

Preparation of Sugar β -Amino Acid Derivatives with Cyclic Structures by Ring-Closing Metathesis

Basker Sundararaju,^[a] Tailor Sridhar,^[b] Mathieu Achard,^[a] Gangavaram V. M. Sharma,^[b] and Christian Bruneau^{*[a]}

Keywords: Amino acids / Metathesis / Ruthenium / Carbohydrates

Efficient syntheses of β -amino acid derivatives with cyclic structures were developed. The key steps involve aza-Michael addition and ruthenium-catalyzed allylation for the construction of new acyclic β -amino acid dienes incorporat-

ing a sugar fragment, and a ruthenium-catalyzed ring-closing metathesis for the construction of the seven- and nine-membered ring compounds.

Introduction

The modification of amino acid derivatives through the introduction of cyclic motives in their structures makes them more rigid, which is assumed to play a crucial role in biological properties and thus has a potential impact in drug design and development.^[1] The ring-closing metathesis reaction is particularly appropriate to create such cyclic substructures from unsaturated substrates.^[2] Indeed, it has been efficiently used in amino acid, peptide, and peptidomimetic science.^[3] The first examples reported the transformations of α -amino esters modified by introduction of two allylic groups at the C α - and N-positions of glycine derivatives, which led to piperidine ring structures.^[2a,4] Because of the growing interest in fluorinated organic compounds due to their specific biological interest,^[5] monofluorinated cyclic α -amino esters have been prepared by using the same strategy starting from *N*-2-fluoroprop-2-enyl substrates.^[6] We have also explored the formation of various cyclic derivatives from α -amino esters containing α -CF₃ and phosphonate analogs.^[7] Other types of non-natural cyclic 1-amino-1-carboxylic acid derivatives of different sizes were also prepared from substrates with two geminal olefinic branches grafted at the α -carbon atom of the final product.^[8] β -Amino esters have also been used as starting substrates for the preparation of cyclic derivatives, wherein, the unsaturated fragments were introduced at all the four avail-

able positions, namely, the C α -, C β -, O-, and N-atoms. *N*-Allylated substrates led to cyclic amines with α -substitution by an alkoxycarbonylmethyl group,^[9] or β -substitution by an alkoxycarbonyl group^[10] starting from C β -allylated and C α -allylated substrates, respectively. Complementarily, another family of β -amino acid products, 1-amino-2-carboxylate cycloalkenes, was obtained when the reactive unsaturated groups were attached to the C α - and C β -positions.^[11] These studies revealed that the ring-closing metathesis reaction was very sensitive to the chemical and steric environment of the reactive olefinic groups.

We now report the preparation of a new family of β -amino esters **I–IV**, with a carbohydrate substituent at the C β -position and unsaturated groups at selected positions, and their transformations through ruthenium-catalyzed ring-closing metathesis to novel cyclic derivatives **V–VIII** (Figure 1).

