $J = 3.4$ Hz, 1H), 5.22 – 5.15 (m, 2H), 3.88 (dd, $J = 15.5$, 2.1 Hz, 1H), 3.68 (m, 1H), 3.12 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (C_6D_6, 100 MHz): $\delta = 143.7$, 130.0, 128.3, 128.0, 127.9, 127.6, 127.5, 96.7, 55.1, 53.1; HRMS (FAB): calcd. for $C_{12}H_{16}NO_3S$ (MH^+): 254.0851; found: 254.0851.

6-Benzyloxy-1-(4-toluenesulfonyl)-1,2,3,6-tetrahydropyridine (40)

Precursor **26** (0.2 g, 0.54 mmol) was reacted according to the general procedure. Column chromatography (pentane/diethyl ether, 4:1 – 2:1) afforded **40** as a colorless oil; yield: 0.13 g (0.37 mmol, 68%); IR (film): $\nu = 3533$, 3022, 2828, 1595, 1450, 1322, 1156 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.72$ (d, $J =$ 8.3 Hz, 2H), 7.39 – 7.32 (m, 5H), 7.27 (d, $J = 8.0$ Hz, 2H), 5.85 – 5.78 (m, 2H), 5.52 (d, $J = 3.7$ Hz, 1H), 4.80 (d, $J = 11.7$ Hz, 1H), 4.64 (d, $J = 12.0$ Hz, 1H), 3.83 – 3.80 (m, 1H), 3.45 – 3.39 (m, 1H), 2.43 (s, 3H), 1.78 – 1.76 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 143.3$, 138.3, 137.9, 129.5, 129.2, 128.3, 128.0, 127.6, 126.9, 124.7, 79.5, 69.6, 37.6, 23.0, 21.4; HRMS (FAB): calcd. for $C_{19}H_{22}NO_3S$ (MH^+): 344.1320; found: 344.1316.

2-Benzyloxy-5-benzyloxymethyl-1-(4-nitrobenzenesulfonyl)-2,5-dihydro-1*H*-pyrrole (41)

Precursor **27** (0.1 g, 0.2 mmol) was reacted following the general method, except that catalyst **31** was used in toluene at 60 °C. Column chromatography (pentane/diethyl ether, 2:1) yielded **41** as a colorless oil; yield: 40.0 mg (0.084 mmol, 42%); IR (film): $\nu = 2920$, 1715, 1529 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): both diastereoisomers: $\delta = 8.15$ (m, 2H), 7.97 (m, 2H), 7.45 – 7.07 (m, 10H), 6.11 (m, 1H), 5.76 (m, 1H), 4.61 – 4.30 (m, 6H), 3.68 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): both diastereoisomers: $\delta = 137.4$, 132.5, 128.6, 128.3, 128.3, 127.8, 127.7, 127.6, 127.5, 127.3, 123.9, 94.4, 73.4, 72.4, 68.0, 65.7, 65.3, 29.6; HRMS (FAB): calcd. for $C_{25}H_{24}N_2O_6SNa$ (MNa^+): 503.1253; found: 503.1250.

Methyl 6-Benzyloxy-1-(4-nitrobenzenesulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (42)

Precursor **28** (3.1 g, 6.7 mmol) was reacted according to the general method. Column chromatography (pentane/diethyl ether, 1:1 – 1:4) afforded **42** as a white solid; yield: 2.59 g (6.0 mmol, 89%); mp 106 – 108 °C; IR (film): $\nu = 3105$, 2952, 1743, 1529, 1349, 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): both

diastereoisomers: δ = 8.29 and 8.14 (d, *J* = 8.9 Hz, 2H), 7.99 (d, *J* = 8.9 Hz, 2H), 5.97 – 5.92 and 5.89 – 5.85 (m, 1H), 5.78 – 5.76 and 5.75 – 5.73 (m, 1H), 5.70 and 5.49 (d, *J* = 3.6 Hz, 1H), 4.76 – 4.67 (m, 2H), 4.54 and 4.23 (d, *J* = 11.4 Hz, 1H), 3.83 and 3.52 (s, 3H), 2.69 – 2.46 (m, 1H), 1.92 – 1.88 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): both diastereoisomers: δ = 170.7, 150.0, 149.8, 146.5, 146.0, 137.2, 136.8, 128.7, 128.2, 128.2, 128.1, 127.8, 127.6, 127.5, 127.4, 127.2, 125.2, 124.1, 123.7, 123.3, 82.3, 79.3, 69.5, 68.1, 55.5, 52.8, 50.8, 27.0, 23.5; HRMS (FAB): calcd. for $C_{20}H_{20}N_2O_7SNa$ (MNa^+): 455.0889; found: 455.0882.

