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

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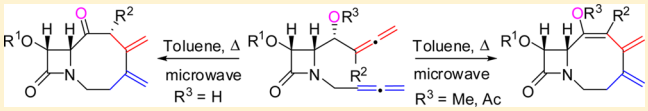
Supporting Information

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(allenes) in the absence of metals have been achieved by the thermolysis of nonconjugated 2-azetidinone-tethered bis(allenes) on application of 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]

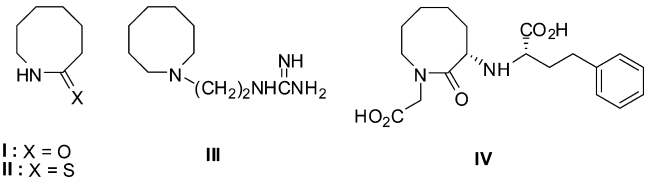


Figure 1. Representative examples of bioactive azocine derivatives.

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

RESULTS AND DISCUSSION

The starting materials, new β-lactam bis(allenes) **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(I) bromide (Crabbé reaction).[9] 2-Azetidinone-tethered allenals **3a**–**c** were prepared from allenyl dioxolanes **2a**–**c** through $BiCl_3$-catalyzed acetonide deprotection followed by oxidative diol cleavage (Scheme 1).[10] 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(allenes) **4a**–**h** with total allenic/propargylic regioselectivity and reasonable syn/anti diastereoselectivity (de 60–100%, by integration of well-resolved signals in the ^{1}H NMR spectra of the crude reaction mixtures before purification). Fortunately, in the cases of absence of total diasteroeselectivity (**4a,c,d**) the diastereomeric bis(allenes) *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(allenes) **5a**–**k** (Scheme 1).

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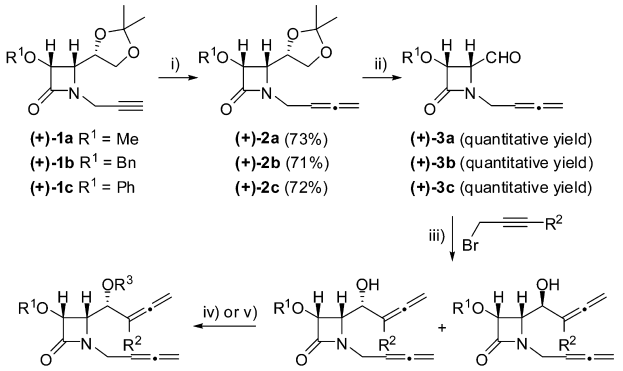
Scheme 1. Preparation of Enantiopure β-Lactam Bis(allenes) 4a–h and 5a–k[a]



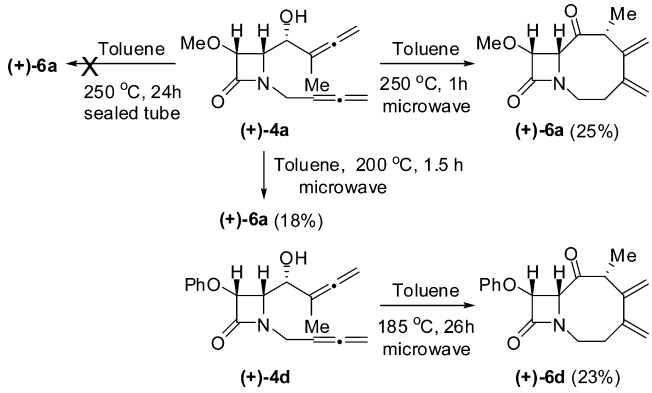
(+)-5a R1 = Me, R2 = Me, R3 = Me (72%)	(+)-*syn*-4a (80%)	(+)-*anti*-4a (8%)
(+)-5b R1 = Me, R2 = Ph, R3 = Me (61%)	(+)-*syn*-4b (68%)	
(+)-5c R1 = Me, R2 = PMP, R3 = Me (63%)	(+)-*syn*-4c (42%)	(+)-*anti*-4c (16%)
(+)-5d R1 = Ph, R2 = Me, R3 = Me (66%)	(+)-*syn*-4d (42%)	(+)-*anti*-4d (15%)
(+)-5e R1 = Ph, R2 = Ph, R3 = Me (59%)	(+)-*syn*-4e (57%)	
(+)-5f R1 = Ph, R2 = PMP, R3 = Me (64%)	(+)-*syn*-4f (48%)	
(–)-5g R1 = Bn, R2 = Me, R3 = Me (80%)	(–)-*syn*-4g (72%)	(+)-*anti*-4g (15%)
(+)-5h R1 = Bn, R2 = Ph, R3 = Me (54%)	(+)-*syn*-4h (56%)	
(+)-5i R1 = Me, R2 = Me, R3 = Ac (64%)	(+)-*syn*-4a (80%)	(+)-*anti*-4a (8%)
(+)-5j R1 = Me, R2 = Ph, R3 = Ac (74%)	(+)-*syn*-4b (68%)	
(+)-5k R1 = Me, R2 = PMP, R3 = Ac (68%)	(+)-*syn*-4c (42%)	(+)-*anti*-4c (16%)

