Ring-Closing Metathesis on Solid Support: Elaboration of a Cyclization/Cleavage Strategy Towards Unsaturated α-Ester-Substituted N-Heterocycles

J. J. N. Veerman[a], Jan H. van Maarseveen[b], Geb M. Visser[b], Chris G. Kruse[b], Hans E. Schoemaker[a], Henk Hiemstra[a], and Floris P. J. T. Rutjes*[a]

Lab. of Organic Chemistry, Institute of Molecular Chemistry, University of Amsterdam[a]
Nieuwe Achtergracht 129, NL-1018 WS Amsterdam, The Netherlands
Fax: (internat.) +31 (0)20 525 5670
E-mail: florisr@org.chem.uva.nl

Solvay Pharmaceuticals[b],
P. O. Box 900, NL-1380 DA Weesp, The Netherlands

Received June 18, 1998

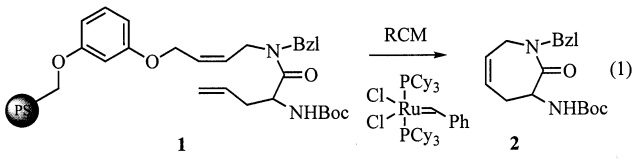
Keywords: Ring-closing metathesis / Cyclization cleavage / N-Heterocycles / Amino acids / Solid phase

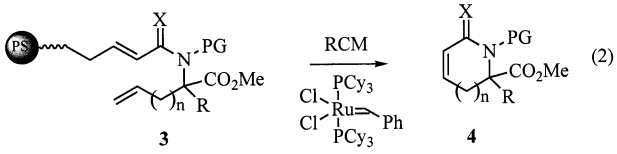
A Ru-mediated strategy for the cleavage of organic substrate molecules from a solid support via ring-closing metathesis is described. Application of this protocol to solid phase-bound olefinic amino acid derivatives provides various highly functionalized unsaturated N-heterocycles of different ring-sizes in moderate to excellent yields. This strategy features the addition of a stoichiometric amount of styrene to the metathesis mixture, which is shown to increase the yield of the reaction.

The synthesis of organic compound libraries has become of major importance for the pharmaceutical industry.[1] As a result, significant efforts are currently devoted to developing novel methodology for solid-phase organic chemistry. Several review articles provide an accurate overview of reaction types that have been carried out on solid support[2] and of their applicability in the synthesis of compound libraries of various structural classes.[3]

A detailed scan of the possibilities revealed two items that to our opinion deserve more attention. One of these subjects concerns 'traceless' linker[4] strategies: cleavage of the substrate molecules from conventional protective group-derived linkers often leads to the formation of a polar functionality such as a carboxylic acid, a hydroxyl group, an amide group, or an amine function. Secondly, most of the currently used cleavage reactions release all of the immobilized substrate molecules, including unwanted side products. Application of a cyclization/cleavage strategy[5] partially solves these problems, since the anchoring group will be encapsulated as a structural element in the ring system. Moreover, cleavage will be restricted to substrate molecules that contain the structural requirements for ring closure. However, most of the existing cyclization/cleavage methods lead to lactams or lactones.[5] Inspired by the numerous examples of Ru-catalyzed ring-closing metathesis (RCM)[6][7][8] in the synthesis of heterocyclic structures, we envisioned that this process would be an ideal way of realizing a novel cyclization/cleavage protocol. There are important advantages to this approach: first, the only trace of this cleavage method is a non-polar double bond which is part of the anticipated ring system, and second, the desired cyclic olefins will be solely released from the resin because only diolefins are suitable substrates for RCM.

In a preliminary communication we presented the first example of this novel cyclization/cleavage strategy[9] consisting of the solid phase preparation of ε-caprolactam derivative **2** from diolefin **1** (Eq. 1).





X = CH_2, O; R = H, Me; n = 1–3
PG = Bz, Bzl, SO_2Ar, PMB

In this article, we wish to present additional results concerning this strategy in full detail. The general protocol is outlined in Eq. 2 and is based on the immobilized amino acid-derived diolefins **3**, which afford the corresponding N-heterocycles **4** after RCM via cyclative cleavage. We will compare the scope and limitations of this useful strategy with the cyclization of similar α-amino acid derivatives, that we previously examined in solution phase approaches.[10] In the course of our work, other reports of Ru-mediated cyclization/cleavage RCM strategies by the groups of Nicolaou,[11] Piscopio,[12] and Blechert[13] appeared in the literature, but they did not provide any mechanistic information.

Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/eurjoc or from the author.

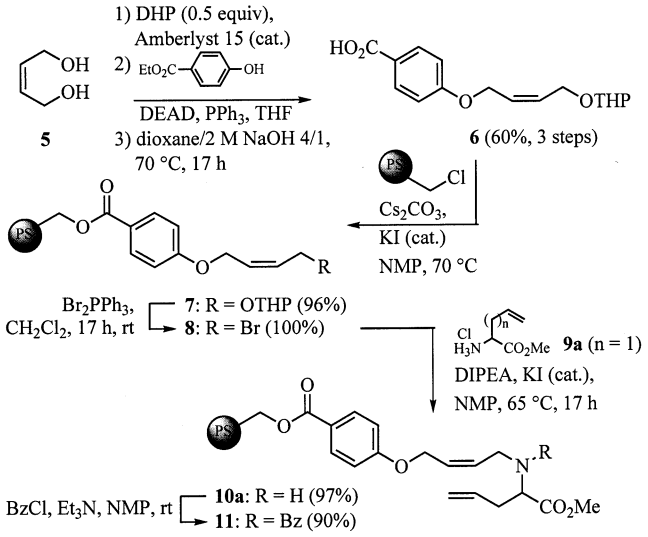
  1434–193X/98/1111–2583 $ 17.50+.50/0

We have studied the influence of olefin additives on the yield of the cyclization/cleavage reaction and performed cleavage experiments to gain insight in the RCM mechanism. Furthermore, the influence of the ring size (n = 1−3 to give six- to eight-membered rings, respectively), the nature of the nitrogen atom (X = H_2, O and PG = Bn, Bz or X = H_2 and PG = SO_2Ph-p-NO_2), the electron density at the central double bond (X = H_2, O) and steric factors (R = H, CH_3) will be discussed.