Methyl 6-Phenoxy-1-(4-toluenesulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (43)

Precursor **29** (0.88 g, 2.27 mmol) was reacted as indicated in the general procedure. Column chromatography (pentane/diethyl ether, 4:1 – 2:1) afforded **43** as a colorless oil; yield: 0.53 g (1.37 mmol, 60%); IR (film): ν = 1749, 1600, 1495, 1357, 1228, 1164 cm^{-1}; ^{1}H NMR (C_6D_6, 500 MHz): δ = 7.66 (d, *J* = 8.3 Hz, 2H), 7.09 – 7.06 (m, 2H), 6.99 (d, *J* = 7.8 Hz, 2H), 6.85 – 6.83 (m, 2H), 6.68 (d, *J* = 8.3 Hz, 2H), 6.46 (s, 1H), 5.55 – 5.54 (m, 2H), 4.62 (d, *J* = 6.8 Hz, 1H), 3.10 (s, 3H), 2.43 – 2.40 (m, 1H), 1.96 – 1.90 (m, 1H), 1.86 (s, 3H); ^{13}C NMR (C_6D_6, 125 MHz): δ = 171.3, 170.6, 143.5, 138.6, 130.2, 129.4, 128.7, 128.4, 123.3, 122.6, 117.6, 78.9, 51.9, 51.6, 25.1, 21.5; HRMS (FAB): calcd. for $C_{20}H_{22}NO_5S$ (MH^+): 388.1219; found: 388.1236.

Methyl 7-Benzyloxy-1-(4-nitrobenzenesulfonyl)-2,3,4,7-tetrahydro-1*H*-azepine-2-carboxylate (44)

Precursor **30** (0.11 g, 0.23 mmol) was reacted according to the general method. Column chromatography (petroleum ether/diethyl ether, 4:1 – 1:1) gave **44** as a colorless oil; yield: 72 mg, (0.16 mmol, 70%); IR (film): ν = 2952, 1745, 1531, 1349, 1163 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): both diastereoisomers: δ = 8.3 and 8.08 (d, *J* = 8.8 Hz, 2H), 8.21 and 7.98 (d, *J* = 8.8 Hz, 2H), 7.35 – 7.24 (m, 4H), 7.09 – 7.07 (m, 1H), 5.86 – 5.82 (m, 0.5H), 5.74 – 5.66 (m, 1H), 5.61 (d, *J* = 5.9 Hz, 0.5H), 5.56 (s, 0.5H), 5.51 – 5.46 (m, 0.5H), 4.82 – 4.74 (m, 1H), 4.62 – 4.55 (m, 1H), 4.32 (d, *J* = 11.6 Hz, 0.5H), 4.21 (d, *J* = 11.6 Hz, 0.5H), 3.78 and 3.65 (s, 3H), 2.58 – 2.52 (m, 0.5H), 2.49 – 2.22 (dm, 3H), 1.82 – 1.75 (m, 0.5H); ^{13}C NMR ($CDCl_3$, 100 MHz): both diastereoisomers: δ = 171.5, 171.3, 146.6, 145.6, 137.3, 136.8, 134.2, 131.9, 129.0, 128.5, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 127.3, 126.9, 123.9, 123.7, 85.5, 84.3, 71.1, 69.5, 60.0, 57.6, 52.4, 29.3, 29.0, 26.9, 23.8.

Methyl 6-Allyl-3,6-dihydro-2*H*-pyran-2-carboxylate (46)

To a solution of **34** (50 mg, 0.291 mmol) and allyltrimethylsilane (92.4 μL, 0.58 mmol) in dry CH_2Cl_2 (3 mL) at 0 °C, was added $BF_3 \cdot OEt_2$ (75 μL, 0.58 mmol). After stirring for 30 min at 0 °C, the mixture was allowed to warm to room temperature in 1 h. Saturated aqueous $NaHCO_3$ (10 mL) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 ' 5 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated. Column chromatography (petroleum ether/diethyl ether, 4:1 – 1:1) afforded **46** as a colorless oil; yield: 34 mg (65%); IR (film): ν = 2954, 2928, 1740, 1216, 1179, 1104 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.89 – 5.79 (m, 2H), 5.70 (dq, *J* = 10.4, 2.0 Hz, 1H), 5.14 – 5.06 (m, 2H), 4.48 (t, *J* = 2.3 Hz, 1H), 4.50 – 4.43 (m, 1H), 3.75 (s, 3H), 2.40-2.28 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.2, 134.0, 128.9, 122.6, 117.3, 71.5, 68.9, 52.0, 39.2, 26.8; HRMS (EI^+): calcd. for $C_{20}H_{22}NO_5S$ (M^+): 182.0943; found: 182.0946.

