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Microwave-Promoted Synthesis of Bicyclic Azocine-β-Lactams from Bis(allene)s

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ABSTRACT: A metal-free preparation of structurally novel bicyclic azocine- β -lactams has been developed. The first examples accounting for the preparation of eight-membered rings from

bis(allene)s in the absence of metals have been achieved by the thermolysis of non-conjugated 2azetidinone-tethered bis(allene)s applying microwave irradiation. This selective carbocyclization reaction has been studied experimentally and additionally, its mechanism has been investigated by a DFT study.

INTRODUCTION

The β -lactam (2-azetidinone) motif has been identified as an attractive synthetic target because of its prevalence in many naturally occurring products and due to their medicinally interesting activities.¹ Apart from their biological interest, the use of β -lactams as intermediates in organic synthesis for the preparation of compounds of biological relevance, such as amino acids, alkaloids, heterocycles, and taxoids, is now well established.² In accordance, efforts devoted to the synthesis of this molecular framework remain highly desirable.

On the other hand, fused nitrogen-containing eight membered ring systems, azocines, are found in a range of bioactive natural products such as the alkaloids apparicine, nakadomarin A, manzamine A, and magallanesine.³ Additionally, synthetic derivatives **I–IV** (Figure 1) exhibited central nervous system activities (**I** and **II**) and antihypertensive activities (**III** and **IV**).⁴

Figure 1. Representative examples of bioactive azocine derivatives



In the last two decades the chemistry of allenes has been extensively studied and many reviews on their preparation and reactivities have appeared.⁵ Allenes have shown an interesting reactivity and selectivity affording complex structures in a limited number of steps. While the

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chemistry of allenes is still developing and many reports appear every year, the study of the reactivity of bis(allene)s is in its infancy.⁶ Taking into account that there is only one report available on the thermal cyclization of non-conjugated bis(allene)s,⁷ we decided to study the reactivity of 2-azetidinone-tethered bis(allene)s under thermal conditions.

RESULTS AND DISCUSSION

Starting materials, new β -lactam bis(allene)s **4a–h** and **5a–k** were obtained in optically pure form from 2-azetidinone-tethered alkynyl dioxolanes **1a–c**.⁸ Terminal alkynes **1** were conveniently converted into allenes **2** by treatment with paraformaldehyde in the presence of diisopropylamine and copper(1) bromide (Crabbé reaction).⁹ 2-Azetidinone-tethered allenals **3a–c** were prepared from allenyl dioxolanes **2a–c** through BiCl₃-catalyzed acetonide deprotection followed by oxidative diol cleavage (Scheme 1).¹⁰ The allenic diol formation was not feasible using a Brønsted acid such as PTSA, because the allene moiety did not survive under these conditions. The indium-mediated Barbier-type carbonyl–allenylation reaction of allenic aldehydes **3a–c** in aqueous media yielded bis(allene)s **4a–h** with total allenic/propargylic regioselectivity and reasonable syn/anti diastereoselectivity (*de* 60–100%, by integration of well-resolved signals in the ¹H NMR spectra of the crude reaction mixtures before purification). Fortunately, in the cases of absence of total diasteroeselectivity (**4a**, **4c**, and **4d**) the diastereomeric bis(allene)s *syn-***4** and *anti-***4** could be easily separated by flash chromatography (Scheme 1). The hydroxy functionality of allenols *syn-***4a–h** was either acetylated or protected in the form of methyl ether under phase transfer conditions to afford β -lactam bis(allene)s **5a–k** (Scheme 1).

Scheme 1. Preparation of enantiopure β -lactam bis(allene)s 4a-h and 5a-k. Reagents and conditions^a



^{*a*}Conditions: i) $(CH_2O)_n$, *i*Pr₂NH, CuBr, dioxane, reflux, 2 h. ii) (a) 50 mol% BiCl₃, MeCN-H₂O, rt, 24 h; (b) NaIO₄, NaHCO₃ (aq. sat.), CH₂Cl₂, rt, 24 h. iii) In, THF/NH₄Cl (aq. sat.) (1:5), rt, 24 h. iv) Me₂SO₄, TBAI, CH₂Cl₂, NaOH (aq 50%) (1:1), rt, 8 h. v) Ac₂O, Et₃N, DMAP (cat), CH₂Cl₂, 0 °C, 2 h. PMP = 4-MeOC₆H₄. DMAP = 4-(Dimethylamino)pyridine.

To explore the reactivity of bis(allene)s **4** and **5** under thermal conditions, 2-azetidinonetethered bis(allene) **4a** was selected as a model substrate. Attempts to generate a polycyclic structure from **4a** either in refluxing toluene or at 250 °C in a sealed tube failed. When the thermolysis was carried out in a microwave by heating a solution of bis(allene) **4a** in toluene at 200 ^oC, bicyclic azocinone-β-lactam **6a** was obtained, albeit in a low 18% yield.¹¹ It should be noted that traditional ring-closure strategies are problematic for eight-membered rings owing to unfavorable enthalpic and entropic contributions.^{12,13} Applying microwave irradiation in toluene at 250 °C and using deactivated silica gel during purification resulted in an increased 25% yield for adduct **6a**, without harming the sensitive β-lactam ring (Scheme 2). Remarkably, this rare carbocyclization reaction was the only operative cyclization mode. When substrate **4d** was used as bis(allene) precursor, low yield of the corresponding bicyclic azocinone-β-lactam **6d** was also obtained; but the reaction best proceeds after long exposure of microwave irradiation at 185 °C (Scheme 2). Bicycles **6a** and **6d** were obtained as single regio- and diastereomers. Probably, the ketone funtionality in adducts **6** arises from a keto–enol isomerization. Any efforts to improve the efficiency of this transformation were in vain. Thus, in order to prevent the isomerization precursors.





Our next effort focused on the application of microwave irradiation to the selective construction of fused azocines starting from bis(allene)s **5** bearing a β -lactam moiety. The use of the above thermal conditions on 2-azetidinone-tethered bis(allene) **5a** retains the reactivity pattern,

but suppresses the keto-enol isomerization while maintaining the same regioselectivity of the cyclization step. Thus, in the case of bis(allene) **5a** we observed exclusive formation of the bicyclic enol ether **7a** in a reasonable 60% yield (Scheme 3). HMQC experiments of derivative **7a** satisfactorily established information about the presence of a new eight-membered azocinone ring. Similarly, adducts **7b-k** were obtained in fair yields in a totally selective fashion using the thermal protocol (Scheme 3), through cyclization by attack of the central allene carbon of one moiety to the central carbon of the other cumulene. Applying standard microwave irradiation conditions to non-β-lactam bis(allene)s **A**-**C** resulted in complex reaction mixtures (Scheme S1; see the Supporting Information), which lead to the exclusion of bis(allene)s **A**-**C** as efficient substrates. Consequently, it can be inferred that the 2-azetidinone nucleus plays a key template role in the cyclization processes.

Scheme 3. Preparation of azocine-β-lactams 7a-k



A conceivable mechanism for the formation of bicycles 7 from bis(allene)s 5 may initially involve the formation of diradical intermediates. When a catalytic amount of hydroquinone was added, the reaction rate was considerably reduced and the product yield fell dramatically. This fact

is consistent with involvement of a radical mechanism. The formation of azocine- β -lactams 7 can be rationalized by a mechanism that includes exocyclic diallylic diradical intermediates 8 through initial carbon–carbon bond formation, involving the central allene carbon atoms of both cumulenic moieties. Species 8 may suffer a ring-closure to produce intermediate tricyclic cyclobutanes 9,¹⁴ which finally give bicycles 7 through a rearrangement process (path A, Scheme 4). An alternative explanation for the thermal cyclization, which leads to bicycles 7 is proposed in path B (Scheme 4). This pathway involves the isomerization of species 8 to allylic diradical 10, which is a resonance form of the final product 7.