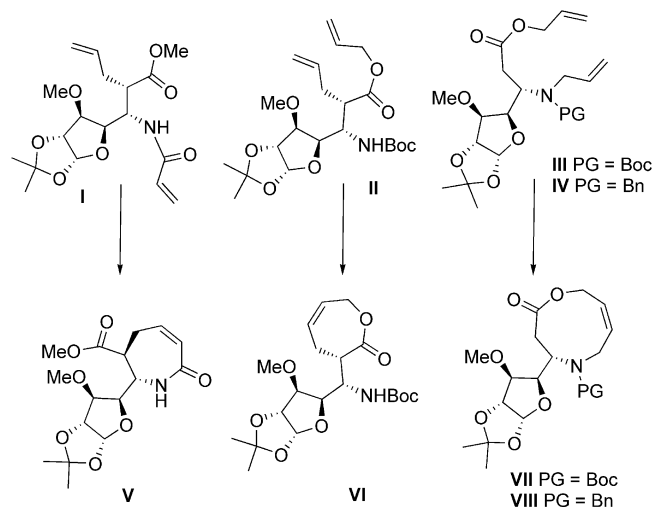


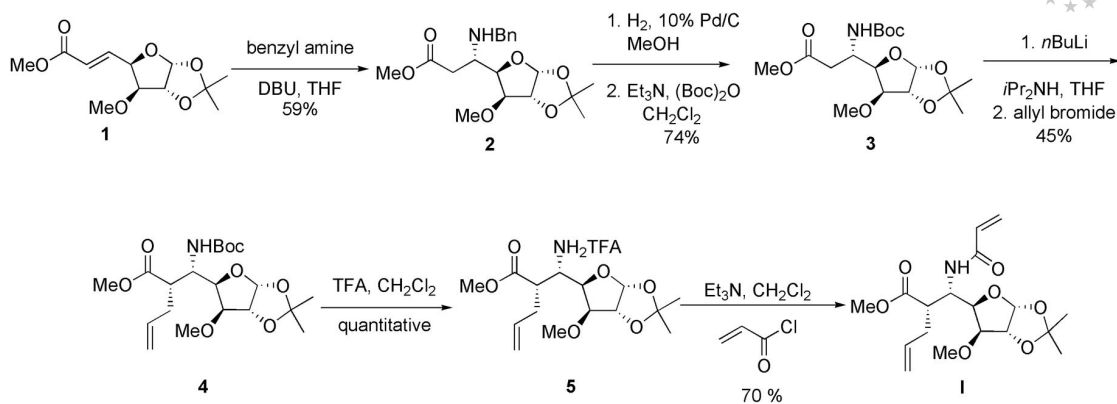
Figure 1. Cyclization of amino acid dienes **I**, **II**, **III**, **IV**.

[a] UMR 6226: CNRS-Université de Rennes 1, Sciences Chimiques de Rennes, Catalyse et Organométalliques, Campus de Beaulieu, 35042 Rennes Cedex, France
Fax: +33-2-23236939

E-mail: christian.bruneau@univ-rennes1.fr

[b] Organic Chemistry Division III, D 211, Discovery Laboratory, Indian Institute of Chemical Technology, Hyderabad 500007, India

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/ejoc.201000923>.

Scheme 1. Synthesis of β -Caa **I**.

Compound **I** featuring an allyl group at the α -position and an acrylamide functionality at the β -position would lead to the formation of seven-membered amide ring **V**, whereas compound **II** containing an allyl group at the α -position and an allyl ester moiety, likewise, may allow the formation of seven-membered unsaturated lactone **VI**. The amine and acid groups in compounds **III/IV** both functionalized with an allyl group may lead after ring-closing metathesis to the formation of the nine-membered ring in **VII/VIII**.

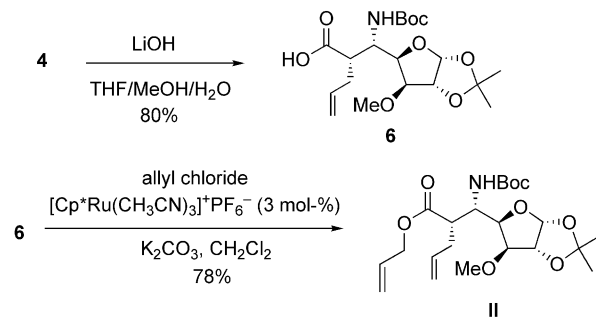
Results and Discussion

Synthesis of **I**

The DBU-mediated aza-Michael addition of benzylamine to ester **1** gave **2** (59%, 94% *de*), which upon catalytic debenzilation with 10% Pd/C in methanol, followed by subsequent treatment with (Boc)₂O afforded the C-linked carbo- β -amino acid ester (β -Caa) **3** in 74% yield. Alkylation of ester **3** at the α -position with allyl bromide by using in situ generated LDA led to the stereoselective formation of **4** in moderate yield (45%). Finally, deprotection of the amine with CF₃COOH (TFA), followed by functionalization of **5** with acryloyl chloride and Et₃N gave acrylamide derivative **I** in 70% yield (Scheme 1).

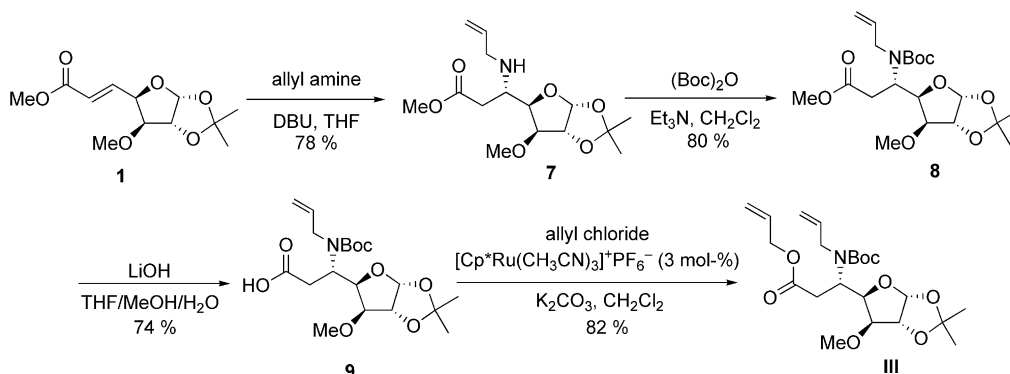
Synthesis of **II**

β -Amino ester diene **II** was prepared from **4**. Base-mediated hydrolysis of ester **4** with LiOH in a THF/MeOH/H₂O (3:1:1) mixture at room temperature furnished acid **6** in 80% yield. Further, ruthenium-catalyzed allylation of the carboxylic group^[12] in **6** at room temperature gave metathesis precursor **II** in 78% yield (Scheme 2).