Results and Discussion

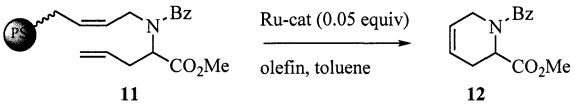
The synthesis of the system that was used for the optimization of the cyclization/cleavage conditions is shown in Scheme 1. The linker system features the olefin function which is required in the cyclization step and an ester function which should enable cleavage of the substrate molecules via transesterification[14] at any stage of the synthesis for analytic purposes. Commercially available *cis*-1,4-dihydroxy-2-butene (**5**) was partially protected as a THP ether, coupled under Mitsunobu conditions[15] with ethyl 4-hydroxybenzoate and saponified to give the benzoic acid derivative **6** in 60% overall yield. Cesium carbonate-mediated coupling[16] of **6** with Merrifield resin provided the solid phase-bound system **7** in 96% yield. The yields of the solid phase reactions were determined by weighing of the resin after work-up, while characterization of the resin-bound products was based on infrared microscopy.[17]

Scheme 1. Construction of the solid phase-bound amino ester **11**



Reaction of the THP ether **7** with triphenylphosphanyl dibromide[18] gave the allylic bromide **8** in 100% yield,[19] which upon reaction with allylglycine derivative **9a**[20] provided the solid phase-bound diolefin **10a** in 97% yield. The amine **10a** was then further functionalized with a benzoyl protecting group to afford the metathesis precursor **11** in excellent yield. This resin-bound allylglycine derivative was chosen for optimization of the cyclization conditions (Table 1). The reactions were carried out in toluene, which enabled a wide range of reaction temperatures. An optimal isolated yield of **12** (56%) was obtained upon treatment of **11** with 5 mol% of the Ru catalyst at 50°C for 18 h (entry 2). Remarkably, after 3 h an isolated yield of 50% was reached (entry 1), showing that the reaction did not proceed much further after a few hours reaction time. Because we previously found[9] that the presence of an olefin additive led to an increased yield, the effect of the addition of different olefins on the yield of the cleavage reaction was studied. Addition of propene gave a disappointing yield of 50% (entry 3), while with the more hindered olefin 3-methyl-1-pentene an improved yield of 66% was obtained (entry 4). The use of styrene, however, resulted in an isolated yield of 86% of the desired unsaturated cyclic amino ester **12** after 18 h at 50°C (entry 7). Interestingly, the isolated yield after 3 h (entry 6) was similar to the reaction without styrene, but was significantly increased in the remaining time.

Table 1. Optimal cyclization/cleavage conditions and influence of the olefin



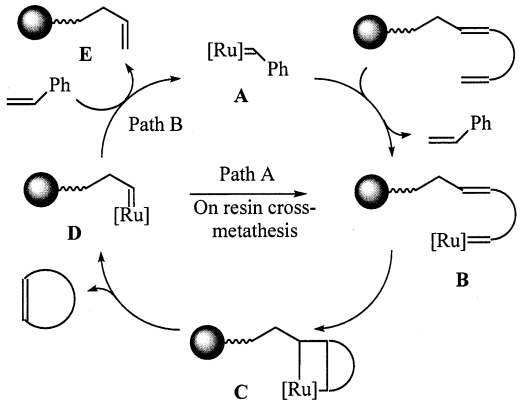
entry	olefin (equiv.)	T (°C)	reaction time (h)	yield (%)
1	styrene (0)	50	3	50
2	styrene (0)	50	18	56
3	propene (3)	50	18	50
4	3-methyl-1-pentene (1)	50	18	66
5	styrene (1)	25	18	50
6	styrene (1)	50	3	50
7	styrene (1)	50	18	86
8	styrene (1)	80	18	80

This result clearly substantiates the use of styrene as a suitable olefin additive.[21] An additional advantage of styrene is its low dimerization rate under the metathesis conditions[22] in contrast with non-conjugated linear terminal alkenes.[9] Therefore, styrene could also be used as an internal standard to monitor the conversion of the reaction by GC analysis.

The role of styrene in the catalytic cycle might be understood as follows (Scheme 2):[23] cross-metathesis of the resin-bound diolefin with the Ru catalyst **A** initially leads to Ru carbene intermediate **B**, which upon ring closure via intermediate **C** and subsequent release of the cyclic olefin gives the Ru-alkylidene species **D**. At this point, the Ru catalyst is immobilized on the resin and can complete the catalytic cycle via two possible mechanisms. On one hand, cross metathesis of the Ru species **D** with a neighbouring resin-bound substrate molecule directly leads to intermediate **B** (Path A), which is also suggested by Piscopio and Blechert.[12][13c] On the other hand, with an excess of styrene present, cross metathesis with intermediate **D** can occur, so that the homogeneous catalyst **A** is formed again (Path B). Although eventually higher yields were obtained in the presence of styrene, the initial reaction rate was not influenced by additional styrene. These observations indicate that initially the reaction primarily proceeds via cross metathesis on the resin. Apparently, in a later stage, forwarding

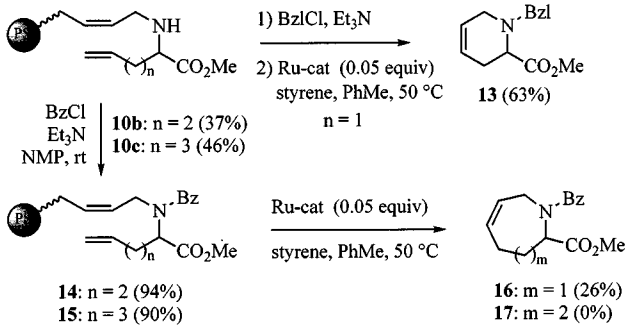
of the Ru catalyst via on-bead cross-metathesis becomes more difficult. This effect might be due to the increased concentration of olefins **E**, which as a result of the shorter tether length are less efficient in forwarding of the Ru species.[13c] At this point, cross metathesis with styrene will lead to a soluble Ru species that can re-enter the catalytic cycle and cause the reaction to proceed. Alternatively, a different explanation that might account for the increased yields in the presence of styrene is that the catalyst then predominantly exists in the more stable benzylidene form, thus enhancing the lifetime of the catalyst.

Scheme 2. Mechanism RCM on solid phase



The optimized conditions were also applied to related cyclization substrates (Scheme 3). Cyclization of benzylated **10a** proceeded smoothly to give the cyclic counterpart **13** in a reasonable 57% yield (over 2 steps). Increasing the ring size dramatically influenced the outcome of the RCM reaction. Closure of precursor **14** (obtained via reaction of **8** with **9b** (n = 2), followed by benzoylation) afforded the seven-membered ring **16** in only 26% yield. Although isolated in a low yield, the azepine **16** was obtained as a single product (according to NMR data of the crude reaction mixture) in addition to some remainder of the catalyst which could be readily removed via filtration through a short path of silica. Despite several attempts, formation of the 8-membered ring **17** from precursor **15** (obtained via a similar sequence as **14**) could not be accomplished.

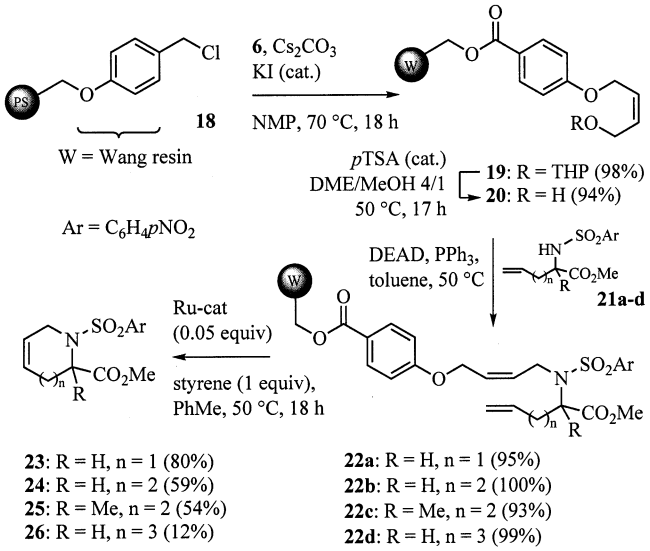
Scheme 3. Additional cyclizations to unsaturated amino esters



In order to obtain information on the exact mechanism, attempts were made to cleave off residual products from the resin for analysis. Unfortunately, despite the use of many conditions (aqueous saponification,[24] transesterification,[25] and amidation using ethylamine),[26] cleavage of the ester linkage failed.