[a]Reagents and conditions: (i) $(CH_2O)_n$, iPr_2NH, CuBr, dioxane, reflux, 2 h; (ii) (a) 50 mol % $BiCl_3$, $MeCN–H_2O$, room temperature, 24 h; (b) $NaIO_4$, $NaHCO_3$ (aqueous saturated), CH_2Cl_2, room temperature, 24 h; (iii) In, THF/NH_4Cl (aqueous saturated) (1/5), room temperature, 24 h; (iv) Me_2SO_4, TBAI, CH_2Cl_2, NaOH (aqueous 50%) (1/1), room temperature, 8 h; (v) Ac_2O, Et_3N, DMAP (cat.), CH_2Cl_2, 0 °C, 2 h. PMP = 4-$MeOC_6H_4$. DMAP = 4-(dimethylamino)pyridine.

To explore the reactivity of bis(allenes) **4** and **5** under thermal conditions, 2-azetidinone-tethered 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 reactor by heating a solution of bis(allene) **4a** in toluene at 200 °C, 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 the bis(allene) precursor, a low yield of the corresponding bicyclic azocinone-β-lactam **6d** was also obtained; however, the reaction proceeds best after a long exposure of microwave irradiation at 185 °C (Scheme 2). Bicycles **6a,d** 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 isomerization involving the allenol group, methyl ethers **5a–h** and acetates **5i–k** were identified as cyclization precursors.

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

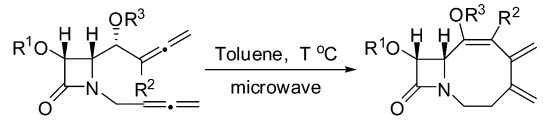
Scheme 2. Preparation of Azocinone-β-Lactams 6a,d[a]



[a]PMP = 4-$MeOC_6H_4$.

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

Scheme 3. Preparation of Azocine-β-Lactams 7a–k



(+)-5a R1 = Me, R2 = Me, R3 = Me	(–)-7a (60%, 250 °C, 0.5 h)
(+)-5b R1 = Me, R2 = Ph, R3 = Me	(–)-7b (50%, 200 °C, 1 h)
(+)-5c R1 = Me, R2 = PMP, R3 = Me	(+)-7c (45%, 200 °C, 1 h)
(+)-5d R1 = Ph, R2 = Me, R3 = Me	(–)-7d (50%, 225 °C, 1 h)
(+)-5e R1 = Ph, R2 = Ph, R3 = Me	(–)-7e (61%, 200 °C, 1 h)
(+)-5f R1 = Ph, R2 = PMP, R3 = Me	(–)-7f (47%, 175 °C, 1 h)
(–)-5g R1 = Bn, R2 = Me, R3 = Me	(–)-7g (54%, 225 °C, 1 h)
(+)-5h R1 = Bn, R2 = Ph, R3 = Me	(–)-7h (52%, 185 °C, 3 h)
(+)-5i R1 = Me, R2 = Me, R3 = Ac	(–)-7i (58%, 200 °C, 2 h)
(+)-5j R1 = Me, R2 = Ph, R3 = Ac	(–)-7j (48%, 200 °C, 1.5 h)
(+)-5k R1 = Me, R2 = PMP, R3 = Ac	(–)-7k (42%, 200 °C, 1 h)

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(allenes) **A–C** resulted in complex reaction mixtures (Scheme S1; see the Supporting Information), which led to the exclusion of bis(allenes) **A–C** as efficient substrates. Consequently, it can be inferred that the 2-azetidinone nucleus plays a key template role in the cyclization processes.