Scheme 2. Preparation of **II**.

Synthesis of **III**

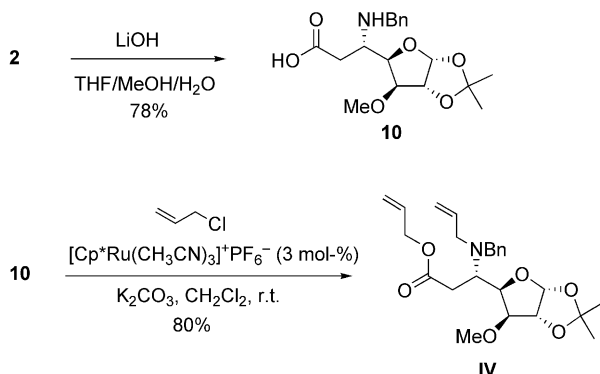
Diene compound **III** was prepared in four steps starting from α,β -unsaturated ester **1**. Compound **1** was subjected to aza-Michael addition with allylamine to give *N*-allylated

Scheme 3. Synthesis of β -Caa **III**.

β -Caa **7** in 78% yield. Further, protection of **7** with (Boc)₂O afforded ester **8** in 80% yield. Treatment of **8** with LiOH gave the corresponding acid **9** in 74% yield, which upon allylation in the presence of a catalytic amount of ruthenium precatalyst gave **III** in 82% yield (Scheme 3).

Synthesis of IV

Ester **2**, upon reaction with LiOH, was converted into acid **10** (78%), which upon further ruthenium-catalyzed allylation of the amine and acid functionalities in the presence of allyl chloride in dichloromethane at room temperature afforded the expected *N*- and *O*-allyl β -amino ester **IV** in 80% yield (Scheme 4).



Scheme 4. Synthesis of **IV**.

Ring-Closing Metathesis

With the expected four dienes **I–IV** in hand, we next investigated the ring-closing metathesis with the benzylidene ruthenium catalysts **GI**, **GII**, and **HGII** (Figure 2).

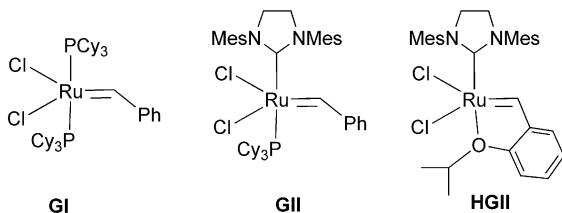


Figure 2. Metathesis catalysts used for RCM reactions.

Ring-closing metathesis of dienes involving an acrylamido group has already been reported,^[13] wherein five- and six-membered lactams were shown to be formed easily with Grubbs catalyst.^[14] However, the construction of seven-membered rings was more difficult and was reported to be more catalyst dependent.^[15] Moreover, in our prepared compounds that contain carbohydrate moieties, the presence of these later would interact with the catalysts and could modify the metathesis process. The results obtained from diene **I**, which is expected to result in a seven-membered ring, are presented in Table 1.

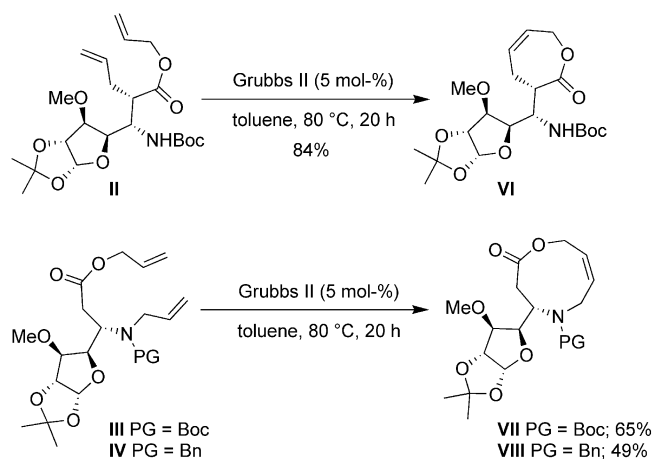
Table 1. Concentration effects in ring-closing metathesis of **I**.^[a]