Density functional theory (DFT) calculations have been carried out to gain more insight into the reaction mechanism of the above discussed microwave-induced azocine formation. The reaction profile involving **5a** is depicted in Figure 2, which shows the corresponding relative energies (zeropoint vibrational energy corrections included) computed in toluene solution at the PCM(toluene)-M06-2X/6-311+G*//B3LYP/6-31+G* level.¹⁵

As stated above, and similar to related transformations involving allenes,¹⁶ the process begins with a stepwise [2+2]-cycloaddition reaction which initially produces the diallylic diradical

intermediate **INT1** in a slightly exothermic reaction ($\Delta E_R = -2.0$ kcal/mol). This species is formed through the transition state **TS1**, which is associated with the C–C bond formation involving both central allene carbon atoms with a computed activation barrier of 33.5 kcal/mol. This relatively high barrier is similar to those computed for related processes¹⁶ and agrees with the harsh reaction conditions used for the synthesis of the bicyclic azocine- β -lactams (see above). The diallylic diradical nature of **INT1** is confirmed by the computed spin densities, which clearly reflect the delocalization of both unpaired electrons on the distal and proximal carbon atoms of the former allene moieties (see the inset in Figure 2). Subsequent diradical ring-closure renders tricyclic intermediate **INT2** in a highly exothermic process ($\Delta E_R = -30.2$ kcal/mol) via **TS2**, a saddle point associated with the formation of the new C–C bond of the cyclobutane moiety (computed activation barrier of 16.1 kcal/mol). Once **INT2** is formed, a 1,5-hydrogen atom migration occurs thus forming species **INT3**, which is 2.4 kcal/mol more stable than its isomer **INT2**. This migration occurs via **TS3** with a considerably high computed barrier of 40.1 kcal/mol. Finally, a ring-opening step of the cyclobutane moiety affords the reaction product **7a** through the transition state **TS4** (computed activation barrier of 35.2 kcal/mol). Figure 2. Computed reaction profile for the transformation of 5a into bicyclic azocine- β -lactam 7a^a



^aRelative energies (zero-point vibrational energies included) and bond distances are given in kcal/mol and angstroms, respectively. Inset: computed spin densities on **INT1**. All data have been computed at the PCM(toluene)M06-2X/6-311+G*//B3LYP/6-31+G* level.

In view of the relatively high activation barriers computed for the steps involving **TS3** and **TS4** (40.1 and 35.2 kcal/mol, respectively), we hypothesized that an alternative reaction pathway may be competitive in the transformation of **5a** into **7a**. Indeed, we were able to locate a transition state (**TS5**) on the potential energy surface, which directly connects the initially formed diradical intermediate **INT1** with the final reaction product **7a**. This saddle point is associated with an analogous 1,5-hydrogen atom migration to that described above (involving **TS3**) but occurring with a much lower computed activation barrier ($\Delta E^{\ddagger} = 26.8$ kcal/mol). Therefore, the conversion of bis(allene) **5** into bicyclic azocine- β -lactams **7** proceeds through the formation of an initial diallylic diradical intermediate which evolves to the final product via a multi-step process, or alternatively,

via a direct 1,5-H migration. Under the harsh reaction conditions used experimentally, both reaction pathways seems to be feasible and competitive.

CONCLUSION

In conclusion, we developed a preparation of structurally novel bicyclic azocine-β-lactams in the absence of metals. The first examples accounting for the metal-free preparation of eight-membered rings from bis(allene)s have been achieved by the thermolysis of non-conjugated 2-azetidinone-tethered bis(allene)s applying microwave irradiation. This selective carbocyclization reaction has been studied experimentally and additionally, its mechanism has been investigated by a DFT study, which suggests the involvement of an initial diallylic diradical intermediate.

Experimental Section

General methods: NMR spectra were recorded at 25 °C on a 300 MHz instrument: ¹H NMR (300 MHz) and ¹³C NMR (75 MHz). Chemical shifts are given in ppm relative to TMS (¹H, 0.0 ppm), or CDCl₃ (¹³C, 76.9 ppm). Low and high resolution mass spectra were taken on a QTOF LC/MS spectrometer using the electronic impact (EI) or electrospray modes (ES). Specific rotation $[\alpha]_D$ is given in 10⁻¹ deg cm² g⁻¹ at 20 °C, and the concentration (*c*) is expressed in g per 100 mL. Microwave irradiation was carried out in a Monowave 300 from Anton Paar GmbH. The reaction temperatures during microwave heating were measured with an internal infrared sensor.

General Procedure for the Preparation of Allenic Dioxolanes 2. A well stirred solution of $(CH_2O)_n$ (0.5 mmol), CuI (0.1 mmol), alkynic dioxolane 1 (0.2 mmol), and *N*,*N*diisopropylethylamine (Hüning's base) (0.36 mmol) in dioxane (1 mL) was refluxed under argon atmosphere. When the reaction was complete as monitored by TLC, it was cooled to RT. Water (5 mL) was added before being extracted with ethyl acetate (3 x 15 mL). The organic phase was washed with water (2 x 5 mL), dried (MgSO₄) and concentrated under reduced pressure.

 Chromatography of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure compounds **2**.

Allenic Dioxolane (+)-2a. From 400 mg (1.66 mmol) of alkynic dioxolane (+)-1a, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent gave compound (+)-2a (307 mg, 73%) as a colorless oil; $[\alpha]_D = +12.4$ (*c* 0.7, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.34 (s, 3H), 1.44 (s, 3H), 3,53 (s, 3H) 3.64 (dd, 1H, *J* = 8.8, 5.6 Hz), 3.74 (m, 2H), 4.12 (m, 2H), 4.29 (m, 1H), 4.43 (d, 1H, *J* = 5.1 Hz), 4.81 (ddd, 1H, *J* = 6.5, 3.3, 2.5 Hz), 5.14 (qd, 1H, *J* = 6.8, 5.7 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.1, 167.3, 109.5, 85.7, 82.8, 76.9, 76.9, 66.7, 59.8, 59.1, 39.3, 26.9, 25.1; IR (CHCl₃) v 1958, 1759; HRMS (ES): calcd for C₁₃H₁₉NO₄[*M*]⁺ 253.1314, found 253.1317.

Allenic Dioxolane (+)-2b. From 700 mg (2.22 mmol) of alkynic dioxolane (+)-1b, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent gave compound (+)-2b (519 mg, 71%) as a colorless oil; $[\alpha]_D = +14.9$ (*c* 0.3, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.33 (s, 3H), 1.43 (s, 3H), 3.65 (dd, 1H, *J* = 8.8, 5.6 Hz), 3.77 (m, 2H), 4.14 (m, 2H), 4.35 (dt, 1H, *J* = 9.1, 6.1 Hz), 4.63 (m, 2H), 4.81 (m, 2H), 4.91 (d, 1H, *J* = 11.8 Hz), 5.14 (m, 1H), 7.32 (m, 5H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.0, 167.3, 136.9, 128.4, 128.0, 127.7, 109.5, 85.6, 80.4, 77.0, 76.8, 72.8, 66.7, 59.8, 39.4, 26.8, 25.1; IR (CHCl₃) v 1945, 1744; HRMS (ES): calcd for C₁₉H₂₃NO₄[*M*]⁺ 329.1627, found 329.1632.

Allenic Dioxolane (+)-2c. From 700 mg (2.32 mmol) of alkynic dioxolane (+)-1c, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent gave compound (+)-2c (527 mg, 72%) as a colorless oil; $[\alpha]_D = +93.1$ (*c* 0.6, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.64 (s, 3H), 1.73 (s, 3H), 3.97 (dd, 1H, J = 8.9, 5.7 Hz), 4.11 (ddt, 1H, J = 15.1, 7.0, 2.4 Hz), 4.20 (dd, 1H, J = 9.1, 5.1 Hz), 4.46 (m, 2H), 4.73 (dt, 1H, J = 9.1, 6.1 Hz), 5.12 (m, 2H), 5.47 (m, 2H), 7.31 (m, 3H), 7.57 (m, 2H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.2, 165.6, 157.3, 129.6,

122.5, 115.6, 109.7, 85.6, 79.9, 77.0, 77.0, 66.8, 59.8, 39.7, 26.8, 25.1; IR (CHCl₃) v 1958, 1762; HRMS (ES) calcd for C₁₈H₂₁NO₄[*M*]⁺ 315.1471, found 315.1477.

General procedure for the preparation of 2-azetidinone-tethered allenals 3. The corresponding allenic dioxolane 2 (1.00 mmol) was dissolved in acetonitrile/water (10 mL; 95:5) and the solution was cooled to 0 °C. BiCl₃ (0.05 mmol) was added, the ice bath was removed and the mixture was stirred at RT for 24 h (monitoring by TLC). The reaction mixture was poured into a satd. aq. solution of NaHCO₃. The aqueous layer was extracted with ethyl acetate (3 x 20 mL), and the combined organic extracts were dried (MgSO₄) and concentrated in vacuo to afford (3R,4S)-1-(buta-2,3-dienyl)-4-[(S)-2,2-dimethyl-1,3-dioxolan-4-yl]-3-alkoxyazetidin-2-ones.

Further purification was not necessary.

Saturated aqueous sodium hydrogen carbonate (100 μ L) was added to a solution of the corresponding diol (1.0 mmol) in dichloromethane (3.3 mL), maintaining the temperature below 25 °C. Solid sodium periodate (2.0 mmol) was added over a 10 min period with vigorous stirring and the reaction was allowed to proceed for 24 h, while the temperature was maintained below 25 °C. The solid was removed by filtration, the filtrate was dried (MgSO₄) and the solvent was removed under reduced pressure. The crude product was used for next step without any further purification. Spectroscopic and analytical data for some representative forms of 4-oxoazetidine-2-carbaldehydes **3** follow.