The introduction of the acid-labile Wang linker enables such a cleavage reaction at different stages of the synthesis (Scheme 4). Loading of chlorinated Wang resin **18**[27] with the initial linker molecule **6** using standard conditions provided resin **19** in 98% yield. Cleavage was effected quantitatively by treatment of the resin with TFA/CH_2Cl_2 (1:1) at room temperature for 4 h. Removal of the THP group by treatment with *p*TSA in DME/MeOH provided the solid phase-bound allylic alcohol **20** in 94% yield. The α-alkenylglycine methyl ester derivatives were activated with a *p*-nitrobenzenesulfonyl[28] group (**21a**–**d**) and coupled with the solid-supported allylic alcohol **20** via a Mitsunobu reaction to provide the cyclization precursors **22a**–**d** in excellent yields. Remarkably, even the sterically congested disubstituted amino acid derivative **21c** was coupled in high yield. Cleavage of the resin-bound cyclization precursors **22a**–**d** with TFA/CH_2Cl_2 (1:1) and subsequent spectral analysis proved the purity and yield of the precursors. Cyclization of **22a** proceeded in 80% isolated yield to give the six-membered ring **23**. Cyclization of **22b** and **c** afforded the seven-membered rings **24** and **25** in 59% and 54%, respectively. Clearly, the additional methyl group does not alter the outcome of the RCM reaction. The corresponding eight-membered ring **26** was also obtained, albeit in a low yield of 12% (entry 5). In solution, however, a similar cyclization could not be accomplished.[10]

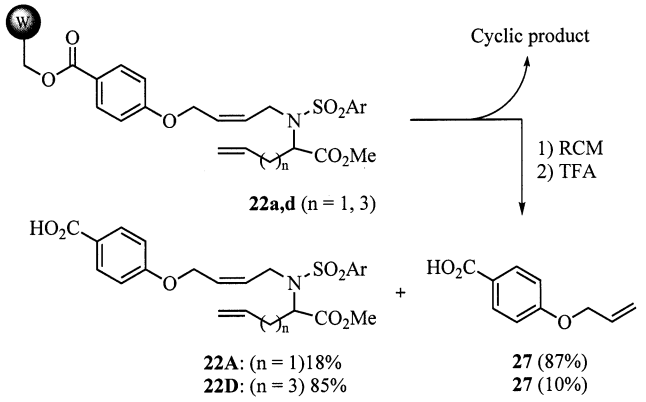
Scheme 4. Solid-phase synthesis of cyclic unasaturated amino esters



At this point, cleavage experiments were carried out to gain mechanistic information on the RCM reaction (Scheme 5). TFA-mediated cleavage of the remainder from resins **23a** and **d** after RCM provided nearly quantitative yields of only two products: the 'starting' compounds **22A** and **D**, respectively, and *O*-allyl-*p*-hydroxybenzoic acid (**27**). Neither dimers (as previously suggested by others),[12] nor cross metathetis products of styrene with the starting mate-

rial or *O*-allyl-*p*-hydroxybenzoic acid (**27**) were found. These results show that dimerization of substrate molecules, in contrast to solution phase reactions, does not take place on the resin.[10]

Scheme 5. TFA-mediated cleavage after RCM

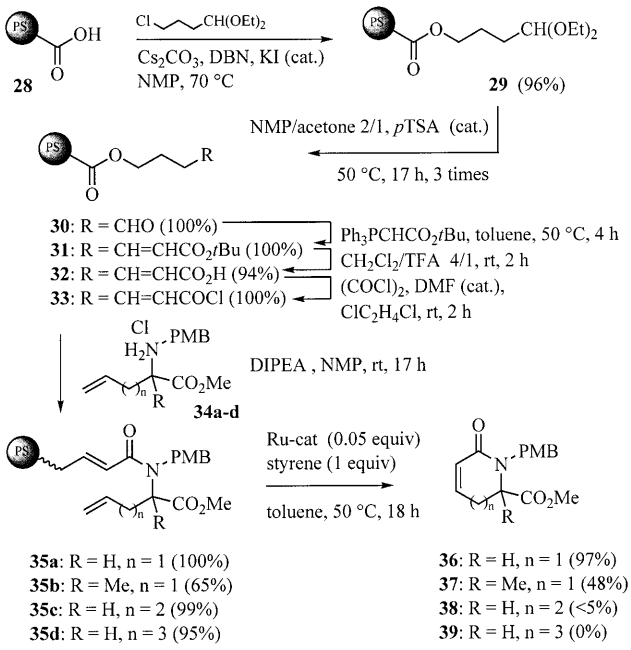


Finally, the applicability of electron-poor olefins as substrates for cyclization/cleavage RCM was studied. The precursor molecules **35a**−**d** were obtained starting from polystyrene-supported benzoic acid **28**, which was prepared according to a literature procedure.[29] Coupling of 1,1-diethoxy-4-chlorobutane at elevated temperature with **28** gave resin **29** in 96% yield. This resin was then treated with *p*TSA in NMP/acetone to liberate the aldehyde,[30] which was then converted into the α,β-unsaturated ester **31** via a Wittig reaction[31] in 100% yield. Removal of the *tert*-butyl group using TFA in CH_2Cl_2[32] and subsequent treatment with oxalyl chloride gave the α,β-unsaturated acid chloride **33** in excellent yield. Reaction with the PMB-protected amino acid derivatives **34a**−**d** in the presence of base provided the cyclization precursors **35a**−**d** in satisfactory yields. The lower yield of **35b** is probably a result of steric factors. These precursors where then subjected to the cyclization procedure. Cyclization of **35a** to six-membered ring **36** proceeded in excellent yield (97%), while the slightly more hindered system **37** was formed in a somewhat lower yield (48%). Unfortunately, ring closure to seven- and eight-membered rings **38** and **39** could not be accomplished. These results are completely in accordance with solution phase results, where subjection of similar systems to the metathesis conditions did not lead to ring-closed products either.[10]

Conclusions

In conclusion, we have demonstrated that solution phase RCM can be readily translated to solid phase without affecting the scope of the reaction. Moreover, it was found that addition of styrene has a beneficial effect on the yield of the reaction. Various heterocyclic six- and seven-membered rings were prepared in moderate to excellent yields, while in a selected case even an eight-membered ring could be formed. Important advantages of RCM on solid phase are: (a) the precursors for cyclization can be prepared in high yields and (b) because by-products are not amenable to RCM, cyclization leads to single products containing a non-polar double bond which may be further functionalized.

Scheme 6. Solid-phase synthesis of α,β-unsaturated lactams



DSM Research (Geleen, The Netherlands) is gratefully acknowledged for providing a research grant. *C. Salomons* and *D. de Boer* (*Solvay Pharmaceuticals*) are kindly acknowledged for measuring and interpreting the IR spectra, technical assistance and helpful discussions.