Entry	Catalyst	Solvent	Conc. [M]	Temp [°C]	Time [h]	Conv. [%] ^[b]
1	GI	CH ₂ Cl ₂	0.01	40	20	0
2	GI	toluene	0.01	80	20	0
3	GI	CH ₂ Cl ₂	0.05	40	20	0
4	GI	CH ₂ Cl ₂	0.004	40	12	10
5	GII	CH ₂ Cl ₂	0.004	40	12	90
6	GII	CH ₂ Cl ₂	0.004	40	20	95(74) ^[c]
7	HGII	CH ₂ Cl ₂	0.004	40	20	75

[a] All reactions were carried out under an inert atmosphere. [b] GC conversion by using tetradecane as an internal standard. [c] Number in parentheses is isolated yield.

Ester **I**, upon RCM in the presence of catalyst (5 mol-%; Table 1, Entry 1), did not give any product and did not undergo a ring-closing or oligomerization reaction. Similar results were observed in refluxing toluene or dichloromethane (Table 1, Entries 2 and 3). Attempts to increase the catalyst loading up to 30 mol-% were unsuccessful. This might be attributed to a substrate concentration that was too high. Interestingly, a lower substrate concentration of 0.004 M led to the complete conversion of **I** (95% after 20 h; Table 1, Entries 5 and 6) and the selective formation of seven-membered unsaturated lactam **V** in 74% yield (Table 1, Entry 6). The first generation **GI** catalyst showed low activity (Table 1, Entry 4), whereas the second generation Grubbs–Hoveyda catalyst **HGII** was able to perform the cyclization of **I** with slightly lower efficiency (Table 1, Entry 7). This reactivity showed high functional group tolerance to ruthenium catalysts **GII** and **HGII**, which accommodate ether, acetal, ester, and amide functionalities. The beneficial effect of low concentration in ring-closing metathesis of functional substrates has recently been observed during the formation of lactones from acrylates^[16] and seven-membered cyclic amines, whereas this effect was not observed in the preparation of five- and six-membered rings.^[17]

These optimal conditions were then applied to the ring-closing metathesis of substrates **II**, **III**, and **IV** (Scheme 5). In the presence of catalyst **GII** (5 mol-%) at 80 °C in toluene for 20 h with a substrate concentration of 0.004 M, the expected seven- and nine-membered lactones **VI**, **VII**, and **VIII** were obtained in 84, 65, and 49% isolated yield, respectively. The low yield obtained from **IV** is due to *N*-deallylation during metathesis. The deallylation is attributed to the isomerization of the *N*-allyl group into an enamine, which can concomitantly lead after hydrolysis to undesired deallylated amine. In all the cases, exclusive formation of the *Z*-type isomer was observed. Cyclization product **VII** was found to be present in different conformers due to the presence of the Boc-carbamate group.

Scheme 5. Synthesis of cyclized β -amino acid derivatives.

Conclusions

In conclusion, a series of new β -amino acid derivatives having a carbohydrate side chain at the C β -position and olefinic groups located at different positions of the core structure were prepared. Efficient procedures were developed to perform the ring-closing metathesis of β -amino acid derivatives to form conformationally constrained cyclic structures. This study has shown the drastic influence of the substrate concentration and also underlined that low concentrations were appropriate for highly selective cyclization reactions in the presence of the second generation Grubbs catalyst. The new cyclic compounds incorporate both the C α - and a β -amido group in **V**, the ester and the C α -carbon in **VI**, or the ester and the amino groups in **VII** and **VIII**.