Allenal (+)-3a. From 400 mg (1.88 mmol) of allenic dioxolane (+)-2a, compound (+)-3a (370 mg, quantitative yield) was obtained as a pale brown oil; $[\alpha]_D = +52.1$ (*c* 0.7, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3,49 (s, 3H) 3.94 (m, 2H), 4.22 (dd, 1H, *J* = 4.9, 3.1 Hz), 4.77 (d, 1H, *J* = 5.0 Hz), 4.82 (dd, 2H, *J* = 6.1, 2.9 Hz), 5.09 (m, 1H), 9.69 (d, 1H, *J* = 3.0 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.6, 198.9, 165.9, 85.8, 84.9, 77.5, 63.5, 59.2, 40.1; IR (CHCl₃) v 1957, 1760; HRMS (ES) calcd for C₉H₁₁NO₃[*M*]⁺ 181.0739; found: 181.0737.

Allenal (+)-3b. From 432 mg (1.49 mmol) of allenic dioxolane (+)-2b, compound (+)-3b (383 mg, quantitative yield) was obtained as a pale yellow oil; $[\alpha]_D = +40.9$ (*c* 0.2, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.91 (m, 1H), 4.01 (m, 1H), 4.19 (dd, 1H, *J* = 5.0, 3.1 Hz), 4.63 (d, 1H, *J* = 11.7 Hz), 4.77 (d, 1H, *J* = 11.7 Hz), 4.83 (m, 2H), 4.93 (d, 1H, *J* = 5.1 Hz), 5.09 (m, 1H, *J* = 6.6 Hz), 7.33 (m, 5H), 9.61 (d, 1H, *J* = 3.1 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.6, 198.8, 166.0, 135.9, 128.5, 128.4, 128.2 (2C), 84.9, 83.4, 77.4, 73.3, 63.6, 40.1; IR (CHCl₃) v 1957, 1742; HRMS (ES) calcd for C₁₅H₁₅NO₃[*M*]⁺ 257.1052; found: 257.1046.

Allenal (+)-3c. From 661 mg (2.40 mmol) of allenic dioxolane (+)-2c, compound (+)-3c (584 mg, quantitative yield) was obtained as a pale brown oil; $[\alpha]_D = +16.8$ (*c* 0.9, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.95 (m, 1H), 4.08 (m, 1H), 4.45 (dd, 1H, *J* = 5.1, 2.8 Hz), 4.86 (m, 2H), 5.13 (m, 1H), 5.46 (d, 1H, *J* = 5.1 Hz), 7.03 (m, 3H), 7.31 (m, 2H), 9.72 (d, 1H, *J* = 2.8 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.6, 197.4, 164.5, 156.8, 129.7 (2C), 122.9, 115.5 (2C), 84.8, 82.1, 77.6, 63.4, 40.3; IR (CHCl₃) v 1957, 1748; HRMS (ES) calcd for C₁₄H₁₃NO₃[*M*]⁺ 243.0895; found: 243.0899.

Indium-promoted reaction between 3-substituted prop-2-ynyl bromides and allenals 3. General procedure for the synthesis of bis(allene)s 5a. 1-Bromobut-2-yne, (3-bromoprop-1ynyl)benzene or 1-(3-bromoprop-1-ynyl)-4-methoxybenzene (3.0 mmol) was added to a well stirred suspension of the appropriate allenal (1.0 mmol) and indium powder (6.0 mmol) in THF/NH4Cl (aq. sat.) (1:5, 5 mL) at 0 °C. After disappearance of the starting material (TLC) the mixture was extracted with ethyl acetate (3 x 5 mL). The organic extract was washed with brine, dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes or dichloromethane/ethyl acetate mixtures gave analytically pure compounds. Spectroscopic and analytical data for pure forms of **5** follow.

Preparation of (+)-*syn*-**4a and (+)**-*anti*-**4a.** From 300 mg (1.65 mmol) of allenal (+)-**3a**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent, 234 mg (80%) of

the less polar compound (+)-*syn*-4a and 36 mg (8%) of the more polar compound (+)-*anti*-4a were obtained.

Bis(allene) (+)-*syn*-4a. Colorless oil; $[\alpha]_D = +26.0$ (*c* 0.4, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.79 (t, 3H, *J* = 3.2 Hz), 3.57 (s, 3H), 3.70 (ddt, 1H, *J* = 15.3, 6.9, 2.5 Hz), 4.02 (dd, 1H, *J* = 4.8, 4.2 Hz), 4.15 (ddt, 1H, *J* = 15.3, 5.5, 3.5 Hz), 4.25 (dd, 1H, *J* = 6.5, 3.1 Hz), 4.47 (d, 1H, *J* = 4.9 Hz), 4.82 (m, 4H, =CH₂), 5.12 (qd, 1H, *J* = 6.9, 5.6 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 208.8, 205.4, 167.4, 99.7, 86.1, 83.6, 77.4, 76.9, 70.1, 59.6, 59.1, 39.7, 16.0; IR (CHCl₃) v 3392, 1958, 1742; HRMS (ES) calcd for C₁₃H₁₇NO₃[*M*]⁺ 235.1208; found: 235.1208.

Bis(allene) (+)-*anti*-4a. Colorless oil; $[\alpha]_D = +61.2$ (*c* 0.8, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.83 (t, 3H, *J* = 3.0 Hz), 3.63 (s, 3H), 3.97 (dd, 1H, *J* = 5.9, 4.9 Hz), 4.09 (m, 2H), 4.32 (d, 1H, *J* = 5.6 Hz), 4.58 (d, 1H, *J* = 4.8 Hz), 4.78 (m, 2H), 4.83(m, 2H), 5.09 (m, 1H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.0, 206.0, 167.2, 98.8, 85.7, 84.4, 77.3, 76.2, 71.0, 59.6, 58.1, 38.5, 15.2; IR (CHCl₃): v 3393, 1960, 1747; HRMS (ES) calcd for C₁₃H₁₇NO₃[*M*]⁺ 235.1208; found: 235.1211.

Bis(allene) (+)-*syn*-4**b.** From 302 mg (1.66 mmol) of allenal (+)-3**a**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (+)-*syn*-4**b** (336 mg, 68%) as a colorless oil; $[\alpha]_D = +28.0$ (*c* 0.5, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 ^oC) δ 3.57 (s, 3H), 3.77 (ddt, 1H, *J* = 15.3, 6.5, 2.6 Hz), 4.10 (t, 1H, *J* = 5.1 Hz), 4.17 (m, 1H), 4.45 (d, 1H, *J* = 4.8 Hz), 4.74 (m, 2H), 4.93 (m, 1H), 5.09 (dt, 1H, *J* = 12.4, 6.2 Hz), 5.26 (qd, 1H, *J* = 12.3, 2.5 Hz), 7.34 (m, 5H); ¹³C-NMR (75 MHz, CDCl₃, 25 ^oC) δ 208.8, 207.6, 167.5, 133.9, 128.6 (2C), 127.3, 126.7 (2C), 107.0, 86.0, 83.5, 80.6, 77.1, 68.4, 59.6, 59.6, 39.7; IR (CHCl₃) v 3391, 1956, 1743; HRMS (ES) calcd for C₁₈H₁₉NO₃[*M*]⁺ 297.1365; found: 297.1365.

Preparation of (+)-*syn*-**4c and (+)**-*anti*-**4c.** From 473 mg (2.60 mmol) of allenal (+)-**3a**, and after chromatography of the residue using dichloromethane/ethyl acetate (9:1) as eluent, 357 mg

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(42%) of the less polar compound (+)-*syn*-4c and 137 mg (16%) of the more polar compound (+)*anti*-4c were obtained.

Bis(allene) (+)-*syn*-4c. Colorless oil; $[\alpha]_D = +41.7$ (*c* 1.2, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 2.61 (brs, 1H), 3.54 (s, 3H), 3.76 (ddd, 1H, *J* = 6.7, 5.6, 2.6 Hz), 3.81 (s, 3H), 4.10 (t, 1H, *J* = 5.0 Hz), 4.19 (ddt, 1H, *J* = 15.3, 5.7, 3.5 Hz), 4.47 (d, 1H, *J* = 4.8 Hz), 4.76 (td, 2H, *J* = 6.4, 3.2 Hz), 4.90 (m, 1H), 5.11 (m, 1H), 5.25 (qd, 2H, *J* = 12.1, 2.8 Hz), 6.90 (d, 2H, *J* = 8.8 Hz), 7.36 (d, 2H, *J* = 8.8 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 208.8, 207.2, 167.4, 159.0, 127.9 (2C), 125.9, 114.3 (2C), 106.5, 86.0, 83.6, 80.6, 77.2, 68.5, 59.6, 59.6, 55.3, 39.7; IR (CHCl₃) v 3398, 1956, 1737; HRMS (ES) calcd for C₁₉H₂₁NO₄[*M*]⁺ 327.1473; found 327.1471.