Methyl 6-Allyl-2-methyl-3,6-dihydro-2*H*-pyran-2-carboxylate (47)

To a solution of **35** (one diastereoisomer, 65 mg, 0.248 mmol) and allyltrimethylsilane (78.8 μL, 0.5 mmol) in dry CH_2Cl_2 (5 mL) at 0 °C, was added $BF_3 \cdot OEt_2$ (63 μL, 0.5 mmol). After stirring for 3 h with the temperature going from 0 °C to room temperature, saturated aqueous $NaHCO_3$ (10 mL) and diethyl ether (10 mL) were added and the layers were separated. The organic layer was washed with brine (5 mL), dried over $MgSO_4$ and concentrated. Column chromatography (heptane/ethyl acetate, 4:1) afforded **47** as a colorless oil; yield: 23 mg (47%); ^{1}H NMR ($CDCl_3$, 300 MHz): 3:1 mixture of diastereoisomers: δ = 5.92 – 5.56 (m, 3H), 5.19 – 5.03 (m, 2H), 4.45 and 4.23 (m, 1H), 3.75 and 3.71 (s, 3H), 2.68-2.25 and 2.12-2.02 (m, 4H), 1.48 and 1.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 175.4, 134.8, 127.6, 123.0, 118.0, 70.3, 65.8, 53.0, 40.1, 32.8, 21.5.

Methyl 6-Cyano-2-methyl-3,6-dihydro-2*H*-pyran-2-carboxylate (48)

To a solution of **35** (one diastereoisomer, 57 mg, 0.218 mmol) and Me_3SiCN (58 μL, 0.44 mmol) in dry CH_2Cl_2 (5 mL) at 0 °C, was added $BF_3 \cdot OEt_2$ (55 μL, 0.44 mmol). After stirring for 2 h with the temperature going from 0 °C to room temperature, saturated aqueous $NaHCO_3$ (10 mL) and diethyl ether (10 mL) were added and the layers separated. The organic layer was washed with brine (5 mL), dried over $MgSO_4$ and concentrated. Column chromatography (heptane/ethyl acetate, 4:1) afforded **48** as a slightly yellow oil; 21 mg (49%); ^{1}H NMR ($CDCl_3$, 300 MHz): 1:1.25 mixture of diastereoisomers: δ = 6.13 – 5.98 (m, 1H), 5.75 – 5.66 (m, 1H), 5.46 – 5.42 and 5.19 – 5.15 (m, 1H), 3.79 and 3.73 (s, 3H), 2.81 – 2.72 (ddt, *J* = 17.6, 11.3, 1.4, 1.1 Hz, 0.57H), 2.70 – 2.60 (dddd, *J* = 17.6, 5.8, 2.7, 1.4, 1.1 Hz, 0.43H), 2.33 – 2.07 (dddd, *J* = 48.0, 17.6, 6.0, 2.8 Hz, 1H), 1.52 and 1.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): both diastereoisomers: δ = 173.1, 127.7, 127.2, 121.1, 120.5, 117.4, 117.1, 72.5, 71.9, 61.8, 61.3, 53.0, 52.6, 32.6, 32.1, 25.9.

2*H*-Chromene-2-carbonitrile (49)

To a solution of **36** (50.5 mg, 0.21 mmol) and Me_3SiCN (58 μL, 0.44 mmol) in dry CH_2Cl_2 (5 mL) at 0 °C, was added $BF_3 \cdot OEt_2$ (55 μL, 0.44 mmol). The solution was allowed to warm to room temperature and saturated aqueous $NaHCO_3$ (10 mL) was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (5 mL). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$ and concentrated. Column chromatography (petroleum ether/ethyl acetate, 40:1) afforded **49** as a colorless oil; yield: 26 mg

(75%); IR (film): $\nu = 2930, 2360, 1240\ cm^{-1}$; ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 7.23$ (dt, $J = 7.8, 1.3$ Hz, 1H), 7.10 (dd, $J = 7.5, 1.6$ Hz, 1H), 7.02 (dt, $J = 7.4, 0.5$ Hz, 1H), 6.94 (br d, $J = 8.1$ Hz, 1H), 6.69 (d, $J = 9.5$ Hz, 1H), 5.77 (dd, $J = 9.5, 4.7$ Hz, 1H), 5.67 (dd, $J = 4.7, 0.6$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta =$ 150.8, 130.5, 127.9, 127.4, 123.2, 120.5, 116.7, 116.1, 116.0, 62.4; HRMS (FAB): calcd. for $C_{10}H_7NO$ (MH^+): 157.0528; found: 157.0538.