A conceivable mechanism for the formation of bicycles **7** from bis(allenes) **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 the 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

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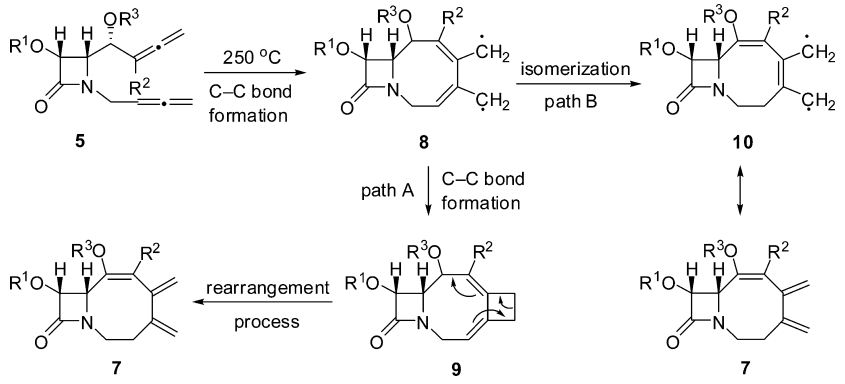
Scheme 4. Rationalization for the Thermal Carbocyclization of Bis(allenes) 5



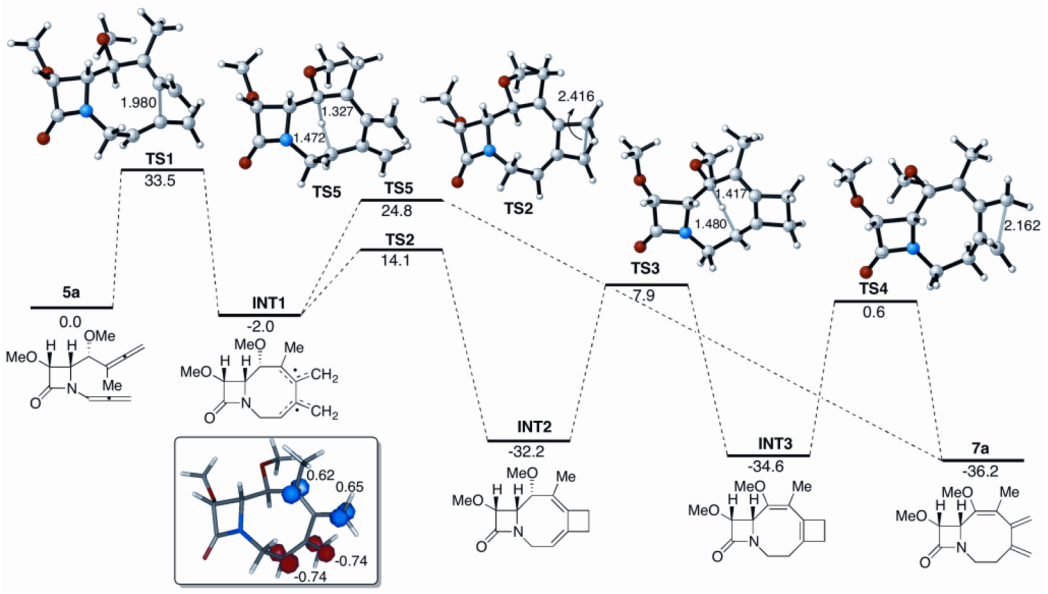


Figure 2. Computed reaction profile for the transformation of **5a** into bicyclic azocine-β-lactam **7a**. Relative energies (zero-point vibrational energies included) and bond distances are given in kcal/mol and angstroms, respectively. Inset: computed spin densities on **INT1**. All data have been computed at the PCM(toluene)M06-2X/6-311+G*//B3LYP/6-31+G* level.

suffer 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 microwave-induced azocine formation discussed above. The reaction profile involving **5a** is depicted in Figure 2, which shows the corresponding relative energies (zero-point 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 (ΔE_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 processes[16] 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 (ΔE_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 the 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).