Bis(allene) (+)-*anti*-4c. Colorless oil; $[\alpha]_D = +28.8$ (*c* 1.5, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.61 (m, 1H), 3.65 (s, 3H), 3.81 (s, 3H), 4.04 (m, 1H), 4.09 (m, 1H), 4.61 (d, 1H, *J* = 4.8 Hz), 4.77 (dt, 2H, *J* = 6.3, 3.0 Hz), 4.87 (m, 1H), 5.06 (m, 1H), 5.25 (m, 2H), 6.89 (d, 2H, *J* = 8.8 Hz), 7.44 (d, 2H, *J* = 8.8 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 208.8, 208.1, 167.2, 158.9, 127.8 (2C), 126.1, 114.0 (2C), 105.8, 85.8, 84.5, 80.6, 77.3, 68.8, 59.6, 58.8, 55.3, 38.5; IR (CHCl₃) v 3422, 1956, 1744; HRMS (ES) calcd for C₁₉H₂₁NO₄[*M*]⁺ 327.1473; found 327.1471.

Preparation of (+)-*syn*-**4d and (+)**-*anti*-**4d.** From 335 mg (1.38 mmol) of allenal (+)-**3c**, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent, 61 mg (15%) of the less polar compound (+)-*anti*-**4d** and 172 mg (42%) of the more polar compound (+)-*syn*-**4d** were obtained.

Bis(allene) (+)-*syn*-4d. Colorless oil; $[\alpha]_D = +70.0$ (*c* 1.2, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.81 (t, 3H, *J* = 3.1 Hz), 3.84 (ddt, 1H, *J* = 15.3, 6.8, 2.6 Hz), 4.19 (m, 2H), 4.39 (dd, 1H, *J* = 5.1, 2.5 Hz), 4.74 (dd, 2H, *J* = 6.5, 3.2 Hz), 4.86 (m, 2H), 5.19 (m, 2H, H3), 7.05 (m, 3H), 7.30 (m, 2H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.0, 205.6, 166.2, 157.6, 129.5 (2C),

122.5, 115.9 (2C), 99.5, 86.0, 80.5, 77.4, 77.2, 70.9, 59.5, 40.1, 15.9; IR (CHCl₃) v 3420, 1957, 1736; HRMS (ES) calcd for C₁₈H₁₉NO₃[*M*]⁺ 297.1365; found 297.1372.

Bis(allene) (+)-*anti*-4d. Colorless solid; mp 91–93 °C; $[\alpha]_D = +120.4$ (*c* 1.6, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.88 (t, 3H, *J* = 3.1 Hz), 2.73 (brs, 1H), 3.68 (ddt, 1H, *J* = 15.4, 7.0, 2.5 Hz), 4.18 (m, 2H, H4), 4.47 (d, 1H, *J* = 5.6 Hz), 4.71 (dd, 2H, *J* = 5.3, 2.4 Hz), 4.88 (m, 2H), 5.15 (m, 1H), 5.32 (d, 1H, *J* = 4.9 Hz), 7.06 (t, 1H, *J* = 7.3 Hz), 7.14 (m, 2H), 7.32 (m, 2H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.1, 206.2, 165.9, 157.4, 129.6 (2C), 122.9, 116.2 (2C), 98.4, 85.6, 82.0, 77.4, 76.4, 70.8, 58.4, 38.8, 15.2; IR (CHCl₃) v 3421, 1957, 1743; HRMS (ES) calcd for C₁₈H₁₉NO₃[*M*]⁺ 297.1365; found: 297.1372.

Bis(allene) (+)-*syn*-4e. From 223 mg (0.92 mmol) of allenal (+)-3c, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent gave compound (+)-*syn*-4e (188 mg, 57%) as a colorless oil; $[\alpha]_D = +85.6$ (*c* 0.8, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.94 (ddt, 1H, J = 15.3, 6.7, 2.6 Hz), 4.28 (m, 2H), 4.85 (m, 2H), 5.09 (m, 1H), 5.17 (m, 2H), 5.23 (m, 2H), 7.00 (m, 2H), 7.36 (m, 8H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.0, 207.8, 166.4, 157.6, 134.0, 129.4 (2C), 128.7 (2C), 127.4, 126.7 (2C), 122.4, 115.9 (2C), 106.9, 85.9, 80.6, 80.4, 77.2, 69.7, 60.0, 40.2; IR (CHCl₃) v 3452, 1959, 1752; HRMS (ES) calcd for C₂₃H₂₁NO₃[*M*]⁺ 359.1521; found 359.1519.

Bis(allene) (+)-*syn*-**4f.** From 256 mg (1.05 mmol) of allenal (+)-**3c**, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent gave compound (+)-*syn*-**4f** (196 mg, 48%) as a colorless oil; $[\alpha]_D = +76.0$ (*c* 0.4, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.87 (s, 3H), 3.99 (m, 1H), 4.30 (m, 2H), 4.88 (m, 2H), 5.06 (m, 1H), 5.12 (d, 1H, J = 2.0 Hz), 5.18 (d, 1H, J = 1.6 Hz), 5.25 (m, 2H), 6.95 (d, 2H, J = 8.9 Hz), 7.03 (m, 3H), 7.31 (dd, 2H, J = 7.4, 1.1 Hz), 7.41 (d, 2H, J = 8.8 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 208.9, 207.5, 166.3, 159.0, 157.6, 129.4 (2C), 127.9 (2C), 126.0, 122.3, 116.0 (2C), 114.2 (2C), 106.4, 85.9, 80.5, 80.4, 77.2, 69.8, 60.0,

55.3, 40.2; IR (CHCl₃) v 3447, 1956, 1753; HRMS (ES) calcd for C₂₄H₂₃NO₄[*M*]⁺ 389.1627; found 389.1622.

Preparation of (–)-*syn*-**4g and (+)**-*anti*-**4g.** From 200 mg (0.78 mmol) of allenal (+)-**3b**, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent, 36 mg (15%) of the less polar compound (+)-*anti*-**4g** and 175 mg (72%) of the more polar compound (–)-*syn*-**4g** were obtained.

Bis(allene) (–)-*syn*-**4g.** Colorless oil; $[\alpha]_D = -163.0$ (*c* 0.5, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.78 (t, 3H, *J* = 3.1 Hz), 3.72 (ddt, 1H, *J* = 15.3, 7.0, 2.5 Hz), 4.02 (m, 1H), 4.19 (m, 2H, OCH), 4.69 (dd, 2H, *J* = 8.2, 3.3 Hz), 4.82 (m, 4H, =CH₂), 4.93 (d, 1H, *J* = 11.6 Hz) 5.11 (m, 1H), 7.35 (s, 5H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 208.9, 205.4, 167.4, 136.6, 128.6 (2C), 128.2, 128.0 (2C), 99.6, 86.1, 81.2, 77.4, 77.1, 73.4, 70.1, 58.9, 39.8, 16.1; IR (CHCl₃) v 3385, 1958, 1741; HRMS (ES) calcd for C₁₉H₂₁NO₃[*M*]⁺ 311.1521; found 311.1527.

Bis(allene) (+)-*anti*-4g. Colorless oil; $[\alpha]_D = +75.2$ (*c* 1.8, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.82 (t, 3H, *J* = 3.1 Hz), 3.01 (brs, 1H), 3.62 (ddt, 1H, *J* = 15.4, 6.9, 2.4 Hz), 3.98 (m, 1H), 4.11 (m, 1H), 4.36 (d, 1H, *J* = 5.9 Hz), 4.75 (m, 4H), 4.84 (m, 2H), 4.97 (d, 1H, *J* = 11.5 Hz), 5.10 (m, 1H), 7.36 (s, 5H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.0, 206.0, 167.1, 136.4, 128.6 (2C), 128.2, 128.0 (2C), 98.8, 85.7, 82.0, 77.2, 76.3, 73.4, 70.9, 58.0, 38.6, 15.1; IR (CHCl₃) v 3420, 1957, 1738; HRMS (ES) calcd for C₁₉H₂₁NO₃[*M*]⁺ 311.1521; found 311.1529.

Bis(allene) (+)-*syn*-**4h.** From 248 mg (0.96 mmol) of allenal (+)-**3b**, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent gave compound (+)-*syn*-**4h** (200 mg, 56%) as a colorless oil; $[\alpha]_D = +174.7$ (*c* 0.2, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.77 (ddt, 1H, *J* = 15.3, 6.8, 2.6 Hz), 4.05 (t, 1H, *J* = 5.1 Hz) 4.18 (ddt, 1H, *J* = 15.3, 5.6, 3.5 Hz), 4.62 (m, 2H), 4.71 (m, 2H), 4.88 (m, 2H), 5.16 (m, 3H), 7.30 (m, 10H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 208.8, 207.6, 167.6, 136.7, 133.9, 128.6 (2C), 128.5 (2C), 128.1, 128.0 (2C),

127.4, 126.7 (2C), 107.0, 86.0, 81.1, 80.7, 77.1, 73.4, 68.6, 59.6, 39.8; IR (CHCl₃) v 3455, 1958, 1742; HRMS (ES) calcd for $C_{24}H_{23}NO_3[M]^+$ 373.1678; found 373.1678.