Methyl (*S*)-1-(4-Nitrobenzenesulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (51)

To a solution of **42** (50 mg, 0.116 mmol) and triethylsilane (55.5 μL, 0.347 mmol) in CH_2Cl_2 (1 mL) at −78 °C, was added $BF_3 \cdot OEt_2$ (44 μL, 0.347 mmol). After 1 h at this temperature, the solution was allowed to warm to room temperature and quenched by adding saturated aqueous $NaHCO_3$ (5 mL). Diethyl ether (10 mL) was added and the layers were separated. The organic layer was washed with H_2O (5 mL) and brine (5 mL), dried over $MgSO_4$ and concentrated. Recrystallization of the crude product afforded **51** as a white solid; yield: 33 mg (88%); mp 119 – 120 °C; $[\alpha]_D$: + 21 (*c* 1, CH_2Cl_2); IR (film): $\nu = 1711, 1531, 1352, 1168\ cm^{-1}$; ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 8.34$ (d, $J = 8.8$ Hz, 2H), 7.97 (d, $J =$ 8.8 Hz, 2H), 5.77 – 5.74 (m, 1H), 5.67 – 5.64 (m, 1H), 4.91 – 4.89 (m, 1H), 4.14 (d, $J = 16.7$ Hz, 1H), 3.80 (d, $J = 16.7$ Hz, 1H), 3.52 (s, 3H), 2.62 – 2.61 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 170.1, 149.0, 144.7, 128.4, 124.0, 122.8, 122.5, 52.9, 52.3, 42.2,$ 27.7; HRMS (FAB): calcd. for $C_{13}H_{15}N_2O_6S$ (MH^+): 327.0651; found: 327.0650.

Methyl (*S,S*)-1-(4-Nitrobenzenesulfonyl)-6-prop-2-ynyl-1,2,3,6-tetrahydropyridine-2-carboxylate (52)

To a solution of **42** (40 mg, 0.095 mmol) and allenyltributylstannane (94 mg, 0.286 mmol) in CH_2Cl_2 (1 mL) at −78 °C, was added $BF_3 \cdot OEt_2$ (36 μL, 0.286 mmol). After 3 h at this temperature, the solution was allowed to warm to room temperature and quenched by adding saturated aqueous $NaHCO_3$ (5 mL). Diethyl ether (10 mL) was added and the layers were separated. The organic layer was washed with H_2O (5 mL) and with brine (5 mL), dried over $MgSO_4$ and concentrated. Column chromatography (petroleum ether/diethyl ether, 4:1 – 1:1) afforded **52** as a white solid; yield: 26 mg (75%); mp 112 – 114 °C; $[\alpha]_D$: + 83.5 (*c* 1.05, CH_2Cl_2); IR (film): $\nu = 3290, 1742, 1530, 1351, 1167\ cm^{-1}$; ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 8.36$ (d, $J = 8.8$ Hz, 2H), 8.03 (d, $J = 8.8$ Hz, 2H), 6.01 – 5.97 (m, 1H), 5.83 – 5.78 (m, 1H), 4.84 (d, $J = 6.2$ Hz, 1H), 4.38 (dd, $J = 6.8, 3.4$ Hz, 1H), 3.72 (s, 3H), 2.83 – 2.81 (m, 1H), 2.79 – 2.63 (m, 1H), 2.58 – 2.51 (m, 1H), 2.10 – 2.03 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 170.6, 149.0, 145.7, 128.2,$ 125.0, 124.4, 123.1, 71.2, 60.3, 52.7, 52.4, 52.0, 25.9, 24.6; HRMS (FAB): calcd. for $C_{16}H_{17}N_2O_6S$ (MH^+): 365.0807; found: 365.0809.

(*S*)-1,2,3,6-Tetrahydropyridine-2-carboxylic Acid (Baikiain, 53)