Experimental Section

Synthesis of Metathesis Precursor I

Methyl (3*S*)-(Benzylamino)-3-{6-methoxy-2,2-dimethyl-(3*aR*,5*R*,6*S*,6*aR*)-perhydrofuro[2,3-*d*][1,3]dioxol-5-yl}propanoate (2): To a stirred solution of compound **1** (0.86 g, 3.33 mmol) and benzylamine (0.36 mL, 3.33 mmol) in THF (5 mL) was added DBU (0.50 mL, 3.33 mmol), and the reaction mixture was stirred at room temperature for 8 h. THF was removed, and the residue was purified by column chromatography (15% ethyl acetate in petroleum ether) to give **2** (0.72 g, 59%) as a pale-yellow syrup. $[\alpha]_D^{20} = -31.1$ ($c = 1.0$, CHCl₃). IR (neat): $\tilde{\nu} = 3370, 2980, 2918, 1718, 1449, 1368, 1072, 1013$ cm⁻¹. ¹H NMR (500 MHz, CDCl₃): $\delta = 7.32$ (m, 2 H), 7.29 (m, 2 H), 7.22 (m, 1 H), 5.91 (d, $J = 3.8$ Hz, 1 H), 4.59 (d, $J = 3.9$ Hz, 1 H), 4.23 (dd, $J = 3.2, 8.7$ Hz, 1 H), 3.86 (ABq, $J = 12.9$ Hz, 2 H), 3.73 (d, $J = 3.2$ Hz, 1 H), 3.69 (s, 3 H, OCH₃), 3.41 (dt, $J = 5.6, 8.7$ Hz, 1 H), 3.37 (s, 3 H, OCH₃), 2.57 (dd, $J = 5.6, 14.9$ Hz, 1 H), 2.46 (dd, $J = 5.6, 14.9$ Hz, 1 H), 1.48 (s, 3 H, CMe₂), 1.32 (s, 3 H, CMe₂) ppm. MS (FAB): m/z (%) = 366 (100) [M + H]⁺, 192 (50), 106 (9), 91 (82), 57 (17).

Methyl (3*S*)-3-[(*tert*-Butoxy)carbonylamino]-3-{6-methoxy-2,2-dimethyl-(3*aR*,6*S*,6*aR*)-perhydrofuro[2,3-*d*][1,3]dioxol-5-yl}propanoate (3): A mixture of ester **2** (0.7 g, 1.91 mmol) and 10% Pd/C (0.5 g) in methanol (3 mL) was stirred at room temperature under a hydrogen atmosphere for 12 h. After completion of the reaction

(TLC analysis), the reaction mixture was filtered, and the filtrate was evaporated. The amine was used as such for further reactions without purification. To the above free amine in CH₂Cl₂ (5 mL) at 0 °C under a nitrogen atmosphere was added Et₃N (0.67 mL, 4.77 mmol). After 10 min, (Boc)₂O (0.46 mL, 2.1 mmol) was added, and the reaction mixture was allowed to stir for 2 h. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (15% ethyl acetate in petroleum ether) to give **3** (0.52 g, 74%) as a pale-yellow solid. M.p. 72–75 °C. $[\alpha]_D^{20} = -26.9$ ($c = 1.1$, CHCl₃). IR (neat): $\tilde{\nu} = 3385, 2980, 2938, 1725, 1705, 1502, 1308, 1161, 1071, 1013$ cm⁻¹. ¹H NMR (500 MHz, CDCl₃): $\delta = 5.91$ (d, $J = 3.8$ Hz, 1 H), 5.09 (br. s, 1 H), 4.57 (d, $J = 3.8$ Hz, 1 H), 4.30 (m, 1 H), 4.298 (m, 1 H), 3.68 (d, $J = 3.1$ Hz, 1 H), 3.68 (s, 3 H, OCH₃), 3.37 (s, 3 H, OCH₃), 2.71 (dd, $J = 3.2, 14.6$ Hz, 1 H), 2.67 (dd, $J = 7.9, 14.6$ Hz, 1 H), 1.48 (s, 3 H, CMe₂), 1.43 (s, 9 H, CMe₃), 1.31 (s, 3 H, CMe₂) ppm. MS (FAB): m/z (%) = 752 (4) [2M + H]⁺, 376 (23) [M + H]⁺, 276 (100) [M + H – Boc]⁺, 320 (12), 218 (11), 133 (15).