In view of the relatively high activation barriers computed for the steps involving **TS3** and **TS4** (40.1 and 35.2 kcal/mol,

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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(allenes) **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 multistep 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(allenes) have been achieved by the thermolysis of nonconjugated 2-azetidinone-tethered bis(allenes) on application of 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: ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz). Chemical shifts are given in ppm relative to TMS (^{1}H, 0.0 ppm) or $CDCl_3$ (^{13}C, 76.9 ppm). Low- and high-resolution mass spectra were taken on a QTOF LC/MS spectrometer using the electronic impact (EI) or electrospray mode (ES). The specific rotation $[\alpha]_D$ is given in 10^{-1} deg cm^2 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 instrument 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 an argon atmosphere. When the reaction was complete as monitored by TLC, the mixture was cooled to room temperature. Water (5 mL) was added before being extracted with ethyl acetate (3 × 15 mL). The organic phase was washed with water (2 × 5 mL), dried ($MgSO_4$) 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, compound (+)-**2a** (307 mg, 73%) was obtained as a colorless oil: $[\alpha]_D$ = +12.4 (c 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1958, 1759 cm^{-1}; HRMS (ES) calcd for $C_{13}H_{19}NO_4$ $[M]^+$ 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, compound (+)-**2b** (519 mg, 71%) was obtained as a colorless oil: $[\alpha]_D$ = +14.9 (c 0.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1945, 1744 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{23}NO_4$ $[M]^+$ 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, compound (+)-**2c** (527 mg, 72%) was obtained as a colorless oil: $[\alpha]_D$ = +93.1 (c 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1958, 1762 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{21}NO_4$ $[M]^+$ 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. $BiCl_3$ (0.05 mmol) was added, the ice bath was removed, and the mixture was stirred at room temperature for 24 h (monitoring by TLC). The reaction mixture was poured into a saturated aqueous solution of $NaHCO_3$. The aqueous layer was extracted with ethyl acetate (3 × 20 mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo to afford (3*R*,4*S*)-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 μL) was added to a solution of the corresponding diol (1.0 mmol) in dichloromethane (3.3 mL), the temperature being maintained 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 ($MgSO_4$), and the solvent was removed under reduced pressure. The crude product was used for the 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, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 209.6, 198.9, 165.9, 85.8, 84.9, 77.5, 63.5, 59.2, 40.1; IR ($CHCl_3$) ν 1957, 1760 cm^{-1}; HRMS (ES) calcd for $C_9H_{11}NO_3$ $[M]^+$ 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, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1957, 1742 cm^{-1}; HRMS (ES) calcd for $C_{15}H_{15}NO_3$ $[M]^+$ 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, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1957, 1748 cm^{-1}; HRMS (ES) calcd for $C_{14}H_{13}NO_3$ $[M]^+$ 243.0895, found 243.0899.

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Indium-Promoted Reaction between 3-Substituted Prop-2-ynyl Bromides and Allenals 3. General Procedure for the Synthesis of Bis(allenes) 4. 1-Bromobut-2-yne, (3-bromoprop-1-ynyl)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/NH_4Cl (aqueous saturated) (1:5, 5 mL) at 0 °C. After disappearance of the starting material (TLC) the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), 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, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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, =CH_2), 5.12 (qd, 1H, *J* = 6.9, 5.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 3392, 1958, 1742 cm^{-1}; HRMS (ES) calcd for $C_{13}H_{17}NO_3$ $[M]^+$ 235.1208, found 235.1208.

*Bis(allene) (+)-anti-**4a**.* Colorless oil: $[\alpha]_D$ = +61.2 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$): ν 3393, 1960, 1747 cm^{-1}; HRMS (ES) calcd for $C_{13}H_{17}NO_3$ $[M]^+$ 235.1208, found 235.1211.

*Bis(allene) (+)-syn-**4b**.* From 302 mg (1.66 mmol) of allenal (+)-**3a**, and after chromatography of the residue using hexanes/ethyl acetate (1/1) as eluent, compound (+)-*syn*-**4b** (336 mg, 68%) was obtained as a colorless oil: $[\alpha]_D$ = +28.0 (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C) 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); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) 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 ($CHCl_3$) ν 3391, 1956, 1743 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{19}NO_3$ $[M]^+$ 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 (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, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C) δ 2.61 (br s, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 3398, 1956, 1737 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{21}NO_4$ $[M]^+$ 327.1473, found 327.1471.

*Bis(allene) (+)-anti-**4c**.* Colorless oil: $[\alpha]_D$ = +28.8 (*c* 1.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 3422, 1956, 1744 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{21}NO_4$ $[M]^+$ 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, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 3420, 1957, 1736 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{19}NO_3$ $[M]^+$ 297.1365, found 297.1372.