To a solution of **51** (150 mg, 0.47 mmol) in DMF (10 mL) was added K_2CO_3 (196 mg, 1.42 mmol) and thiophenol (58.2 μL, 0.57 mmol), followed by stirring at room temperature for 24 h. The solvent was removed and the crude mixture was lyophilized. The residue was again dissolved in methanol (2 mL) and H_2O (2 mL) was added, followed by lithium hydroxide (1.1 equiv.). The mixture was stirred for 24 h. Diethyl ether (5 mL) was added and a white solid precipitated, which was filtered off. The aqueous layer was then lyophilized to yield **53** as an amorphous solid; yield: 32.5 mg (61%); $[\alpha]_D$: −182.6 (*c* 0.3, H_2O); IR (KBr): $\nu = 2924, 1712, 1404, 1189\ cm^{-1}$; ^1H NMR (CD_3OD, 400 MHz): $\delta = 6.01$ (br s, 1H), 5.80 – 5.78 (m, 1H), 4.07 – 4.03 (m, 1H), 3.74 (br s, 2H), 3.31 (br s, 3H), 2.76 – 2.72 (m, 1H), 2.53 – 2.46 (m, 1H); ^{13}C NMR (D_2O, 100 MHz): $\delta =$ 173.6, 128.0, 122.6, 58.0, 44.7, 28.4. Data were identical to literature values.[16]

(*S,S*)-6-Prop-2-ynyl-1,2,3,6-tetrahydropyridine-2-carboxylic Acid (54)

To a solution of **52** (1.47 g, 4.05 mmol) in DMF (50 mL) was added K_2CO_3 (1.68 g, 12.15 mmol) and thiophenol (500 μL, 4.86 mmol), followed by stirring at room temperature for 24 h. The solvent was removed by lyophilization. The crude residue was again dissolved in methanol (10 mL) and H_2O (10 mL) was added, followed by lithium hydroxide (2.0 equiv.). The resulting mixture was stirred for 24 h. Diethyl ether (10 mL) was added and a white solid precipitated, which was filtered off. The aqueous layer was then lyophilized to afford **54** as an amorphous solid; yield: 344 mg (52%); $[\alpha]_D$: −106.8 (*c* 0.5, MeOH); IR (KBr): $\nu = 3184, 3012, 2659, 2526, 1601, 1409\ cm^{-1}$; ^1H NMR (CD_3OD, 400 MHz): $\delta = 6.08 – 6.01$ (m, 1H), 5.81 (d, $J = 9.3$ Hz, 1H), 4.00 – 3.98 (m, 1H), 3.72 – 3.66 (m, 1H), 2.74 – 2.56 (dm, 4H), 2.43 – 2.34 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz): $\delta = 173.8, 128.3, 124.9, 78.6, 73.9, 57.8, 54.3, 27.6,$ 23.4; HRMS (FAB): calcd. for $C_9H_{12}NO_2$ (MH^+): 166.0868; found: 166.0866.

Methyl (*S,S*)-6-Allyl-1-(4-nitrobenzenesulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (55)

To a solution of **42** (1.00 g, 2.31 mmol) and allyltributylstannane (2.15 mL, 6.93 mmol) in CH_2Cl_2 (20 mL) at −78 °C was added $BF_3 \times OEt_2$ (0.87 mL, 6.94 mmol). This mixture was stirred at −78 °C for 4 h and allowed to warm to room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ (20 mL) and diethyl ether (20 mL) was added. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 20 mL). The organic layers were washed with brine (20 mL), dried over $MgSO_4$ and concentrated. Column chromatography (pentane/diethyl ether, 2:1) afforded **55** as a white solid; yield: 0.88 g (100%); mp 113 – 114 °C; $[\alpha]_D$: + 59.1 (*c* 1, CH_2Cl_2); IR (film): $\nu = 3105, 2953,$ 1741, 1531, 1216, 1095, 923 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 8.4$ (d, $J = 8.8$ Hz, 2H), 8.1 (d, $J = 8.8$ Hz, 2H), 5.84 – 5.66 (m, 3H), 5.10 – 5.06 (m, 2H), 4.83 (d, $J = 6.3$ Hz, 1H), 4.30 – 4.26 (m, 1H), 3.72 (s, 3H), 2.64 (dd, $J = 17.8, 5.8$ Hz, 1H), 2.55 – 2.48 (m, 1H), 2.22 (dt, $J = 13.6, 9.0$ Hz, 1H), 2.08 – 2.01 (m, 1H);

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.7, 149.8, 146.0, 133.7, 128.1, 125.4, 124.0, 122.6, 118.0, 53.4, 52.3, 51.6, 40.2, 24.0; HRMS (FAB): calcd. for $C_{13}H_{20}O_2N$ (MH^+): 367.0964; found: 367.0975.