***tert*-Butyl (1*S*,2*S*)-2-(Methoxycarbonyl)-1-[(3*aR*,5*R*,6*S*,6*aR*)-tetrahydro-6-methoxy-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl]pent-4-enylcarbamate (4):** To a solution of *N,N*-diisopropylamine (0.65 mL, 4.66 mmol) in THF (5 mL) was added *n*BuLi (2.6 M in *n*-hexane, 1.79 mL, 4.66 mmol) at –78 °C under a nitrogen atmosphere, and the mixture was stirred for 30 min at 0 °C. A solution of **3** (0.5 g, 1.33 mmol) in THF (8 mL) was added at –78 °C, and the mixture was stirred for an additional 30 min at the same temperature. Allyl bromide (0.17 mL, 1.99 mmol) was added to the reaction mixture at –78 °C, and the mixture was stirred for 2 h. The reaction mixture was quenched with cold aqueous NH₄Cl solution (8 mL), and the product was extracted with EtOAc (2 × 20 mL). The extracts were washed with water (2 × 10 mL) and brine (10 mL) and then dried (Na₂SO₄). The solvent was evaporated under reduced pressure, and the residue purified by column chromatography (12% ethyl acetate in petroleum ether) to give **4** (0.25 g, 45%) as a light-yellow syrup. $[\alpha]_D^{20} = -67.84$ ($c = 1.1$, CHCl₃). ¹H NMR (400 MHz, CDCl₃, 298 K): $\delta = 5.84$ (d, $J = 3.9$ Hz, 1 H), 5.80–5.70 (m, 1 H), 5.13–5.01 (m, 3 H), 4.49 (d, $J = 3.9$ Hz, 1 H), 4.24–4.19 (m, 1 H), 4.00–3.98 (m, 1 H), 3.67 (s, 3 H, OCH₃), 3.59 (d, $J = 3.1$ Hz, 1 H), 3.36 (s, 3 H, OCH₃), 2.57–2.53 (m, 1 H), 2.45–2.28 (m, 2 H), 1.44 (s, 12 H, CMe₂ + CMe₃), 1.28 (s, 3 H, CMe₂) ppm. ¹³C NMR (75 MHz, CDCl₃, 298 K): $\delta = 174.1, 155.7, 134.8, 117.1, 111.3, 104.6, 84.1, 81.1, 80.0, 79.0, 57.4, 51.6, 49.7, 46.8, 33.4, 28.3, 26.6, 26.2$ ppm. HRMS (ESI): calcd. for C₂₀H₃₃NO₈ [M + Na] 438.2103; found 438.2119.

(*S*)-Methyl 2-[(*S*)-(acrylamido){(3*aR*,5*R*,6*S*,6*aR*)-tetrahydro-6-methoxy-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl}methyl]pent-4-enoate (1): A solution of ester **4** (0.60 g, 1.44 mmol) and CF₃COOH (0.60 mL) in CH₂Cl₂ (3 mL) was stirred at room temperature under a nitrogen atmosphere for 2 h. The solvent was evaporated under reduced pressure to get intermediate amine **5**, which was dried under high vacuum and used as such without any further purification. To a stirred solution of amine **5** in dry CH₂Cl₂ (5 mL) was added sequentially Et₃N (0.3 mL, 2.16 mmol) and acryloyl chloride (0.14 mL, 1.73 mmol) under a nitrogen atmosphere at 0 °C, and the mixture was stirred at room temperature for 8 h. The reaction mixture was diluted with CH₂Cl₂ (8 mL) and washed with aqueous 1 M HCl (10 mL), saturated NaHCO₃ (10 mL), water (8 mL), and brine (15 mL). The organic layers were dried (Na₂SO₄) and evaporated under reduced pressure, and the residue was purified by column chromatography (35% ethyl acetate in petroleum ether) to give **1** (0.37 g, 70%) as a light-yellow syrup. $[\alpha]_D^{20} = -82.6$ ($c = 0.5$, CHCl₃). ¹H NMR (300 MHz, CDCl₃, 298 K): $\delta = 6.42$ –6.08 (m, 3 H), 5.83 (d, $J = 3.77$ Hz, 1 H), 5.79–5.60 (m, 1 H), 5.09–5.00 (m, 2 H), 4.69

(m, 1 H), 4.48 (d, $J = 3.7$ Hz, 1 H), 4.06 (dd, $J = 3.3$, 6.4 Hz, 1 H), 3.69 (s, 3 H, OCH₃), 3.62 (d, $J = 3.02$ Hz, 1 H), 3.36 (s, 3 H, OCH₃), 2.70–2.60 (m, 1 H), 2.35 (m, 2 H), 1.44 (s, 3 H, CMe₂), 1.29 (s, 3 H, CMe₂) ppm. ¹³C NMR (125 MHz, CDCl₃, 298 K): $\delta = 174.6$, 165.5, 134.4, 131.1, 126.4, 117.4, 111.3, 104.6, 83.9, 81.1, 79.8, 57.4, 51.9, 47.9, 46.1, 33.7, 26.7, 25.9 ppm. HRMS (ESI): calcd. for C₁₈H₂₇NO₇ [M + Na]⁺ 392.1685; found 392.1669.

General Procedure for Ring-Closing Metathesis (RCM): In a typical experiment, a solution of the diene substrate in toluene or CH₂Cl₂ ($c = 0.004$ M) was stirred under an inert atmosphere. The solution was purged under an atmosphere of argon for 10 min and then Grubbs II catalyst (5 mol-%) was added, and the reaction mixture was stirred at the specified temperature. The conversion was determined by gas chromatography and also TLC indicated when the reaction was complete. The reaction mixture was then concentrated under vacuum. The product was purified by column chromatography with the appropriate solvent mixture.