Experimental Section

General: Reagents were purchased at highest commercial quality and used without further purification unless stated otherwise. Fluka Merrifield resin (200−400 mesh, 1% DVB, 1.7 mmol Cl/g) and Rapp Polymere Polystyrene PHB resin (Wang resin, 100−200 mesh, 1.07 mmol OH/g) were used. Toluene was distilled from CaH_2, and stored under nitrogen. − R_f values were obtained by using thin-layer chromatography on silica gel-coated plastic sheets (Merck silica gel 60 F_{245}) using UV light as visualizing agent or $KMnO_4$ solution and heat as developing agents. − Chromatographic purification refers to flash chromatography using the indicated solvent (mixture) and ACROS silica gel (particle size 35−70 μm). − IR: Nicolet Magna 550 FTIR coupled with a NIC-Plan IR microscope. − NMR: Bruker AM 400 (400 MHz and 100.6 MHz, for ^1H and ^{13}C, respectively). Chemical shifts in $CDCl_3$ are given in ppm downfield from tetramethylsilane. − The resins were washed according to the following sequence, unless indicated otherwise: CH_2Cl_2, MeOH, CH_2Cl_2, MeOH, CH_2Cl_2, Et_2O, CH_2Cl_2, Et_2O, CH_2Cl_2. The resin was allowed to swell/shrink for 1 minute before each filtration. − Supporting Information: Experimental procedures for the cleavage of the precursor molecules from resins **20**, **22a**−**d** as well as spectral data are available on the WWW under http://www.wiley-vch.de/home/eurjoc of from the authors.

Resin **7**: A mixture of Merrifield resin (10.1 g, 17 mmol), **6** (14.6 g, 50 mmol), Cs_2CO_3 (24.4 g, 75 mmol), and KI (0.28 g, 1.7 mmol)

in NMP (500 ml) was swirled for 17 h at 65°C. The reaction mixture was filtered, washed and dried in a vacuum stove to afford resin **7** (14.3 g, 16.5 mmol) in 96% yield. − IR (neat): $\tilde{\nu}$ = 1725 cm^{-1} (C=O).

Resin **8**: A mixture of resin **7** (11.6 g, 13.3 mmol) and Br_2PPh_3 (16.9 g, 40 mmol) in CH_2Cl_2 (150 ml) was swirled for 17 h at r.t. Then the resin was filtered, washed, and dried in a vacuum stove to give resin **8** (11.3 g, 13.3 mmol) in 100% yield. − IR (neat): $\tilde{\nu}$ = 1715 cm^{-1} (C=O).

Resin **10a**: A suspension of resin **8** (629 mg, 0.75 mmol), methyl 2-amino-4-pentenoate × HCl **9a** (376 mg, 2.27 mmol), DIPEA (0.53 ml, 3.02 mmol), and KI (13 mg, 78 μmol) in NMP (10 ml) was swirled for 17 h at 65°C. The reaction mixture was filtered, washed, and dried in a vacuum stove to provide resin **10a** (664 mg, 0.73 mmol) in 97% yield. − IR (neat): $\tilde{\nu}$ = 3400 cm^{-1} (NH), 2980, 1735 (C=O), 1715 (C=O).

Resin **10b**. A suspension of resin **8** (3.54 g, 3.06 mmol), methyl 2-amino-5-hexenoate × HCl **9b** (1.63 g, 9.09 mmol), DIPEA (2.16 ml, 12.2 mmol) and KI (51 mg, 0.31 mmol) in NMP (100 ml) was swirled for 17 h at 65°C. The reaction mixture was filtered, washed, and dried in a vacuum stove to furnish resin **10b** (3.61 g, 1.13 mmol) in 37% yield. − IR (neat): $\tilde{\nu}$ = 1730 cm^{-1} (C=O), 1715 (C=O).

Resin **10c**. A suspension of resin **8** (3.65 g, 3.16 mmol), methyl 2-amino-6-heptenoate × HCl **9c** (2.01 g, 10.4 mmol), DIPEA (2.4 ml, 13.8 mmol), and KI (51 mg, 0.31 mmol) in NMP (100 ml), was swirled for 17 h at 65°C. The reaction mixture was filtered, washed, and dried in a vacuum stove to yield resin **10c** (3.76 g, 1.45 mmol, 46%). − IR (neat): $\tilde{\nu}$ = 1730 cm^{-1} (C=O), 1715 (C=O).

Resin **11**: A suspension of resin **10a** (619 mg, 0.69 mmol), benzoyl chloride (0.24 ml, 2.08 mmol), and Et_3N (0.29 ml, 2.08 mmol) in NMP (10 ml) was swirled for 17 h at r.t. The reaction mixture was filtered, washed, and dried in a vacuum stove to afford resin **11** (683 mg, 0.62 mmol) in 90% yield. − IR (neat): $\tilde{\nu}$ = 1740 cm^{-1} (C=O), 1715 (C=O), 1645.

Resin **14**: A suspension of resin **10b** (557 mg, 0.18 mmol), benzoyl chloride (60 μl, 0.54 mmol), and Et_3N (80 μl, 0.54 mmol) in NMP (10 ml) was swirled for 17 h at r.t. The reaction mixture was filtered, washed, and dried in a vacuum stove to give resin **14** (575 mg, 0.17 mmol) in 94% yield. − IR (neat): $\tilde{\nu}$ = 1740 cm^{-1} (C=O), 1715 (C=O), 1645.

Resin **15**: A suspension of resin **10c** (531 mg, 0.20 mmol), benzoyl chloride (70 μl, 0.60 mmol), and Et_3N (80 μl, 0.60 mmol) in NMP (10 ml) was swirled for 17 h at r.t. The reaction mixture was filtered, washed, and dried in a vacuum stove to afford resin **15** (550 mg, 0.18 mmol) in 90% yield. − IR (neat): $\tilde{\nu}$ = 1740 cm^{-1} (C=O), 1715 (C=O), 1650.

Resin **19**: A suspension of resin **18** (5.73 g, 4.01 mmol), **6** (5.27 g, 18.0 mmol), Cs_2CO_3 (6.62 g, 20.3 mmol), and KI (66 mg, 0.4 mmol) in NMP (100 ml) was swirled for 18 h at 70°C. This procedure was applied twice. The resin was then filtered, washed, and dried in a vacuum stove to provide resin **19** (6.74 g, 3.95 mmol) in 98% yield. − IR (neat): $\tilde{\nu}$ = 1715 cm^{-1} (C=O).

Resin **20**: To a suspension of resin **19** (1.72 g, 1.01 mmol) in MeOH/DME (25 ml, 4:1), a catalytic amount of *p*TSA (17 mg, 0.1 mmol) was added. After swirling for 18 h at 50°C, the resin was filtered, washed, and dried in a vacuum stove to yield resin **20** (1.64 g, 0.95 mmol) in 94%. IR (neat): $\tilde{\nu}$ = 3500 cm^{-1} (NH), 1725 (C=O), 1720 (C=O).

General Procedure A for Loading Allylic Alcohol Resin **20**. Resin **20** was suspended in toluene (ca. 5 ml/100 mg resin). Then the corresponding *p*-nitrobenzenesulfonyl-protected amino acid (3 equiv), PPh_3 (3 equiv.), and DEAD (3 equiv.) were added and the reaction mixture was swirled for 18 h at 50°C. The resin was then filtered, washed, and dried in a vacuum stove.