*Bis(allene) (+)-anti-**4d**.* Colorless solid: mp 91−93 °C; $[\alpha]_D$ = +120.4 (*c* 1.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C) δ 1.88 (t, 3H, *J* = 3.1 Hz), 2.73 (br s, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 3421, 1957, 1743 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{19}NO_3$ $[M]^+$ 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, compound (+)-*syn*-**4e** (188 mg, 57%) was obtained as a colorless oil: $[\alpha]_D$ = +85.6 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 3452, 1959, 1752 cm^{-1}; HRMS (ES) calcd for $C_{23}H_{21}NO_3$ $[M]^+$ 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, compound (+)-*syn*-**4f** (196 mg, 48%) was obtained as a colorless oil: $[\alpha]_D$ = +76.0 (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 3447, 1956, 1753 cm^{-1}; HRMS (ES) calcd for $C_{24}H_{23}NO_4$ $[M]^+$ 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, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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, =CH_2), 4.93 (d, 1H, *J* = 11.6 Hz), 5.11 (m, 1H), 7.35 (s, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 3385, 1958, 1741 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{21}NO_3$ $[M]^+$ 311.1521, found 311.1527.

*Bis(allene) (+)-anti-**4g**.* Colorless oil: $[\alpha]_D$ = +75.2 (*c* 1.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C) δ 1.82 (t, 3H, *J* = 3.1 Hz), 3.01 (br s, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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

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($CHCl_3$) ν 3420, 1957, 1738 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{21}NO_3$ $[M]^+$ 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, compound (+)-*syn*-**4h** (200 mg, 56%) was obtained as a colorless oil: $[\alpha]_D$ = +174.7 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 3455, 1958, 1742 cm^{-1}; 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. Tetrabutylammonium 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 mixture 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 × 15 mL), the combined organic extracts were dried ($MgSO_4$) 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, compound (+)-**5a** (115 mg, 72%) was obtained as a colorless oil: $[\alpha]_D$ = +10.4 (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1960, 1747 cm^{-1}; HRMS (ES) calcd for $C_{14}H_{19}NO_3$ $[M]^+$ 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, compound (+)-**5b** (98 mg, 61%) was obtained as a colorless oil: $[\alpha]_D$ = +11.8 (*c* 1.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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), 7.46 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1956, 1744 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{21}NO_3$ $[M]^+$ 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, compound (+)-**5c** (92 mg, 63%) was obtained as a colorless oil: $[\alpha]_D$ = +12.4 (*c* 1.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1957, 1753 cm^{-1}; HRMS (ES) calcd for $C_{20}H_{23}NO_4$ $[M]^+$ 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, compound (+)-**5d** (47 mg, 66%) was obtained as a colorless oil: $[\alpha]_D$ = +20.0 (*c* 0.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1958, 1762 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{21}NO_3$ $[M]^+$ 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, compound (+)-**5e** (46 mg, 59%) was obtained as a colorless oil: $[\alpha]_D$ = +44.4 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1959, 1760 cm^{-1}; HRMS (ES) calcd for $C_{24}H_{23}NO_3$ $[M]^+$ 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, compound (+)-**5f** (36 mg, 64%) was obtained as a colorless oil: $[\alpha]_D$ = +26.0 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1957, 1759 cm^{-1}; HRMS (ES) calcd for $C_{25}H_{25}NO_4$ $[M]^+$ 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, compound (−)-**5g** (60 mg, 80%) was obtained as a colorless oil: $[\alpha]_D$ = −5.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1957, 1752 cm^{-1}; HRMS (ES) calcd for $C_{20}H_{23}NO_3$ $[M]^+$ 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, compound (+)-**5h** (44 mg, 54%) was obtained as a colorless oil: $[\alpha]_D$ = +17.0 (*c* 0.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1959, 1758 cm^{-1}; HRMS (ES) calcd for $C_{25}H_{25}NO_3$ $[M]^+$ 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 warmed 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 × 5 mL) and brine (3 × 5 mL). The organic layer was dried ($MgSO_4$) 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, compound (+)-**5i** (57 mg, 64%)

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was obtained as a colorless oil: $[\alpha]_D$ = +27.1 (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1958 (C═C═C), 1748 (C═O) cm^{-1}; HRMS (ES) calcd for $C_{15}H_{19}NO_4$ $[M]^+$ 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, compound (+)-**5j** (43 mg, 74%) was obtained as a colorless oil: $[\alpha]_D$ = +37.1 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1957, 1753 cm^{-1}; HRMS (ES) calcd for $C_{20}H_{21}NO_4$ $[M]^+$ 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, compound (+)-**5k** (123 mg, 68%) was obtained as a colorless oil: $[\alpha]_D$ = +9.8 (*c* 1.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C) 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); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) 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 ($CHCl_3$) ν 1957, 1753 cm^{-1}; HRMS (ES) calcd for $C_{21}H_{23}NO_5$ $[M]^+$ 369.1576, found 369.1584.