General procedure for the preparation of bis(allenyl) methyl ethers 5a–h. Tetrabutyl ammonium iodide (cat), 50% aqueous sodium hydroxide (18 mL) and dimethyl sulfate (0.60 mmol) were sequentially added at room temperature to a solution of the corresponding bis(allenyl) alcohol **4** (0.92 mmol) in dichloromethane (18 mL). The reaction was stirred until disappearance of the starting material (TLC). Then aqueous ammonia (30%) was added (2.5 mL), before being partitioned between dichloromethane and water. The aqueous phase was extracted with dichloromethane (3 x 15 mL), the combined organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for some representative pure forms of compounds **5a–h** follow.

Bis(allenyl) methyl ether (+)-5a. From 150 mg (0.64 mmol) of bis(allenyl) alcohol (+)-*syn*-**4a**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (+)-**5a** (115 mg, 72%) as a colorless oil; $[\alpha]_D = +10.4$ (*c* 0.7, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.72 (t, 3H, *J* = 3.2 Hz), 3.30 (s, 3H) 3.48 (s, 3H), 3.77 (ddt, 1H, *J* = 15.3, 6.9, 2.5 Hz), 3.90 (m, 2H), 4.08 (ddt, 1H, *J* = 15.1, 5.8, 3.4 Hz), 4.42 (dd, 1H, *J* = 3.0, 1.3 Hz), 4.74 (q, 2H, *J* = 3.2 Hz), 4.81 (m, 2H), 5.12 (qd, 1H, *J* = 6.9, 5.6 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 208.8, 207.9, 167.6, 95.3, 86.1, 83.5, 82.2, 76.9, 75.1, 59.5, 58.9, 55.6, 39.8, 14.6; IR (CHCl₃) v 1960, 1747; HRMS (ES) calcd for C₁₄H₁₉NO₃[*M*]⁺ 249.1365; found 249.1360.

Bis(allenyl) methyl ether (+)-5b. From 150 mg (0.64 mmol) of bis(allenyl) alcohol (+)-*syn*-**4b**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (+)-**5b** (98 mg, 61%) as a colorless oil; $[\alpha]_D = +11.8$ (*c* 1.6, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.26 (s, 3H), 3.31 (s, 3H), 3.75 (ddt, 1H, *J* = 15.1, 6.8, 2.6 Hz), 4.08 (m, 2H), 4.30 (d, 1H, *J* = 4.8 Hz), 4.43 (d, 1H, *J* = 9.3 Hz), 4.74 (m, 2H), 5.10 (m, 3H), 7.23 (m, 3H),

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7.46 (m, 2H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 210.0, 209.9, 167.6, 134.6, 128.5 (2C), 127.2, 126.9 (2C), 103.1, 86.1, 83.6, 80.5, 78.5, 76.9, 59.6, 59.4, 55.4, 39.9; IR (CHCl₃) v 1956, 1744; HRMS (ES) calcd for C₁₉H₂₁NO₃[*M*]⁺ 311.1521; found 311.1508.

Bis(allenyl) methyl ether (+)-5c. From 140 mg (0.43 mmol) of bis(allenyl) alcohol (+)-*syn*-**4c**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (+)-**5c** (92 mg, 63%) as a colorless oil; $[\alpha]_D = +12.4$ (*c* 1.5, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.32 (s, 3H), 3.39 (s, 3H), 3.84 (m, 4H), 3.81 (s, 3H), 4.14 (m, 2H), 4.37 (d, 1H, *J* = 4.7 Hz), 4.47 (d, 1H, *J* = 9.3 Hz), 4.82 (m, 2H), 5.16 (m, 3H), 6.89 (d, 2H, *J* = 8.8 Hz), 7.45 (d, 2H, *J* = 8.8 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.9, 209.2, 167.8, 159.1, 128.4 (2C), 127.0, 114.3 (2C), 102.9, 86.4, 83.9, 80.9, 78.7, 77.2, 60.0, 59.3, 55.6, 55.5, 40.2; IR (CHCl₃) v 1957, 1753; HRMS (ES) calcd for C₂₀H₂₃NO₄[*M*]⁺ 341.1627; found 341.1616.

Bis(allenyl) methyl ether (+)-5d. From 68 mg (0.23 mmol) of bis(allenyl) alcohol (+)-*syn*-**4d**, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent gave compound (+)-5d (47 mg, 66%) as a colorless oil; $[\alpha]_D = +20.0$ (*c* 0.1, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.69 (t, 3H, *J* = 3.2 Hz), 3.32 (s, 3H), 3.85 (m, 1H), 4.06 (m, 2H), 4.15 (m, 1H), 4.37 (m, 1H), 4.60 (m, 1H), 4.84 (m, 2H), 5.19 (m, 2H), 7.00 (m, 3H), 7.27 (m, 2H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 210.0, 208.3, 166.1, 157.9, 129.3 (2C), 122.0, 115.6 (2C), 94.6, 86.0, 82.3, 79.9, 77.0, 75.0, 58.4, 55.6, 40.2, 14.2; IR (CHCl₃) v 1958, 1762; HRMS (ES) calcd for C₁₉H₂₁NO₃[*M*]⁺ 311.1521; found 311.1522.

Bis(allenyl) methyl ether (+)-5e. From 77 mg (0.21 mmol) of bis(allenyl) alcohol (+)-*syn*-**4e**, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent gave compound (+)-**5e** (46 mg, 59%) as a colorless oil; $[\alpha]_D = +44.4$ (*c* 0.2, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.41 (s, 3H), 3.92 (m, 1H), 4.24 (m, 1H), 4.31 (dd, 1H, *J* = 9.2, 4.9 Hz), 4.62 (d, 1H, *J* = 9.1 Hz), 4.78 (d, 1H, *J* = 12.4 Hz), 4.85 (m, 2H), 4.99 (d, 1H, *J* = 12.5 Hz), 5.14 (d, 1H, *J* = 4.9 Hz), 5.21 (m, 1H), 6.81 (m, 2H), 6.99 (m, 2H), 7.29 (m, 4H), 7.48 (m, 2H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 210.5, 209.2, 166.2, 157.8, 134.4, 129.2 (2C), 128.5 (2C), 127.2 (3C), 121.9, 115.6 (2C), 102.3, 85.9, 81.2, 79.8, 78.1, 77.2, 58.7, 55.5, 40.4); IR (CHCl₃) v 1959, 1760; HRMS (ES) calcd for C₂₄H₂₃NO₃[*M*]⁺ 373.1678; found 373.1690.

Bis(allenyl) methyl ether (+)-5f. From 54 mg (0.14 mmol) of bis(allenyl) alcohol (+)-*syn*-4f, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent gave compound (+)-**5f** (36 mg, 64%) as a colorless oil; $[\alpha]_D = +26.0$ (*c* 0.2, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.40 (s, 3H), 3.83 (s, 3H), 3.92 (m, 1H), 4.24 (m, 1H), 4.30 (dd, 1H, *J* = 9.2, 4.9 Hz), 4.57 (d, 1H, *J* = 9.2 Hz), 4.71 (d, 1H, *J* = 12.2 Hz), 4.86 (m, 2H), 4.95 (d, 1H, *J* = 12.2 Hz), 5.13 (d, 1H, *J* = 4.8 Hz), 5.21 (m, 1H), 6.86 (m, 4H), 6.98 (t, 1H, *J* = 7.4 Hz), 7.24 (m, 2H), 7.40 (d, 2H, *J* = 8.8 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 210.2, 209.2, 166.1, 158.9, 157.9, 129.2 (2C), 128.4 (2C), 126.4, 121.9, 115.7 (2C), 114.0 (2C), 101.6, 85.9, 81.5, 79.8, 77.9, 77.2, 58.6, 55.4, 55.3, 40.3; IR (CHCl₃) v 1957, 1759; HRMS (ES) calcd for C₂₅H₂₅NO₄[*M*]⁺ 403.1784; found 403.1781.