Methyl (2*R*,3*S*)-2-((3*aR*,6*S*,6*aR*)-6-methoxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-7-oxo-2,3,4,7-tetrahydro-1*H*-azepine-3-carboxylate (V): RCM reaction on **I** (0.19 g, 0.53 mmol) at 40 °C in CH₂Cl₂ (120 mL, $c = 0.004$ M) for 20 h, as described above gave **V** (0.13 g, 74%) as a colorless oil. $[\alpha]_D^{20} = -70.0$ ($c = 0.1$, CH₂Cl₂). ¹H NMR (500 MHz, CD₂Cl₂): $\delta = 6.33$ – 6.25 (m, 1 H), 6.07 (br. s, 1 H, NH), 5.93–5.87 (m, 2 H), 4.67 (d, $J = 3.8$ Hz, 1 H), 4.52 (dd, $J = 3.2$, 8.9 Hz, 1 H HC=CH), 3.96 (m, 1 H), 3.81 (d, $J = 3.4$ Hz, 1 H), 3.74 (s, 3 H, OCH₃), 3.42 (s, 3 H, OCH₃), 3.0–2.98 (m, 1 H), 2.88–2.81 (m, 1 H), 2.60–2.53 (m, 1 H), 1.51 (s, 3 H, CMe₂), 1.35 (s, 3 H, CMe₂) ppm. ¹³C NMR (125 MHz, CD₂Cl₂): $\delta = 171.8$, 168.5, 138.0, 125.8, 111.7, 104.9, 83.7, 81.1, 79.5, 57.3, 52.2, 51.9, 45.3, 31.4, 26.5, 26.0 ppm. HRMS: calcd. for C₁₆H₂₄NO₇ [M + H]⁺ 342.1544; found 342.1552.

Supporting Information (see footnote on the first page of this article): Protocols and characterization data for compounds **II**, **III**, **IV**, **VI**, **VII**, and **VIII**.

Acknowledgments

The authors wish to thank Indo-French Centre for the Promotion of Advanced Research CEFIPRA/IFCPAR (IFC/A/3805-2/2008/1720) for a grant to B.S. T.S. thanks the Council of Scientific and Industrial Research (CSIR) India for a research fellowship.

- [1] M. Goodman, H. Shao, *Pure Appl. Chem.* **1996**, 68, 1303–1308.
- [2] Selected references: a) S. J. Miller, R. H. Grubbs, *J. Am. Chem. Soc.* **1995**, 117, 5855–5856; b) F. P. J. T. Rutjes, L. B. Wolf, H. E. Schoemaker, *J. Chem. Soc. Perkin Trans. 1* **2000**, 4197–4212; c) T. Hoffmann, R. Waibel, P. Gmeiner, *J. Org. Chem.* **2003**, 68, 62–69; d) S. Zaman, P. Campaner, A. D. Abell, *Bioorg. Med. Chem.* **2006**, 14, 8323–8331; e) S. Brass, H.-D. Gerber, S. Dörr, W. E. Diederich, *Tetrahedron* **2006**, 62, 1777–1786; f) J. Gardiner, S. G. Aitken, S. B. McNabb, S. Zaman, A. D. Abell, *J. Organomet. Chem.* **2006**, 5487–5496; g) A. J. Vernall, S. Ballet, A. D. Abell, *Tetrahedron* **2008**, 64, 3980–3997; h) S.-Y. Han, S. Chang, “General Ring-Closing Metathesis” in *Handbook of Metathesis* (Ed.: R. H. Grubbs), Wiley, Weinheim, **2003**, vol. 2, pp. 5–127.
- [3] A. Brik, *Adv. Synth. Catal.* **2008**, 350, 1661–1675.