Methyl (*S,S*)-1,6-Diallyl-1,2,3,6-tetrahydropyridine-2-carboxylate (56)

To a solution of **55** (487 mg, 1.32 mmol) in acetonitrile (20 mL) was added K_2CO_3 (551 mg, 3.98 mmol) and thiophenol (164 μL, 1.59 mmol). This suspension was stirred for 24 h, during which more thiophenol was added (2 × 75 μL). After evaporation of the acetonitrile, the product was purified by column chromatography (pentane/diethyl ether, 1:2) to yield the free amine *methyl 6-allyl-1,2,3,6-tetrahydropyridine-2-carboxylate* (yield: 178 mg, 74%) as a colorless oil, which was dissolved again in dry acetonitrile (10 mL), followed by the addition of K_2CO_3 (271 mg, 1.96 mmol) and allyl bromide (178 mg, 1.47 mmol). The solution was stirred at 60 °C for 24 h during which additional allyl bromide (89 mg, 0.74 mmol) was added. The solvent was removed under vacuum and the crude product was purified by column chromatography (pentane/diethyl ether, 20:1), to afford **56** as a yellow oil; yield: 147 mg (50%); $[\alpha]_{436}$: +60.2 (*c* 1.05 CH_2Cl_2); IR (film): ν = 2923, 1735, 1459 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.75 (m, 4H), 5.11 (m, 4H), 3.70 (s, 3H), 3.53 (d, *J*=5.1 Hz, 1H), 3.42 (d, *J*=1.3 Hz, 2H), 3.24 (m, 1H), 2.41 (m, 2H), 2.20 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 135.9, 131.1, 128.8, 122.2, 118.9, 116.2, 58.9, 57.8, 55.7, 51.9, 37.8, 30.1; HRMS (FAB): calcd. for $C_{13}H_{20}O_2N$ (MH^+): 222.1494; found: 222.1491.

Methyl (*S,S*)-3,6,9,9a-Tetrahydro-4*H*-quinolizine-4-carboxylate (57)

A solution of **56** (147 mg, 0.665 mmol) in dry toluene (30 mL) was degassed using argon. Ruthenium catalyst **32** (5.7 mg, 1 mol %) was added and the solution was heated at 80 °C for 6 h. Air was bubbled through the solution to destroy the active catalyst and the solvent was removed under vacuum. Column chromatography (pentane/diethyl ether, 2:1) gave **57** as a white solid; yield: 99 mg (77%); $[\alpha]_D$: −74 (*c* 0.98, CH_2Cl_2); IR (film): ν = 3025, 1742 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.58 (m, 4H) 3.76 (s, 3H), 3.37 (d, *J* = 15.1 Hz, 1H), 3.18 (dd, *J* = 6.8 Hz, 3.9 Hz, 1H), 2.96 (m, 1H), 2.82 (m, 1H), 2.54 (dd, *J* = 2.4 Hz, 1.7 Hz, 1H), 2.23 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 173.4, 129.0, 125.5, 124.6, 122.4, 64.2, 56.6, 52.0, 51.9, 32.7, 30.0; HRMS (FAB): calcd. for $C_{11}H_{16}O_2N$ (MH^+): 194.1181; found: 194.1181.

(*S,S*)-3,6,9,9′-Tetrahydro-4*H*-quinolizine-4-carboxylic Acid (58)

A solution of ester **57** (50 mg, 0.259 mmol) in methanol/H_2O (3:1, 4 mL) was treated with lithium hydroxide (11.9 mg, 0.28 mmol) and stirred for 24 h. The crude solution was purified using a strong basic Amberlite column (IRA-416): washing with 5% NH_3/H_2O and collecting with acetic acid (1 M) as the eluent. After lyophilizing off the aqueous acetic acid, the free amino acid **58** was obtained as a white solid; yield: 23 mg (50%); IR (film): ν = 3030, 1738, 1169 cm^{-1}; ^{1}H NMR (D_2O, 400 MHz): δ = 6.04 (m, 1H), 5.99 – 5.68 (m, 2H), 4.21 (m, 2H), 4.08 (m, 1H), 3.73 (m, 1H), 2.80-2.58 (m, 3H), 2.41 (m, 1H); ^{13}C NMR (D_2O, 100 MHz): δ = 137.7, 128.4, 126.8, 126.6, 122.6, 66.5, 60.8, 53.5, 32.0, 30.3; HRMS (FAB): calcd. for $C_{10}H_{14}O_2N$ (MH^+): 180.1025; found: 180.1021.

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References and Notes

[1] For review articles, see: a) A. Fürstner, *Angew. Chem. Int. Ed*. **2000**, *39*, 3012; b) T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, *34*, 18; c) R. H. Grubbs, S. Chang, *Tetrahedron* **1998**, *54*, 4413. d) A. Fürstner, *Top. Organomet. Chem*. **1998**, *1*, 37.