Bis(allenyl) methyl ether (-)-5g. From 71 mg (0.23 mmol) of bis(allenyl) alcohol (-)-*syn*-4g, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent gave compound (-)-5g (60 mg, 80%) as a colorless oil; $[\alpha]_D = -5.5$ (*c* 1.0, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.71 (t, 3H, *J* = 3.2 Hz), 3.31 (s, 3H), 3.79 (ddt, 1H, *J* = 15.1, 6.6, 2.6 Hz), 3.94 (m, 2H), 4.11 (m, 1H), 4.61 (m, 4H), 4.82 (m, 3H), 5.15 (m, 4H), 7.32 (m, 5H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 208.9, 207.9, 167.8, 137.3, 128.3 (2C), 127.7, 127.6 (2C), 95.2, 86.1, 82.3, 81.0, 76.9, 75.2, 72.9, 58.5, 55.5, 39.9, 14.7; IR (CHCl₃) v 1957, 1752; HRMS (ES) calcd for C₂₀H₂₃NO₃[*M*]⁺ 325.1678; found 325.1681.

Bis(allenyl) methyl ether (+)-5h. From 75 mg (0.20 mmol) of bis(allenyl) alcohol (+)-*syn*-**4h**, and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent gave compound (+)-**5h** (44 mg, 54%) as a colorless oil; $[\alpha]_D = +17.0$ (*c* 0.1, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 3.35 (s, 3H), 3.84 (ddt, 1H, *J* = 15.0, 6.8, 2.6 Hz), 4.16 (m, 2H), 4.57 (m, 3H), 4.75 (d, 1H, *J* = 11.9 Hz), 4.81 (m, 2H), 5.03 (q, 2H, *J* = 12.5 Hz), 5.16 (td, 1H, *J* = 12.5, 6.7 Hz), 7.29 (m, 8H), 7.51 (m, 2H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 210.1, 209.0, 167.9, 137.2, 134.7, 128.5 (2C), 128.2 (2C), 127.7, 127.7 (2C), 127.2, 127.0 (2C), 103.0, 86.1, 81.0, 80.5, 78.5, 76.9, 73.1, 58.7, 55.3, 40.0; IR (CHCl₃) v 1959, 1758; HRMS (ES) calcd for C₂₅H₂₅NO₃[*M*]⁺ 387.1834; found 387.1830.

General procedure for the preparation of bis(allenyl) acetates 5i–k. Triethylamine (0.94 mmol) and acetic anhydride (0.47 mmol) were sequentially added dropwise via syringe to a solution of the corresponding bis(allenyl) alcohol **4** (0.39 mmol) and DMAP (cat) in dichloromethane (4 mL) at 0 °C under argon. The resulting mixture was allowed to warm to room temperature and stirred for 2 h. The crude mixture was diluted with CH_2Cl_2 (10 mL) and washed with saturated aqueous ammonium chloride (3 x 5 mL) and brine (3 x 5 mL). The organic layer was dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for some representative pure forms of compounds **5i–k** follow.

Bis(allenyl) acetate (+)-5i. From 75 mg (0.32 mmol) of bis(allenyl) alcohol (+)-*syn*-4a, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (+)-**5i** (57 mg, 64%) as a colorless oil; $[\alpha]_D = +27.1$ (*c* 0.4, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 1.76 (t, 3H, J = 3.2 Hz), 2.08 (s, 3H) 3.51 (s, 3H), 3.56 (m, 1H), 4.10 (m, 2H), 4.46 (d, 1H, J = 4.9 Hz), 4.84 (m, 4H), 5.08 (td, 1H, J = 12.4, 6.8 Hz), 5.39 (m, 1H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 208.9, 206.9, 169.9, 167.6, 97.7, 85.7, 83.5, 77.4, 77.3, 72.6, 59.5, 58.3, 39.6, 21.1, 16.4; IR (CHCl₃) v 1958 (C=C=C), 1748 (C=O); HRMS (ES) calcd for C₁₅H₁₉NO₄[M]⁺ 277.1314; found: 277.1315.

Bis(allenyl) acetate (+)-5j. From 50 mg (0.17 mmol) of bis(allenyl) alcohol (+)-*syn*-4b, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (+)-5j (43 mg, 74%) as a colorless oil; $[\alpha]_D = +37.1$ (*c* 0.8, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 2.06 (s, 3H), 3.39 (s, 3H), 3.57 (m, 1H), 4.24 (m, 2H), 4.46 (d, 1H, *J* = 4.8 Hz), 4.81 (m, 2H),

5.08 (m, 1H), 5.28 (m, 2H), 6.09 (dt, 1H, J = 7.1, 1.8 Hz) 7.35 (m, 3H), 7.46 (m, 2H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 209.1, 209.0, 169.9, 169.6, 128.6 (2C), 127.5, 126.8 (2C), 106.6, 105.5, 85.6, 83.6, 80.6, 77.3, 70.2, 59.6, 58.6, 39.7, 21.1; IR (CHCl₃) v 1957, 1753; HRMS (ES) calcd for C₂₀H₂₁NO₄[M]⁺ 339.1471; found 339.1460.

Bis(allenyl) acetate (+)-5k. From 160 mg (0.49 mmol) of bis(allenyl) alcohol (+)-*syn*-4c, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (+)-**5k** (123 mg, 68%) as a colorless oil; $[\alpha]_D = +9.8$ (*c* 1.7, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 ^oC) δ 2.05 (s, 3H), 3.38 (s, 3H), 3.53 (m, 1H), 3.80 (s, 3H), 4.19 (m, 2H), 4.45 (d, 1H, *J* = 4.9 Hz), 4.82 (m, 2H) , 5.07 (qd, 1H, *J* = 6.9, 5.5 Hz), 5.24 (dd, 2H, *J* = 3.6, 1.8 Hz), 6.05 (dt, 1H, *J* = 7.2, 1.8 Hz), 6.87 (d, 2H, *J* = 8.9 Hz), 7.37 (d, 2H, *J* = 8.9 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 ^oC) δ 209.0, 208.7, 169.7, 167.6, 159.0, 127.9 (2C), 125.3, 114.0 (2C), 104.9, 85.5, 83.5, 80.6, 77.3, 70.2, 59.6, 58.6, 55.2, 39.6, 21.1; IR (CHCl₃) v 1957, 1753; HRMS (ES) calcd for C₂₁H₂₃NO₅[*M*]⁺ 369.1576; found 369.1584.

General procedure for the microwave-promoted reaction of β -lactam bis(allene)s 4. Preparation of azocinone- β -lactams 6. A stirred solution of the corresponding bis(allene) 4 (0.1 mmol) in toluene (2.0 mL) was heated at the appropriate temperature under microwave irradiation until disappearance of the starting material (TLC). The reaction was allowed to cool to room temperature, concentrated under vacuum, and purified by flash column chromatography eluting with ethyl acetate/dichloromethane mixtures. Spectroscopic and analytical data for pure forms of compounds 6 follow.

Azocinone-β-lactam (+)-6a. Microwave heating (toluene, 250 °C, 1h). From 40 mg (0.16 mmol) of bis(allene) (+)-4a, and after chromatography of the residue using dichloromethane/ethyl acetate (9:1) as eluent gave compound (+)-6a (10 mg, 25%) as a colorless oil; $[\alpha]_D = +156.0$ (*c* 0.7, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 5.22 (d, 1H, 0.6 Hz), 5.12 (d, 1H, J = 1.7 Hz), 4.91 (t, 1H, J = 1.1 Hz), 4.89 (m, 1H), 4.68 (dd, 1H, J = 4.8, 0.7 Hz), 4.13 (m, 2H), 3.92 (dq, 1H, J = 1.2 Hz)

6.5, 0.7 Hz), 3.46 (s, 3H), 2.83 (m, 1H), 2.58 (m, 1H), 2.45 (ddd, 1H, J = 14.9, 5.1, 2.8 Hz), 1.23 (d, 3H, J = 6.7 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ : 208.9, 166.6, 148.4, 148.2, 115.7, 114.6, 86.5, 67.0, 59.4, 45.4, 43.3, 33.8, 13.4; IR (CHCl₃) v 1755, 1719; HRMS (ES) calcd for C₁₃H₁₇NO₃[M]⁺ 235.1208; found 235.1215.

Azocinone-β-lactam (+)-6d. Microwave heating (toluene, 185 °C, 26h). From 40 mg (0.13 mmol) of bis(allene) (+)-4d, and after chromatography of the residue using dichloromethane/ethyl acetate (9:1) as eluent gave compound (+)-6d (9 mg, 23%) as a colorless oil; $[\alpha]_D = +111.8$ (*c* 0.5, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 7.30 (m, 2H), 7.04 (m, 3H), 5.39 (d, 1H, *J* = 5.2 Hz), 5.23 (s, 1H), 5.15 (d, 1H, *J* = 1.5 Hz), 4.94 (d, 2H, *J* = 1.0 Hz), 4.35 (d, 1H, *J* = 5.2 Hz), 4.18 (ddd, 1H, *J* = 13.9, 5.8, 3.2 Hz), 3.98 (q, 1H, *J* = 6.6 Hz), 2.93 (m, 1H), 2.60 (m, 1H), 2.47 (m, 1H), 1.24 (d, 3H, *J* = 6.7 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 208.0, 165.4, 157.1, 148.2 (2C), 129.6 (2C), 122.9, 116.0, 115.9 (2C), 114.7, 83.2, 66.7, 45.9, 43.5, 33.7, 13.7; IR (CHCl₃) v 1768, 1722; HRMS (ES) calcd for C₁₈H₁₉NO₃[*M*]⁺ 297.1365; found 297.1355.