Resin **22a**: Resin **20** (213 mg, 0.116 mmol) was coupled with **21a** according to general procedure **A** to give resin **22a** (246 mg, 0.11 mmol) in 95% yield. − IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 1740 (C=O), 1715 (C=O).

Resin **22b**: Resin **20** (360 mg, 0.197 mmol) was coupled with **21b** according to general procedure **A** to afford resin **22b** (421 mg, 0.197 mmol) in 100% yield. − IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 1740 (C=O), 1710 (C=O), 1640.

Resin **22c**: Resin **20** (228 mg, 0.125 mmol) was coupled with **21c** according to general procedure **A** to give resin **22c** (266 mg, 0.116 mmol) in 93% yield. − IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 1740 (C=O), 1715 (C=O), 1640.

Resin **22d**: Resin **20** (108 mg, 0.059 mmol) was coupled with **21d** according to general procedure **A** to afford resin **22d** (126 mg, 0.058 mmol) in 99% yield. − IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 1740 (C=O), 1720 (C=O), 1640.

Resin **29**: A mixture of resin **28** (1.89 g, 1.2 mmol), Cs_2CO_3 (1.0 g, 3.07 mmol), KI (25 mg, 0.15 mmol), DBN (19 μl, 0.15 mmol), and 1,1-diethoxy-4-chlorobutane (0.83 g, 4.6 mmol) in NMP (20 ml) was swirled for 72 h at 70°C. The reaction mixture was filtered, washed, and dried in a vacuum stove to supply resin **29** (2.05 g, 1.15 mmol) in 96% yield. − IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 1720 (C=O).

Resin **30**: A suspension of resin **29** (11.3 g, 5.94 mmol) and *p*-TSA (102 mg, 0.59 mmol) in NMP/acetone (150 ml, 2:1) was swirled for 3 h at 50°C. The resin was filtered, washed, and dried in a vacuum stove. The resin was subjected to this procedure three times to yield resin **30** (10.8 g, 5.94 mmol) in 100% yield. − IR (neat): $\tilde{\nu}$ = 2720 cm^{-1}, 1720 (2 × C=O).

Resin **31**: A suspension of resin **30** (1.27 g, 0.636 mmol) and *tert*-butyl (triphenylphosphoranylidene)acetate (681 mg, 1.81 mmol) in toluene (40 ml) was swirled for 4 h at 50°C. Then the resin was filtered, washed, and dried in a vacuum stove to provide resin **31** (1.33 g, 0.636 mmol) in 100% yield. − IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 1720 (2 × C=O).

Resin **32**: A suspension of resin **31** (10.6 g, 4.42 mmol) in CH_2Cl_2/TFA (125 ml, 4:1) was swirled for 2 h at r. t. The reaction mixture was then filtered, washed, and dried in a vacuum stove to afford resin **32** (10.4 g, 4.15 mmol) in 94% yield. − IR (neat): $\tilde{\nu}$ = 3600−2400 cm^{-1} (CO_2H), 1725 (C=O), 1720 (C=O), 1695.

Resin **33**: To a suspension of resin **32** (1.20 g, 0.50 mmol) in dichloroethane (20 ml), oxalyl chloride (218 μl, 2.5 mmol) and DMF (1 drop) were added. After swirling for 2 h at r. t., the reaction mixture was filtered. The residue was then washed successively with: CH_2Cl_2, ether, CH_2Cl_2, ether, CH_2Cl_2, and dried in a vacuum stove to give resin **33** (1.21 g, 0.50 mmol) in 100% yield. − IR (neat): $\tilde{\nu}$ = 1760 cm^{-1} (C=O), 1720 (C=O).

General Procedure B for Loading Acid Chloride Resin **33**: Resin **33** was suspended in NMP (5 ml/200 mg). Then the appropriate PMB-protected amino acid (3 equiv) and DIPEA (4 equiv) were added and the reaction mixture was swirled for 17 h at r.t. The resin was then filtered, washed, and dried in a vacuum stove.

Resin **35a**: Resin **33** (308 mg, 0.127 mmol) was treated with **34a** using general procedure **B** to give resin **35a** (335 mg, 0.127 mmol)

in 100% yield. − IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 1740 (C=O), 1720 (C=O), 1660.

Resin **35b**: Resin **33** (186 mg, 0.077 mmol) was treated with **34b** using general procedure **B** to afford resin **35b** (197 mg, 0.050 mmol) in 65% yield. − IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 1780 (C=O), 1745 (C=O), 1725 (C=O), 1660.

Resin **35c**: Resin **33** (251 mg, 0.103 mmol) was treated with **34c** using general procedure **B** to provide resin **35c** (274 mg, 0.103 mmol) in 99% yield. − IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 1740 (C=O), 1720 (C=O), 1660.

Resin **35d**: Resin **33** (431 mg, 0.177 mmol) was treated with **34d** using general procedure **B** to yield resin **35d** (471 mg, 0.168 mmol) in 95%. − IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 1740 (C=O), 1725 (C=O), 1660.

General Procedure C for Cyclization of Resin-Bound Diolefin Precursor: The resin was suspended in dry, degassed toluene (5 ml) under a nitrogen atmosphere. Then styrene (1 equiv) and the Ru catalyst (0.05 equiv) were added and the mixture was gently stirred for 18 h at 50°C. The resin was then filtered and washed. The filtrate was evaporated and further purified by flash chromatography with the indicated eluent (mixture).

Methyl 1-Benzoyl-1,2,3,6-tetrahydropyridine-2-carboxylate (**12**): Resin **11** (505 mg, 0.44 mmol) was treated according to procedure **C**. Flash chromatography (EtOAc/hexanes, 1:1) afforded 93 mg (86%) of **12**. − R_f = 0.35. − IR (film): $\tilde{\nu}$ = 1740 cm^{-1} (C=O), 1649. − ^{1}H NMR ($CDCl_3$): data of the major of two rotamers δ = 7.38−7.47 (m, 5 H), 5.78−5.82 (m, 1 H), 5.51−5.73 (br d, 1 H), 4.59−4.63 (m, 1 H), 4.03−4.07 (br d, 1 H), 3.82−3.87 (br d, 1 H), 3.77 (s, 3 H), 2.50−2.79 (m, 2 H). − ^{13}C NMR ($CDCl_3$): Two rotamers δ = 171.2, 135.7, 129.6, 128.5, 128.2, 126.6, 126.2, 123.9, 123.2, 122.2, 55.7, 52.4, 52.2, 49.4, 45.3, 40.6, 26.7, 26.0. − HRMS FAB (MH^+): $C_{14}H_{16}NO_3$ (246.1130); found 246.1134.