[2] For several investigations into new RCM catalysts, see: a) J. Huang, E. D. Stevens, S. P. Nolan, J. L. Petersen, *J. Am. Chem. Soc.* **1999**, *121*, 2674; b) M. Scholl, T. M. Trnka, J. P. Morgan, R. H. Grubbs, *Tetrahedron Lett*. **1999**, *40*, 2247; c) M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett*. **1999**, *1*, 953; d) S. S. Zhu, D. R. Cefalo, D. S. La, J. Y. Jamieson, W. M. Davis, A. H. Hoveyda, R. R. Schrock, *J. Am. Chem. Soc*. **1999**, *121*, 8251; e) G. S. Wheaterhead, J. G. Ford, E. J. Alexanian, R. R. Schrock, A. H. Hoveyda, *J. Am. Chem. Soc*. **2000**, *122*, 1828; f) A. Fürstner, L. Ackermann, B. Gabor, R. Goddard, C. W. Lehmann, R. Mynott, F. Stelzer, O. R. Thiel, *Chem. Eur. J.* **2001**, *7*, 3236.

[3] a) F. P. J. T. Rutjes, T. M. Kooistra, H. Hiemstra, H. E. Schoemaker, *Synlett* **1998**, 192; b) M. T. Crimmins, B. W. King, *J. Am. Chem. Soc*. **1998**, *120*, 9084; c) H. Ovaa, M. A. Leeuwenburgh, H. S. Overkleeft, G. A. van der Marel, J. H. van Boom, *Tetrahedron Lett*. **1998**, *39*, 3025; d) P. A. V. van Hooft, M. A. Leeuwenburgh, H. S. Overkleeft, G. A. van der Marel, C. A. A. van Boeckel, J. H. van Boom, *Tetrahedron Lett*. **1998**, *39*, 6061; e) M. Scholl, R. H. Grubbs, *Tetrahedron Lett*. **1999**, *40*, 1425; f) M. J. Bassindale, P. Hamley, A. Leitner, J. P. A. Harrity, *Tetrahedron Lett*. **1999**, *40*, 3247; g) K. C. M. F. Tjen, S. S. Kinderman, H. E. Schoemaker, H. Hiemstra, F. P. J. T. Rutjes, *Chem. Commun*. **2000**, 699; h) R. Doodeman, F. P. J. T. Rutjes, H. Hiemstra, *Tetrahedron Lett*. **2000**, *41*, 5979; i) J. Mulzer, M. Hanbauer, *Tetrahedron Lett*. **2000**, *41*, 33. For a silicon tethered example, see: T. R. Hoye, M. A. Promo, *Tetrahedron Lett*. **1999**, *40*, 1429 and references cited therein.

[4] Some recent selected examples on dihydropyrans: a) B. Schmidt, H. Wildemann, *Eur. J. Org. Chem*. **2000**, 3145; b) A. K. Ghosh, H. Lei, *J. Org. Chem*. **2000**, *65*, 4779; c) D. P. Steinhuebel, J. J. Fleming, J. Du Bois, *Org. Lett*. **2002**, *4*, 293; d) T. B. Durham, M. J. Miller, *Org. Lett*. **2002**, *4*, 135. For examples on tetrahydropyridines and

azepines, see: e) J. Åhman, P. Somfai, *Tetrahedron Lett*. **1995**, *36*, 303; f) S. N. Osipov, N. M. Kobelíkova, G. T. Shchetnikov, A. F. Kolomiets, C. Bruneau, P. H. Dixneuf, *Synlett* **2001**, 621; g) W. H. Pearson, A. Aponick, *Org. Lett*. **2001**, *3*, 1327. For examples on chromenes, see: h) B. M. Trost, F. D. J. Toste, *J. Am. Chem. Soc*. **1998**, *120*, 9074. i) K. S. Atwal, G. J. Grover, F. N. Ferrara, S. Z. Ahmd, P. G. Sleph, S. Dzwonczyk, D. E. Normandin, *J. Med. Chem.* **1995**, *38*, 1966.

[5] For examples, see: a) S. A. Angle, J. G. Breitenbucher, *Tetrahedron Lett*. **1993**, *34*, 3985; b) T. Hamada, T. Zenkoh, H. Sato, O. Yonemitsu, *Tetrahedron Lett*. **1991**, *32*, 1649; c) T. Bauer, C. Chapuis, A. Jezewski, J. Kozak, J. Jurczak, *Tetrahedron: Asymmetry* **1996**, *7*, 1391; d) T. Bauer, A. Jezewski, J. Jurczak, *Tetrahedron: Asymmetry* **1996**, *7*, 1405; e) M. Terada, K. Mikami, T. Nakai, *Tetrahedron Lett*. **1991**, *32*, 935. The dihydropyran as a useful building block in the total synthesis of fostriecin (CI-920): f) D. L. Boger, S. Ichikawa, W. Zhong, *J. Am. Chem. Soc*. **2001**, *123*, 4161.