General procedure for the microwave-promoted reaction of β -lactam bis(allene)s 5. Preparation of azocine- β -lactams 7. A stirred solution of the corresponding bis(allene) 5 (0.1 mmol) in toluene (2.0 mL) was heated at the appropriate temperature under microwave irradiation until disappearance of the starting material (TLC). The reaction was allowed to cool to room temperature, concentrated under vacuum, and purified by flash column chromatography eluting with hexanes/ethyl acetate or ethyl acetate/dichloromethane mixtures. Spectroscopic and analytical data for pure forms of compounds 7 follow.

Azocine-β-lactam (–)-7a. Microwave heating (toluene, 250 °C, 0.5h). From 50 mg (0.2 mmol) of bis(allene) (+)-5a, and after chromatography of the residue using dichloromethane/ethyl acetate (9:1) as eluent gave compound (–)-7a (30 mg, 60%) as a colorless oil; $[\alpha]_D = -106.0$ (*c* 0.6, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 5.29 (d, 1H, J = 2.0 Hz), 5.13 (d, 1H, J = 1.3), 4.83

(t, 1H, J = 1.8 Hz), 4.70 (d, 1H, J = 2.0 H), 4.52 (dd, 1H, J = 4.6, 1.2 Hz), 4.22 (d, 1H, J = 4.5), 3.71 (td, 1H, J = 13.7, 4.0 Hz), 3.60 (s, 3H), 3.51 (s, 3H), 3.03 (m, 1H), 2.66 (m, 1H), 2.18 (ddd, 1H, J = 14.3, 3.8, 2.1 Hz),1.79 (d, 3H, J = 0.8 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 167.1, 148.4, 148.3, 144.8, 123.9, 113.9, 112.7, 85.1, 59.2, 58.7, 58.4, 41.1, 32.0, 18.2; IR (CHCl₃) v 1753; HRMS (ES) calcd for C₁₄H₁₉NO₃[M]⁺ 249.1365; found 249.1365.

Azocine-β-lactam (-)-7b. Microwave heating (toluene, 200 °C, 1h). From 40 mg (0.13 mmol) of bis(allene) (+)-5b, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent gave compound (-)-7b (21 mg, 50%) as a colorless oil; $[\alpha]_D = -34.0$ (*c* 0.4, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 7.31 (m, 5H), 5.48 (d, 1H, J = 2.0 Hz), 5.10 (s, 1H), 4.86 (m, 2H), 4.63 (d, 1H, J = 4.6), 4.35 (d, 1H, J = 4.6), 3.78 (td, 1H, J = 13.7, 4.0 Hz), 3.56 (s, 3H), 3.38 (s, 3H), 3.11 (dd, 1H, J = 13.6, 4.8 Hz), 2.82 (m, 1H), 2.24 (m, 1H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 167.0, 148.8, 147.0, 146.9, 138.3, 128.5 (2C), 128.0 (2C), 126.9, 125.2, 117.1, 113.2, 85.6, 61.0, 59.0, 58.9, 41.2, 32.0; IR (CHCl₃) v 1759; HRMS (ES) calcd for C₁₉H₂₁NO₃[M]⁺ 311.1521; found 311.1516.

Azocine-β-lactam (+)-7c. Microwave heating (toluene, 200 °C, 1h). From 40 mg (0.12 mmol) of bis(allene) (+)-5c, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (+)-7c (18 mg, 45%) as a colorless oil; $[\alpha]_D = +42.7$ (*c* 0.4, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 7.38 (d, 2H, *J* = 8.9 Hz), 6.84 (d, 2H, *J* = 8.9 Hz), 5.48 (d, 1H, *J* = 2.0 Hz), 5.10 (d, 1H, *J* = 1.6 Hz), 4.84 (m, 2H), 4.61 (d, 1H, *J* = 4.6 Hz), 4.34 (d, 1H, *J* = 4.6 Hz), 3.80 (m, 4H), 3.55 (s, 3H), 3.39 (s, 3H), 3.10 (dd, 1H, *J* = 13.3, 5.3 Hz), 2.78 (m, 1H), 2.21 (m, 1H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 167.1, 158.4, 148.0, 147.2, 147.1, 130.4, 129.7 (2C), 124.8, 116.9, 113.4 (2C), 113.1, 85.6, 61.1, 58.8, 58.8, 55.2, 41.2, 32.0; IR (CHCl₃) v 1756; HRMS (ES) calcd for C₂₀H₂₃NO₄[*M*]⁺ 341.1627; found: 341.1625. **Azocine-β-lactam** (-)-7d. Microwave heating (toluene, 225 °C, 1h). From 40 mg (0.13 mmol) of bis(allene) (+)-5d, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (-)-7d (21 mg, 50%) as a colorless oil; $[\alpha]_D = -49.5$ (*c* 0.6, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 7.31 (dd, 1H, *J* = 7.0, 1.7 Hz), 7.09 (dd, 2H, *J* = 8.7, 1.0 Hz), 7.01 (m, 2H), 5.29 (d, 1H, *J* = 1.9 Hz), 5.25 (dd, 1H, *J* = 4.7, 1.1 Hz), 5.17 (d, 1H, *J* = 1.4 Hz), 4.87 (t, 1H, *J* = 1.7 Hz), 4.72 (d, 1H, *J* = 1.9 H), 4.41 (d, 1H, *J* = 4.7 Hz), 3.80 (td, 1H, *J* = 13.8, 4.2 Hz), 3.56 (s, 3H), 3.10 (dd, 1H, *J* = 13.7, 5.0 Hz), 2.70 (td, 1H, *J* = 14.1, 5.0 Hz), 2.21 (ddd, 1H, *J* = 14.2, 4.0, 1.9 Hz), 1.80 (d, 3H, *J* = 0.8 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 165.9, 157.6, 148.5, 146.0, 144.8, 129.5 (2C) 124.2, 122.1, 115.9 (2C) 114.0, 113.0, 81.8, 60.2, 58.4, 41.3, 32.0, 18.1; IR (CHCl₃) v 1760; HRMS (ES) calcd for C₁₉H₂₁NO₃[*M*]⁺ 311.1521; found 311.1518.

Azocine-β-lactam (-)-7e. Microwave heating (toluene, 200 °C, 1h). From 40 mg (0.11 mmol) of bis(allene) (+)-5e, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent gave compound (-)-7e (24 mg, 61%) as a colorless oil; $[\alpha]_D = -109.4$ (*c* 0.2, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 7.34 (m, 5H), 7.21 (d, 1H, J = 7.2 Hz), 7.04 (m, 4H), 5.53 (d, 1H, J = 2.0 Hz), 5.37 (dd, 1H, J = 4.7, 0.9 Hz), 5.09 (d, 1H, J = 1.4 Hz), 4.97 (d, 1H, J = 1.9 Hz), 4.83 (m, 1H), 4.58 (d, 1H, J = 4.7 Hz), 3.87 (td, 1H, J = 13.7, 4.3 Hz), 3.20 (m, 1H), 3.13 (s, 3H), 2.83 (m, 1H), 2.22 (m, 1H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 165.7, 157.3, 151.2, 151.0, 146.4, 138.2, 137.4, 129.5 (2C), 128.6 (2C), 128.1 (2C), 127.1, 122.2, 117.1, 115.5 (2C), 113.5, 81.8, 62.1, 59.5, 41.4, 32.1; IR (CHCl₃) v 1763; HRMS (ES) calcd for C₂₄H₂₃NO₃[M]⁺ 373.1678; found: 373.1692.

Azocine-β-lactam (–)-7f. Microwave heating (toluene, 175 °C, 1h). From 50 mg (0.12 mmol) of bis(allene) (+)-5f, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent gave compound (–)-7f (24 mg, 47%) as a colorless oil; $[\alpha]_D = -30.0$ (*c* 0.4, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 7.31 (m, 4H, Ph), 7.08 (m, 3H), 6.83 (d, 2H, J = 8.9 Hz), 5.53

(d, 1H, J = 2.0 Hz), 5.36 (dd, 1H, J = 4.7, 0.8 Hz), 5.10 (d, 1H, J = 2.0 Hz), 4.94 (d, 1H, J = 2.0 Hz), 4.83 (m, 1H), 4.57 (d, 1H, J = 4.7 Hz), 3.80 (m, 4H), 3.19 (m, 1H), 3.15 (s, 3H), 2.79 (m, 1H), 2.21 (m, 1H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 167.0, 157.4, 151.8, 146.9, 138.2, 136.6, 129.8 (2C), 129.5 (2C), 126.5, 126.2, 125.2, 115.5 (2C), 113.6, 113.5 (2C), 113.5, 78.9, 63.5, 55.0, 53.10, 41.4, 30.1; IR (CHCl₃) v 1764; HRMS (ES) calcd for C₂₅H₂₅NO₄[M]⁺ 403.1784; found 403.1782.