Methyl 1-Benzyl-1,2,3,6-tetrahydropyridine-2-carboxylate (**13**): A suspension of resin **10a** (805 mg, 0.92 mmol), benzyl chloride (106 ml, 9.2 mmol), DIPEA (1.61 ml, 9.2 mmol), and KI (17 mg, 0.1 mmol) in NMP (20 ml) was swirled for 17 h at 70°C. The reaction mixture was filtered, washed, and dried in a vacuum stove to provide benzylated **10a** (881 mg, 0.84 mmol). − IR (neat): $\tilde{\nu}$ = 1730 cm^{-1} (C=O), 1715 (C=O). This resin (423 mg, 0.40 mmol) was treated according to procedure **C**. Flash chromatography (EtOAc/hexanes, 2:5) provided 58 mg (57% over two steps) of **13**. − R_f = 0.59. − IR (film): $\tilde{\nu}$ = 3032 cm^{-1} (NH), 2950, 2843, 1737 (C=O). − ^{1}H NMR ($CDCl_3$): δ = 7.23−7.37 (m, 5 H), 5.67−5.74 (m, 2 H), 3.88 (d, *J* = 13.3 Hz, 1 H), 3.81 (d, *J* = 13.3 Hz, 1 H), 3.71 (s, 3 H), 3.59 (dd, *J* = 3.2, 6.3 Hz, 1 H), 3.44 and 3.16 (br AB system, 2 H), 2.54 and 2.41 (br AB system, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 173.4, 138.5, 128.8, 128.2, 127.0, 125.6, 122.2, 59.3, 57.8, 51.1, 48.5, 28.4. HRMS EI (M^+): $C_{14}H_{17}NO_2$ (231.1259); found 231.1243.

Methyl 1-Benzoyl-2,3,4,7-tetrahydro-1H-azepine-2-carboxylate (**16**): Resin **14** (334 mg, 0.104 mmol) was treated according to procedure **C**. Flash chromatography (EtOAc/hexanes, 1:2) gave 7 mg (26%) of **16**. − R_f = 0.31. − IR (film): $\tilde{\nu}$ = 2951 cm^{-1}, 1713 (C=O), 1639, 1417. − ^{1}H NMR ($CDCl_3$): data of the major of two rotamers δ = 7.33−7.50 (m, 5 H), 5.84−5.89 (m, 1 H), 5.56−5.61 (m, 1 H), 5.12 (dd, *J* = 4.5, 12.6 Hz, 1 H), 4.04−4.09 (br d, 1 H), 3.94 (dd, *J* = 6.5, 18.1 Hz), 3.78 (s, 3 H), 2.10−2.44 (m, 4 H). − ^{13}C NMR ($CDCl_3$): data of the major of two rotamers) δ = 172.3, 135.6, 132.0, 129.8, 128.0, 127.2, 126.8, 57.7, 51.9, 45.1, 28.5, 26.9. − HRMS EI (M^+): $C_{15}H_{17}NO_3$ (259.1208); found 259.1205.

Methyl 1-(4-Nitrobenzensulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (**23**): Resin **22a** (99 mg, 0.040 mmol) was treated according to procedure **C**. Flash chromatography (EtOAc/hexanes, 1:2) gave 10 mg (80%) of **23**. − R_f = 0.38. − IR (film): $\tilde{\nu}$ = 2955 cm^{-1}, 2922, 2852, 1742 (C=O), 1531, 1436. − ^{1}H NMR ($CDCl_3$): δ = 8.35 (d, *J* = 8.9 Hz, 2 H), 7.97 (d, *J* = 8.9 Hz, 2 H), 5.73−5.78 (m, 1 H), 5.64−5.69 (m, 1 H), 4.90 (dd, *J* = 3.3, 5.0 Hz, 1 H), 4.12−4.17 (m, 1 H), 3.78−3.83 (m, 1 H), 3.53 (s, 3 H), 2.59−2.63 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 170.1, 144.6, 128.3, 123.8, 122.7, 122.4, 52.8, 52.1, 42.1, 27.6. − HRMS FAB (MH^+): $C_{13}H_{15}N_2O_6S$ (327.0651); found 327.0807.

Methyl 1-(4-Nitrobenzensulfonyl)-2,3,4,7-tetrahydro-1H-azepine-2-carboxylate (**24**): Resin **22b** (128 mg, 0.047 mmol) was treated according to procedure **C**. Flash chromatography (EtOAc/hexanes, 1:2) afforded 9 mg (59%) of **24**. − R_f = 0.30. − IR (film): $\tilde{\nu}$ = 2923 cm^{-1}, 2853, 1741 (C=O), 1606, 1528. − ^{1}H NMR ($CDCl_3$): δ = 8.31 (d, *J* = 8.9 Hz, 2 H), 8.00 (d, *J* = 8.9 Hz, 2 H), 5.58−5.67 (m, 2 H), 4.60 (dd, *J* = 4.8, 11.2 Hz, 1 H), 4.31 (dd, *J* = 6.0, 18.5 Hz, 1 H), 4.06 (d, *J* = 18.5 Hz, 1 H), 3.64 (s, 3 H), 2.24−2.31 (m, 2 H), 1.97−2.08 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 171.6, 149.4, 146.1, 131.6, 128.4, 126.5, 124.0, 59.7, 52.4, 43.4, 30.0, 26.4. − HRMS FAB (MH^+): $C_{14}H_{17}N_2O_6S$ (341.0807); found 341.0838.

Methyl 2-Methyl-1-(4-nitrobenzensulfonyl)-2,3,4,7-tetrahydro-1H-azepine-2-carboxylate (**25**): Resin **22c** (104 mg, 0.045 mmol) was treated according to procedure **C**. Flash chromatography (EtOAc/hexanes, 1:2) provided 9 mg (54%) of **25**. − IR (film): $\tilde{\nu}$ = 2922 cm^{-1}, 2851, 1735 (C=O), 1606, 1529. − R_f = 0.28. − ^{1}H NMR ($CDCl_3$): δ = 8.31 (d, *J* = 8.9 Hz, 2 H), 8.17 (d, *J* = 8.9 Hz, 2 H), 5.66−5.70 (m, 1 H), 5.45−5.50 (m, 1 H), 4.12−4.18 (m, 1 H), 3.99 (dd, *J* = 6.4, 18.3 Hz, 1 H), 3.77 (s, 3 H), 2.55−2.59 (m, 1 H), 2.12−2.26 (m, 3 H), 1.72 (s, 3 H). − ^{13}C NMR ($CDCl_3$): δ = 173.3, 149.7, 147.3, 132.4, 128.6, 124.1, 123.8, 66.7, 52.5, 42.4, 37.5, 25.6, 23.5. − HRMS FAB (MH^+): $C_{15}H_{19}N_2O_6S$ (355.0964); found 355.0953.

Methyl 1-(4-Nitrobenzensulfonyl)-1,2,3,4,5,8-hexahydroazocine-2-carboxylate (**26**): Resin **22d** (316 mg, 0.159 mmol) was treated according to procedure **C**. Flash chromatography (EtOAc/hexanes, 1:2) furnished 7 mg (12%) of **26**. − R_f = 0.35. − IR (film): $\tilde{\nu}$ = 2938 cm^{-1}, 1741 (C=O), 1531, 1349. − ^{1}H NMR ($CDCl_3$): δ = 8.32 (d, *J* = 9.0 Hz, 2 H), 7.95 (d, *J* = 9.0 Hz, 2 H), 5.70−5.73 (m, 1 H), 5.51−5.55 (m, 1 H), 5.75 (dd, *J* = 4.4, 9.6 Hz, 1H), 4.37−4.42 (br d, 1 H), 3.91−3.97 (br d, 1 H), 3.47 (s, 3 H), 2.92−3.05 (m, 1 H), 1.89−2.06 (m, 4 H), 1.68−1.77 (m, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 171.1, 145.4, 128.2, 127.6, 127.5, 123.9, 59.9, 51.9, 46.3, 26.5, 26.2, 22.2. − HRMS EI ($M^+ - CO_2Me$): $C_{13}H_{15}N_2O_4S$ (295.0752); found 295.0770.