- [4] a) S. J. Miller, H. E. Blackwell, R. H. Grubbs, *J. Am. Chem. Soc.* **1996**, 118, 9606–9614; b) F. P. J. T. Rutjes, H. E. Schoemaker, *Tetrahedron Lett.* **1997**, 38, 677–680; c) K. C. M. F. Tjen, S. S. Kinderman, H. E. Schoemaker, H. Hiemstra, F. P. J. T. Rutjes, *Chem. Commun.* **2000**, 699–700.
- [5] a) F. Leroux, P. Jeschke, M. Schlosser, *Chem. Rev.* **2005**, 105, 827–856; b) D. F. Halpern in *Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications* (Eds.: R. Filler, Y. Kobayashi, L. Yagupolskii), Elsevier, Amsterdam, **1993**, pp. 101–133; c) D. F. Halpern in *Organofluorine Chemistry: Principles and Commercial Applications* (Eds.: R. E. Banks, B. E. Smart, J. C. Tatlow), Plenum Press, New York, **1994**, pp. 543–554.
- [6] V. De Matteis, F. L. van Delft, J. Tiebes, F. P. J. T. Rutjes, *Eur. J. Org. Chem.* **2006**, 1166–1176.
- [7] a) S. N. Osipov, C. Bruneau, M. Picquet, P. H. Dixneuf, *Chem. Commun.* **1998**, 2053–2054; b) S. N. Osipov, O. I. Artyushin, A. F. Kolomiets, C. Bruneau, P. H. Dixneuf, *Synlett* **2000**, 1031–1033; c) S. N. Osipov, N. M. Kobelikova, G. T. Shchetnikov, A. F. Kolomiets, C. Bruneau, P. H. Dixneuf, *Synlett* **2001**, 621–622; d) S. N. Osipov, O. I. Artyushin, A. F. Kolomiets, C. Bruneau, M. Picquet, P. H. Dixneuf, *Eur. J. Org. Chem.* **2001**, 3891–3897.
- [8] a) S. Kotha, N. Sreenivasachary, *Bioorg. Med. Chem. Lett.* **1998**, 8, 257–260; b) T. Ohwada, D. Kojima, T. Kiwada, S. Futaki, Y. Sugiura, K. Yamaguchi, Y. Nishi, Y. Kobayashi, *Chem. Eur. J.* **2004**, 10, 617–626; c) D. Casabona, C. Cativiela, *Synthesis* **2006**, 2440–2443; d) D. Casabona, A. I. Jimenez, C. Cativiela, *Tetrahedron* **2007**, 63, 5056–5061; e) K. Hammer, K. Undheim, *Tetrahedron* **1997**, 53, 2309–2322; f) K. Hammer, K. Undheim, *Tetrahedron* **1997**, 53, 5925–5936.
- [9] a) A. M. Chippindale, S. G. Davies, K. Iwamoto, R. M. Parkin, C. A. P. Smethurst, A. D. Smith, H. Rodriguez-Solla, *Tetrahedron* **2003**, 59, 3253–3265.
- [10] a) S. Brass, N.-S. Chan, C. Gerlach, T. Luksch, J. Böttcher, W. E. Diederich, *J. Organomet. Chem.* **2006**, 691, 5406–5422; b) J. Gardiner, S. G. Aitken, S. B. McNabb, S. Zaman, A. D. Abell, *J. Organomet. Chem.* **2006**, 691, 5487–5496.
- [11] a) A. D. Abell, J. Gardiner, *Org. Lett.* **2002**, 4, 3663–3666; b) P. Perlmutter, M. Rose, F. Vounatsos, *Eur. J. Org. Chem.* **2003**, 756–760; c) S. Fustero, A. Bartolomé, J. F. Sanz-Cervera, M. Sanchez-Rosello, J. Garcia Soler, C. Ramirez de Arellano, A. S. Fuentes, *Org. Lett.* **2003**, 5, 2523–2526; d) J. Gardiner, K. H. Anderson, A. Downard, A. D. Abell, *J. Org. Chem.* **2004**, 69, 3375–3382.
- [12] B. Sundararaju, M. Achard, G. V. M. Sharma, C. Bruneau, *Org. Biomol. Chem.* **2009**, 7, 3906–3909.
- [13] Some examples of RCM from acrylamide: a) Y. Du, D. F. Wiemer, *Tetrahedron Lett.* **2001**, 42, 6069–6072; b) S. Lebrun, A. Couture, E. Deniau, P. Grandclaudeon, *Synthesis* **2008**, 2771–2775; c) J. Minville, J. Poulin, C. Dufresne, C. F. Sturino, *Tetrahedron Lett.* **2008**, 49, 3677–3681.
- [14] a) S. P. Chavan, A. B. Pathak, A. N. Dhawane, U. R. Kalkote, *Synth. Commun.* **2007**, 37, 1503–1510; b) A. Fürstner, O. R. Thiel, L. Ackermann, H.-J. Schanz, S. P. Nolan, *J. Org. Chem.* **2000**, 65, 2204–2207.
- [15] S. B. Hoyt, C. London, M. Park, *Tetrahedron Lett.* **2009**, 50, 1911–1913.
- [16] B. Schmidt, D. Geißler, *ChemCatChem* **2010**, 2, 423–429.
- [17] K. M. Kuhn, T. M. Champagne, S. H. Hong, W.-H. Wei, A. Nickel, C. W. Lee, S. C. Virgil, R. H. Grubbs, R. L. Pederson, *Org. Lett.* **2010**, 12, 984–987.

Received: June 28, 2010

Published Online: September 13, 2010