General Procedure for the Microwave-Promoted Reaction of β-Lactam Bis(allenes) 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 mixture was cooled to room temperature, concentrated under vacuum, and purified by flash column chromatography with ethyl acetate/dichloromethane mixtures as eluents. Spectroscopic and analytical data for pure forms of compounds **6** follow.

*Azocinone-β-Lactam (+)-**6a**.* Microwave heating (toluene, 250 °C, 1 h). From 40 mg (0.16 mmol) of bis(allene) (+)-**4a**, and after chromatography of the residue using dichloromethane/ethyl acetate (9/1) as eluent, compound (+)-**6a** (10 mg, 25%) was obtained as a colorless oil: $[\alpha]_D$ = +156.0 (*c* 0.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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* = 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1755, 1719 cm^{-1}; HRMS (ES) calcd for $C_{13}H_{17}NO_3$ $[M]^+$ 235.1208, found 235.1215.

*Azocinone-β-Lactam (+)-**6d**.* Microwave heating (toluene, 185 °C, 26 h). From 40 mg (0.13 mmol) of bis(allene) (+)-**4d**, and after chromatography of the residue using dichloromethane/ethyl acetate (9/1) as eluent, compound (+)-**6d** (9 mg, 23%) was obtained as a colorless oil: $[\alpha]_D$ = +111.8 (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1768, 1722 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{19}NO_3$ $[M]^+$ 297.1365, found 297.1355.

General Procedure for the Microwave-Promoted Reaction of β-Lactam Bis(allenes) 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 mixture was cooled to room temperature, concentrated under vacuum, and purified by flash column chromatography with hexanes/ethyl acetate or ethyl acetate/dichloromethane mixtures as eluents. Spectroscopic and analytical data for pure forms of compounds **7** follow.

*Azocine-β-Lactam (−)-**7a**.* Microwave heating (toluene, 250 °C, 0.5 h). From 50 mg (0.2 mmol) of bis(allene) (+)-**5a**, and after chromatography of the residue using dichloromethane/ethyl acetate (9/1) as eluent, compound (−)-**7a** (30 mg, 60%) was obtained as a colorless oil: $[\alpha]_D$ = −106.0 (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1753 cm^{-1}; HRMS (ES) calcd for $C_{14}H_{19}NO_3$ $[M]^+$ 249.1365, found 249.1365.

*Azocine-β-Lactam (−)-**7b**.* Microwave heating (toluene, 200 °C, 1 h). From 40 mg (0.13 mmol) of bis(allene) (+)-**5b**, and after chromatography of the residue using hexanes/ethyl acetate (2/1) as eluent, compound (−)-**7b** (21 mg, 50%) was obtained as a colorless oil: $[\alpha]_D$ = −34.0 (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1759 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{21}NO_3$ $[M]^+$ 311.1521, found 311.1516.

*Azocine-β-Lactam (+)-**7c**.* Microwave heating (toluene, 200 °C, 1 h). From 40 mg (0.12 mmol) of bis(allene) (+)-**5c**, and after chromatography of the residue using hexanes/ethyl acetate (1/1) as eluent, compound (+)-**7c** (18 mg, 45%) was obtained as a colorless oil: $[\alpha]_D$ = +42.7 (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1756 cm^{-1}; HRMS (ES) calcd for $C_{20}H_{23}NO_4$ $[M]^+$ 341.1627, found 341.1625.

*Azocine-β-Lactam (−)-**7d**.* Microwave heating (toluene, 225 °C, 1 h). From 40 mg (0.13 mmol) of bis(allene) (+)-**5d**, and after chromatography of the residue using hexanes/ethyl acetate (1/1) as eluent, compound (−)-**7d** (21 mg, 50%) was obtained as a colorless oil: $[\alpha]_D$ = −49.5 (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1760 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{21}NO_3$ $[M]^+$ 311.1521, found 311.1518.