Azocine-β-lactam (–)-7g. Microwave heating (toluene, 225 °C, 1h). From 50 mg (0.15 mmol) of bis(allene) (–)-5g, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (–)-7g (27 mg, 54%) as a colorless oil; $[\alpha]_D = -65.9$ (*c* 0.5, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 7.35 (m, 5H), 5.28 (d, 1H, *J* = 1.9 Hz), 5.14 (d, 1H, *J* = 1.6 Hz), 4.83 (s, 1H), 4.70 (m, 4H), 4.24 (d, 1H, *J* = 4.4 Hz), 3.73 (td, 1H, *J* = 13.8, 3.9 Hz), 3.61 (s, 3H), 3.04 (dd, 1H, *J* = 13.6, 4.6 Hz), 2.68 (td, 1H, *J* = 14.1, 4.9 Hz), 2.19 (ddd, 1H, *J* = 14.4, 3.7, 2.0 Hz), 1.80 (s, 3H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 167.0, 148.8, 146.4, 144.9, 137.4, 128.3 (2C), 127.9 (2C), 127.7, 124.0, 114.0, 112.7, 82.9, 72.2, 59.4, 58.5, 41.2, 32.0, 18.2; IR (CHCl₃) v 1757; HRMS (ES) calcd for C₂₀H₂₃NO₃[*M*]⁺ 325.1678; found 325.1693.

Azocine-β-lactam (–)-7h. Microwave heating (toluene, 185 °C, 3h). From 40 mg (0.10 mmol) of bis(allene) (+)-5h, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent gave compound (–)-7h (21 mg, 52%) as a colorless oil; $[\alpha]_D = -29.7$ (*c* 0.4, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ: 7.28 (m, 10H), 5.48 (d, 1H, J = 2.0 Hz), 5.10 (d, 1H, J = 1.8 Hz), 4.83 (m, 5H), 4.38 (d, 1H, J = 4.7 Hz), 3.79 (m, 1H), 3.39 (s, 3H), 3.12 (dd, 1H, J = 13.4, 4.5 Hz), 2.83 (m, 1H), 2.25 (ddd, 1H, J = 14.1, 3.9, 1.7 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ: 167.5, 159.9, 148.8, 147.1, 146.9, 141.2, 130.3, 128.4 (3C), 128.4 (2C), 128.0 (2C), 127.7, 127.6 (2C), 115.3, 113.2, 83.3, 72.5, 59.0, 53.4, 41.2, 32.2; IR (CHCl₃) v 1758; HRMS (ES) calcd for C₂₅H₂₅NO₃[*M*]⁺ 387.1834; found 387.1828.

Azocine-β-lactam (–)-7**i.** Microwave heating (toluene, 200 °C, 2h). From 40 mg (0.14 mmol) of bis(allene) (+)-5**i**, and after chromatography of the residue using hexanes/ethyl acetate (1:2) as eluent gave compound (–)-7**i** (23 mg, 58%) as a colorless oil; $[\alpha]_D = -37.5$ (*c* 0.8, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 5.35 (d, 1H, J = 1.7 Hz), 5.16 (d, 1H, J = 1.9 Hz), 4.86 (t, 1H, J = 1.7 Hz), 4.76 (d, 1H, J = 1.7 Hz), 4.52 (dd, 1H, J = 4.3, 1.1 Hz), 4.08 (d, 1H, J = 4.2 Hz), 3.74 (m, 1H), 3.49 (s, 3H), 3.04 (m, 2H), 2.23 (s, 3H), 2.18 (m, 1H), 1.70 (d, 3H, J = 0.8 Hz); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 169.4, 166.6, 148.1, 146.0, 137.1, 128.3, 114.4, 113.2, 85.2, 60.0, 58.8, 41.4, 31.8, 20.6, 18.8; IR (CHCl₃) v 1755; HRMS (ES) calcd for C₁₅H₁₉NO₄[M]⁺ 277.1314; found: 277.1315.

Azocine-β-lactam (-)-7j. Microwave heating (toluene, 200 °C, 1.5h). From 50 mg (0.15 mmol) of bis(allene) (+)-5j, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (-)-7j (24 mg, 48%) as a colorless oil; $[\alpha]_D = -25.3$ (*c* 0.5, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 7.26 (m, 5H), 5.48 (d, 1H, *J* = 1.5 Hz), 5.18 (d, 1H, *J* = 1.9 Hz), 4.95 (t, 1H, *J* = 1.7 Hz), 4.87 (d, 1H, *J* = 1.5 Hz), 4.64 (dd, 1H, *J* = 4.3, 1,1 Hz), 4.19 (d, 1H, *J* = 4.3 Hz), 3.79 (td, 1H, *J* = 13.2, 3.8 Hz), 3.58 (s, 3H), 3.31 (m, 1H), 3.17 (m, 1H), 2.36 (ddd, 1H, *J* = 13.9, 3.7, 1.6 Hz), 1.94 (s, 3H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 169.4, 166.2, 147.0, 146.7, 139.2, 132.3, 128.1 (2C), 127.4 (2C), 127.4, 119.6, 117.0, 113.8, 85.8, 60.5, 58.9, 41.6, 31.8, 20.7; IR (CHCl₃) v 1759; HRMS (ES) calcd for C₂₀H₂₁NO₄[*M*]⁺ 339.1471; found: 339.1469.

Azocine-β-lactam (–)-7k. Microwave heating (toluene, 200 °C, 1h). From 50 mg (0.14 mmol) of bis(allene) (+)-5k, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent gave compound (–)-7k (21 mg, 42%) as a colorless oil; $[\alpha]_D = -5.1$ (*c* 0.6, CHCl₃); ¹H-NMR (300 MHz, CDCl₃, 25 °C) δ 7.21 (d, 2H, J = 8.9 Hz), 6.82 (d, 2H, J = 8.9 Hz), 5.48 (d, 1H, J = 1.6 Hz), 5.19 (d, J = 1.8 Hz), 4.94 (s, 1H), 4.85 (d, 1H, J = 1.5 Hz), 4.62 (dd, 1H, J = 4.2, 0.9 Hz), 4.18 (d, 1H, J = 4.3 Hz), 3.76 (m, 4H), 3.56 (s, 3H), 3.23 (m, 2H), 2.34 (m, 1H), 1.99 (s, 1H), 4.85 (d, 1H), 4.85 (d, 2H), 2.34 (m, 2H), 4.99 (s), 4.18 (d, 2H), J = 4.3 Hz), 3.76 (m, 4H), 3.56 (s), 3H), 3.23 (m, 2H), 2.34 (m, 2H), 1.99 (s), 4.18 (d, 2H), J = 4.3 Hz), 3.76 (m, 4H), 3.56 (s), 3H), 3.23 (m, 2H), 2.34 (m, 2H), 1.99 (s), 4.18 (d, 2H), J = 4.3 Hz), 3.76 (m, 4H), 3.56 (s), 3H), 3.23 (m, 2H), 2.34 (m, 2H), 1.99 (s), 4.18 (d, 2H), J = 4.3 Hz), 3.76 (m, 4H), 3.56 (s), 3H), 3.23 (m, 2H), 2.34 (m, 2H), 1.99 (s), 4.18 (d, 2H), J = 4.3 Hz), 3.76 (m, 4H), 3.56 (s), 3H), 3.23 (m, 2H), 2.34 (m, 2H), 1.99 (s), 4.18 (d, 2H), J = 4.3 Hz), 3.76 (m, 4H), 3.56 (s), 3H), 3.23 (m, 2H), 2.34 (m, 2H), 3.90 (s), 4.18 (d, 2H), J = 4.3 Hz), 3.76 (m, 4H), 3.56 (s), 3H), 3.23 (m, 2H), 2.34 (m, 2H), 3.90 (s), 4.18 (d, 2H), 4.28 (d, 2H), 4.

3H); ¹³C-NMR (75 MHz, CDCl₃, 25 °C) δ 169.5, 166.3, 158.7, 147.2, 147.0, 138.4, 131.7, 131.2, 128.8 (2C), 117.0, 113.6, 113.4 (2C), 85.7, 60.6, 58.8, 55.2, 41.5, 31.8, 20.8; IR (CHCl₃) v 1757; HRMS (ES) calcd for C₂₁H₂₃NO₅[*M*]⁺ 369.1576; found: 369.1571.

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Supporting Information Available: Computational details, cartesian coordinates as well as copies of the ¹H NMR and ¹³C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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