Methyl 1-(4-Methoxybenzyl)-6-oxo-1,2,3,6-tetrahydropyridine-2-carboxylate (**36**): Resin **35a** (504 mg, 0.113 mmol) was treated according to procedure **C**. Flash chromatography (EtOAc/hexanes, 9:1) furnished 30 mg (97%) of **36**. − R_f = 0.43. − IR (film): $\tilde{\nu}$ = 3002 cm^{-1}, 2954, 2837, 1742 (C=O), 1668, 1615, 1514. − ^{1}H NMR ($CDCl_3$): δ = 7.18 (d, *J* = 8.5 Hz, 2 H), 6.84 (d, *J* = 8.5 Hz, 2 H), 6.39−6.43 (m, 1 H), 5.99 (dd, *J* = 2.7, 9.9 Hz, 1 H), 5.42 (d, *J* = 14.9 Hz, 1 H), 4.0 (d, *J* = 6.9 Hz, 1 H), 3.79 (d, *J* = 14.9 Hz, 1 H), 3.78 (s, 3 H), 3.69 (s, 3 H), 2.7 (ddd, *J* = 1.4, 6.0, 18.1 Hz, 1 H), 2.58 (ddt, *J* = 2.6, 7.3, 18.2 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 171.6, 163.9, 159.0, 136.4, 129.5, 128.8, 125.6, 113.9, 55.8, 55.1, 52.5, 48.1, 27.3. − HRMS FAB (MH^+): $C_{15}H_{18}NO_4$ (276.1236); found 276.1230.

Methyl 1-(4-Methoxybenzyl)-2-methyl-6-oxo-1,2,3,6-tetrahydropyridine-2-carboxylate (**37**): Resin **35b** (170 mg, 0.043 mmol) was treated according to procedure **C**. Flash chromatography (Et_2O)

yielded 6 mg (48%) of **37**. – R_f = 0.34. – IR (film): $\tilde{\nu}$ = 2952 cm^{-1}, 2836, 1738 (C=O), 1670, 1616, 1513. – ^1H NMR ($CDCl_3$): δ = 7.19 (d, *J* = 8.7 Hz, 2 H), 6.83 (d, *J* = 8.7 Hz, 2 H), 6.47 (ddd, *J* = 2.4, 6.0, 9.8 Hz, 1 H), 6.04 (dd, *J* = 2.7, 9.8 Hz, 1 H), 5.31 (d, *J* = 16.0 Hz, 1 H), 4.11 (d, *J* = 16.0 Hz, 1 H), 3.78 (s, 3 H), 3.68 (s, 3 H), 2.87 (dd, *J* = 6.0, 17.9 Hz, 1 H), 2.49 (dt, *J* = 2.6, 17.9 Hz, 1 H), 1.49 (s, 3 H). – ^{13}C NMR ($CDCl_3$): δ = 174.2, 165.8, 158.3, 136.7, 131.6, 128.1, 125.6, 113.7, 63.8, 55.1, 52.7, 45.7, 36.4, 24.4. – HRMS EI (M^+): $C_{16}H_{19}NO_4$ (289.1314); found 289.1320.

[1] [1a] Special issue on combinatorial chemistry: *Acc. Chem. Res.* **1996**, *29* (3). – [1b] M. A. Gallop, R. W. Barrett, W. J. Dower, S. P. A. Fodor, E. M. Gordon, *J. Med. Chem.* **1994**, *37*, 1233. – [1c] E. M. Gordon, R. W. Barrett, W. J. Dower, S. P. A. Fodor, M. A. Gallop, *J. Med. Chem.* **1994**, *37*, 1386.

[2] [2a] P. H. H. Hermkens, H. C. J. Ottenheijm, D. Rees, *Tetrahedron* **1996**, *52*, 4527. – [2b] P. H. H. Hermkens, H. C. J. Ottenheijm, D. Rees, *Tetrahedron* **1997**, *53*, 5643.

[3] [3a] F. Balkenhohl, C. Von dem Bussche-Hünnefeld, A. Lansky, Zechel, C., *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2288. – [3b] L. A. Thompson, J. A. Ellman, *Chem. Rev.* **1996**, *96*, 555. – [3c] J. S. Früchtel, G. Jung, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 17. – [3d] N. K. Terrett, M. Gardner, D. W. Gordon, R. S. Kobylecki, J. Steele, *Tetrahedron* **1995**, *51*, 8135. – [3e] A. Nefzi, J. M. Ostresh, R. A. Houghten, *Chem. Rev.* **1997**, *97*, 449.

[4] [4a] M. J. Plunkett, J. A. Ellman, *J. Org. Chem.* **1995**, *60*, 6006. – [4b] B. C. Chenera, J. A. Finkelstein, D. F. Veber, *J. Am. Chem. Soc.* **1995**, *117*, 11999. – [4c] F. X. Woolard, J. Paetsch, J. A. Ellman, *J. Org. Chem.* **1997**, *62*, 6102. – [4d] M. J. Plunkett, Ellman, J. A,. *J. Org. Chem.* **1997**, *62*, 2885. – [4e] Y. Han, S. D. Walker, R. N. Young, *Tetrahedron Lett.* **1996**, *37*, 270. – [4f] T. L. Boehm, H. D. H. Showalter, *J. Org. Chem.* **1996**, *61*, 6498.

[5] [5a] A. L. Smith, C. G. Thomson, P. D. Leeson, *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1483 and references cited therein. – [5b] J. Kowalski, M. A. Lipton, *Tetrahedron Lett.* **1996**, *37*, 5839. – [5c] B. A. Dressman, L. A. Spangle, S. W. Kaldor, *Tetrahedron Lett.* **1996**, *37*, 937.

[6] For reviews, see: [6a] H.-G. Schmalz, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1833. – [6b] J. C. Mol, K. J. Ivin *Olefin Metathesis and Metathesis Polymerization* Academic Press: London, 1997. – [6c] M. Schuster, S. Blechert, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2036. – [6d] R. H. Grubbs, S. Chang, *Tetrahedron* **1998**, *54*, 4413.