*Azocine-β-Lactam (−)-**7e**.* Microwave heating (toluene, 200 °C, 1 h). From 40 mg (0.11 mmol) of bis(allene) (+)-**5e**, and after chromatography of the residue using hexanes/ethyl acetate (2/1) as eluent, compound (−)-**7e** (24 mg, 61%) was obtained as a colorless oil: $[\alpha]_D$ = −109.4 (*c* 0.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 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,

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1H), 2.22 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1763 cm^{-1}; HRMS (ES) calcd for $C_{24}H_{23}NO_3$ $[M]^+$ 373.1678, found 373.1692.

*Azocine-β-Lactam (−)-**7f**.* Microwave heating (toluene, 175 °C, 1 h). From 50 mg (0.12 mmol) of bis(allene) (+)-**5f**, and after chromatography of the residue using hexanes/ethyl acetate (2/1) as eluent, compound (−)-**7f** (24 mg, 47%) was obtained as a colorless oil: $[\alpha]_D$ = −30.0 (*c* 0.4, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1764 cm^{-1}; HRMS (ES) calcd for $C_{25}H_{25}NO_4$ $[M]^+$ 403.1784, found 403.1782.

*Azocine-β-Lactam (−)-**7g**.* Microwave heating (toluene, 225 °C, 1 h). From 50 mg (0.15 mmol) of bis(allene) (−)-**5g**, and after chromatography of the residue using hexanes/ethyl acetate (1/1) as eluent, compound (−)-**7g** (27 mg, 54%) was obtained as a colorless oil: $[\alpha]_D$ = −65.9 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1757 cm^{-1}; HRMS (ES) calcd for $C_{20}H_{23}NO_3$ $[M]^+$ 325.1678, found 325.1693.

*Azocine-β-Lactam (−)-**7h**.* Microwave heating (toluene, 185 °C, 3 h). From 40 mg (0.10 mmol) of bis(allene) (+)-**5h**, and after chromatography of the residue using hexanes/ethyl acetate (2/1) as eluent, compound (−)-**7h** (21 mg, 52%) was obtained as a colorless oil: $[\alpha]_D$ = −29.7 (*c* 0.4, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1758 cm^{-1}; HRMS (ES) calcd for $C_{25}H_{25}NO_3$ $[M]^+$ 387.1834, found 387.1828.

*Azocine-β-Lactam (−)-**7i**.* Microwave heating (toluene, 200 °C, 2 h). From 40 mg (0.14 mmol) of bis(allene) (+)-**5i**, and after chromatography of the residue using hexanes/ethyl acetate (1/2) as eluent, compound (−)-**7i** (23 mg, 58%) was obtained as a colorless oil: $[\alpha]_D$ = −37.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1755 cm^{-1}; HRMS (ES) calcd for $C_{15}H_{19}NO_4$ $[M]^+$ 277.1314, found 277.1315.

*Azocine-β-Lactam (−)-**7j**.* Microwave heating (toluene, 200 °C, 1.5 h). From 50 mg (0.15 mmol) of bis(allene) (+)-**5j**, and after chromatography of the residue using hexanes/ethyl acetate (1/1) as eluent, compound (−)-**7j** (24 mg, 48%) was obtained as a colorless oil: $[\alpha]_D$ = −25.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1759 cm^{-1}; HRMS (ES) calcd for $C_{20}H_{21}NO_4$ $[M]^+$ 339.1471, found 339.1469.

*Azocine-β-Lactam (−)-**7k**.* Microwave heating (toluene, 200 °C, 1 h). From 50 mg (0.14 mmol) of bis(allene) (+)-**5k**, and after chromatography of the residue using hexanes/ethyl acetate (1/1) as eluent, compound (−)-**7k** (21 mg, 42%) was obtained as a colorless oil: $[\alpha]_D$ = −5.1 (*c* 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 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, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 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 ($CHCl_3$) ν 1757 cm^{-1}; HRMS (ES) calcd for $C_{21}H_{23}NO_5$ $[M]^+$ 369.1576, found 369.1571.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures, text, and tables giving computational details, Cartesian coordinates for the calculated structures, and the ^{1}H NMR and ^{13}C 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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Notes

The authors declare no competing financial interest.

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