[6] a) G. C. Fu, S. T. Nguyen, R. H. Grubbs, *J. Am. Chem. Soc*. **1993**, *115*, 9856; b) A. G. M. Barrett, S. P. D. Baugh, D. C. Braddock, K. Flack, V. C. Gibson, M. R. Giles, E. L. Marshall, P. A. Procopiou, A. J. P. White, D. J. Williams, *J. Org. Chem*. **1998**, *63*, 7893.

[7] For an entry into applications of the strongly related *N*-acyliminium ion intermediates, see: W. N. Speckamp, M. J. Moolenaar, *Tetrahedron* **2000**, *56*, 3817.

[8] A detailed account on mechanistic aspects of Pd-mediated coupling reactions of alkoxyallenes with amines and alcohols will be published in the near future.

[9] For a discussion on metathesis cyclizations of vinylglycine-derived substrates, see: J.-M. Campagne, L. Ghosez, *Tetrahedron Lett*. **1998**, *39*, 6175.

[10] a) L. B. Wolf, T. Sonke, K. C. M. F. Tjen, B. Kaptein, Q. B. Broxterman, H. E. Schoemaker, F. P. J. T. Rutjes, *Adv. Synth. Catal.* **2001**, *343*, 662; b) T. Sonke, B. Kaptein, W. H. J. Boesten, Q. B. Broxterman, J. Kamphuis, F. Formaggio, C. Toniolo, F. P. J. T. Rutjes, H. E. Schoemaker, in *Stereoselective Biocatalysis*, (Ed.: R. N. Patel), Marcel Dekker, New York, **2000**, pp. 23 – 59.

[11] For examples of formation of sulfonyl-protected *N*,*O*-acetals, see e. g.: a) T. Shono, Y. Matsumura, S. Katoh, K. Takeuchi, K. Sasaki, T. Kamada, R. Shimizu, *J. Am. Chem. Soc*. **1990**, *112*, 2368; b) R. Consonni, P. D. Croce, R. Ferraccioli, *J. Heterocycl. Chem*. **1990**, *27*, 427.

[12] For recent examples of Pd-catalyzed allylic *O*,*O*-acetal formation and subsequent functionalization in natural product synthesis, see e. g.: a) C. Held, R. Fröhlich, P. Metz, *Angew. Chem. Int. Ed*. **2001**, *40*, 1058; b) G. T. Nadolski, B. S. Davidson, *Tetrahedron Lett*. **2001**, *42*, 797.

[13] For alternative metathesis approaches towards substituted chromenes, see e. g.: a) S. Chang, R. H. Grubbs, *J. Org. Chem*. **1998**, *63*, 864; b) J. P. A. Harrity, D. S. La, D. R. Cefalo, M. S. Visser, A. H. Hoveyda, *J. Am. Chem. Soc*. **1998**, *120*, 2343; c) P. Wipf, W. S. Weiner, *J. Org. Chem*. **1999**, *64*, 5321.

[14] L. Brandsma, H. D. Verkruijsse, *Synthesis of acetylenes, allenes and cumulenes, a laboratory manual*, in *Studies in Organic Chemistry*, Vol. 8, Elsevier, Amsterdam, **1981**.

[15] S. D. Bull, S. G. Davies, S. W. Epstein, M. A. Leech, J. V. A. Ouzman, *J. Chem. Soc. Perkin Trans. 1* **1998**, 2321.

[16] Isolation: F. E. King, T. J. King and A. J. Warwick, *J. Chem. Soc.* **1950**, 3590. For other recent enantiopure syntheses of baikiain, see: a) X. Ginesta, M. A. Pericàs, A. Riera, *Tetrahedron Lett*. **2002**, *43*, 779; b) G. Guillena, C. Nájera, *J. Org. Chem*. **2000**, *65*, 7310; c) A. Mazon, C. Nájera, *Tetrahedron: Asymmetry* **1997**, *11*, 1855.

[17] Such a high diastereoselectivity has been observed in comparable systems without the unsaturation: C. Yang, Y. Xu, L. Liao, W. Zhou, *Tetrahedron Lett*. **1998**, *39*, 9228 and references cited therein.

[18] For a highlight on methyl propadienyl ether: R. Pulz, *Synlett* **2000**, 1697.

[19] For a review on alkoxy-1,2-propadienes, see: R. Zimmer, *Synthesis* **1993**, 167.