[7] For a selection of recent examples, see: [7a] A. Fürstner, K. Langemann, *J. Am. Chem. Soc.* **1997**, *119*, 9130. – [7b] Z. Yang, Y. He, D. Vourloumis, H. Vallberg, K. C. Nicolaou, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 166. – [7c] A. G. M. Barrett, S. P. D. Baugh, V. C. Gibson, M. R. Giles, E. L. Marshall, P. A. Procopiou, *J. Chem. Soc., Chem. Commun.* **1997**, 155. – [7d] D. F. Meng, D. S. Su, A. Balog, P. Bertinato, E. J. Sorensen, S. J. Danishefsky, Y. H. Zheng, T. C. Chou, L. F. He, S. B. Horwitz, *J. Am. Chem. Soc.* **1997**, *119*, 2733. – [7e] M. Schuster, J. Pernerstorfer, S. Blechert, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1979. – [7f] S. H. Kim, I. Figueroa, P. L. Fuchs, *Tetrahedron Lett.* **1997**, *38*, 2601. – [7g] A. B. Dyatkin, *Tetrahedron Lett.* **1997**, *38*, 2065. – [7h] Y.-S. Shon, Lee, T. R. *Tetrahedron Lett.* **1997**, *38*, 1283. – [7i] T. A. Kirkland, R. H. Grubbs, *J. Org. Chem.* **1997**, *62*, 7310. – [7j] J. P. A. Harrity, D. S. La, D. R. Cefalo, M. S. Visser, A. H. Hoveyda, *J. Am. Chem. Soc.* **1998**, *120*, 2343. – [7k] A. K. Ghosh, K. A. Hussain, *Tetrahedron Lett.* **1998**, *39*, 1881.

[8] For applications onto amino acid derivatives, see: [8a] K. Hammer, K. Undheim, *Tetrahedron* **1997**, *53*, 2309. – [8b] K. Hammer, K. Undheim, *Tetrahedron* **1997**, *53*, 5925. – [8c] K. Hammer, K. Undheim, *Tetrahedron* **1997**, *53*, 10603. – [8d] T. D. Clark, M. R. Ghadiri, *J. Am. Chem. Soc.* **1995**, *117*, 12364. – [8e] S. J. Miller, H. E. Blackwell, R. H. Grubbs, *J. Am. Chem. Soc.* **1996**, *118*, 9606. – [8f] F. Garro-Hélion, F. Guibé, *J. Chem. Soc., Chem. Commun.* **1996**, 641. – [8g] D. J. O'Leary, S. J. Miller, R. H. Grubbs, *Tetrahedron Lett.* **1998**, *39*, 1689.

[9] J. H. Van Maarseveen, J. A. J. Den Hartog, V. Engelen, E. Finner, G. Visser, C. G. Kruse, *Tetrahedron Lett.* **1996**, *37*, 8249.

[10] F. P. J. T. Rutjes, H. E. Schoemaker, *Tetrahedron Lett.* **1997**, *38*, 677.

[11] K. C. Nicolaou, N. Winssinger, J. Pastor, S. Ninkovic, F. Sarabia, Y. He, D. Vourloumis, Z. Yang, T. Li, P. Giannakakou, E. Hamel, *Nature* **1997**, *387*, 268.

[12] [12a] A. D. Piscopio, J. F. Miller, K. Koch, *Tetrahedron Lett.* **1997**, *38*, 7143. – [12b] A. D. Piscopio, J. F. Miller, K. Koch, *Tetrahedron Lett.* **1998**, *39*, 2667.

[13] [13a] J.-U. Peters, S. Blechert, *Synlett* **1997**, 348. – [13b] M. Schuster, J. Pernerstorfer, S. Blechert, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1979. – [13c] J. Pernerstorfer, M. Schuster, S. Blechert, *J. Chem. Soc., Chem. Commun.* **1997**, 1949.

[14] S. Marquais, M. Arlt, *Tetrahedron Lett.* **1996**, *37*, 5491.

[15] O. Mitsunobu, *Synthesis*, **1981**, 1.

[16] B. F. Gisin, *Helv. Chim. Acta.* **1973**, *56*, 1476.

[17] B. Yan, G. Kumaravel, *Tetrahedron* **1996**, *52*, 843.

[18] M. Schwarz, J. E. Oliver, P. E. Sonnet, *J. Org. Chem.* **1975**, *40*, 2410.

[19] This sequence was repeated on a Wang-resin, followed by TFA-mediated cleavage and full characterization of the residue to confirm the yield of the bromination reaction.

[20] The amino esters were prepared according to literature procedures: [20a] L. Ghosez, J.-P. Antoine, E. Deffense, M. Navarro, V. Libert, M. J. O'Donnell, W.A. Bruder, K. Willey, K. Wojciechowski, *Tetrahedron Lett.* **1982**, *23*, 4255. – [20b] M. J. O'Donnell, B. LeClef, D. B. Rusterholz, L. Ghosez, J.-P. Antoine, M. Navarro, *Tetrahedron Lett.* **1982**, *23*, 4259. – [20c] M. J. O'Donnell, J. M. Boniece, S. E. Earp, *Tetrahedron Lett.* **1978**, *19*, 2641. – [20d] M. J. O'Donnell, R. L. Polt, *J. Org. Chem.* **1982**, *47*, 2663.

[21] Under the optimized conditions, the solid phase cyclization of ε-caprolactam (Eq. 1) was effected in a significantly improved yield of 89%.

[22] Reaction of styrene with 5 mol% of Ru catalyst in toluene for 17 h at 50°C resulted in the formation of 2% of stilbene (determined by GC analysis).

[23] For a general mechanistic study of RCM, see: E. L. Dias, S. T. Nguyen, R. H. Grubbs, *J. Am. Chem. Soc.* **1997**, *119*, 3887.

[24] C. Sylvain, A. Wagner, C. Mioskowski, *Tetrahedron Lett.* **1997**, *38*, 1043.

[25] [25a] L. F. Tietze, A. Steinmetz, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 651. – [25b] D. R. Tortolani, S. A. Biller, *Tetrahedron Lett.* **1996**, *37*, 5687. – [25c] R. Frenette, R. W. Friesen, *Tetrahedron Lett.* **1994**, *35*, 9177.

[26] L. Yang, L. Guo, *Tetrahedron Lett.* **1996**, *37*, 5041.

[27] [27a] M. Mergler, R. Nijfeler, J. Gosteli, *Tetrahedron Lett.* **1989**, *30*, 6741. – [27b] K. Ngu, D.V. Patel, *Tetrahedron Lett.* **1997**, *38*, 973.

[28] T. Fukuyama, C.-K. Jow, M. Cheung, *Tetrahedron Lett.* **1995**, *36*, 6373.

[29] [29a] X. Beebe, N. E. Schore, M. J. Kurth, *J. Am. Chem. Soc.* **1992**, *114*, 10061. – [29b] X. Beebe, N. E. Schore, M. J. Kurth, *J. Org. Chem.* **1995**, *60*, 4196. – [29c] J. M. Frechet, C. Schuerch, *J. Am. Chem. Soc.* **1971**, *93*, 492.

[30] E. W. Colvin, R. A. Raphael, J. S. Roberts, *J. Chem. Soc., Chem. Commun.* **1971**, 858.

[30] [31a] D. P. Rotella, *J. Am. Chem. Soc.* **1996**, *118*, 12246. – [31b] C. Chen, Ahlberg L. A. Randall, R. B. Miller, A. D. Jones, M. J. Kurth, *J. Am. Chem. Soc.* **1994**, *116*, 2661. – [31c] C. C. Leznoff, J. Y. Wong, *Can. J. Chem.* **1973**, *51*, 3756.

[32] D. B. Bryan, R. F. Hall, K. G. Holden, W. F. Huffman, J. G. Gleason, *J. Am. Chem. Soc.* **1977**, *99*, 2353.

[98268]