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New Regiocontrolled Synthesis of Functionalized Pyrroles from 2-Azetidinone-Tethered Allenols

Benito Alcaide,*[a] Pedro Almendros,*[b] Rocío Carrascosa,[a, b] and María C. Redondo[a]

Dedicated to Professor Miguel A. Yus on the occasion of his 60th birthday

Abstract: A new one-pot approach to synthesize densely substituted racemic and enantiopure pyrroles from β-lactams has been developed. The approach relies on the regiocontrolled cyclization of β-allenamine intermediates derived from the ring opening of 2-azetidinone-tethered allenols. In this approach four points of diversity are introduced, one of which is the position of the allene moiety on the β-lactam ring.

Keywords: allenes · domino reactions · lactams · nitrogen heterocycles · rearrangement

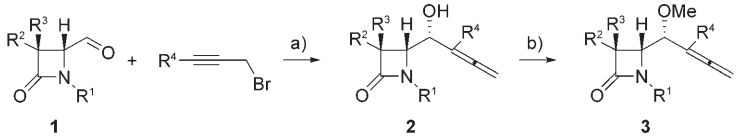
Introduction

Pyrroles constitute an important compound class owing to their wide profile of biological activity.[1] Additionally, the pyrrole nucleus is a useful building block for the synthesis of heterocycles and natural products,[2] and this heterocyclic core is widely used in materials science and molecular recognition.[3] Recently, organometallic transformations have been pursued with renewed interest to achieve the elusive addition reaction of the N–H bond across allenes.[4] In addition to the key role that β-lactams have played in the fight against pathogenic bacteria, the use of 2-azetidinones as chiral building blocks in organic synthesis is now well established.[5] Although much effort has been made in these fields, the direct preparation of the pyrrole ring from β-lactams has not yet been reported. Furthermore, little attention has been given to the use of the allenamine building block for the synthesis of pyrroles.[6] Following our work on heterocyclic chemistry,[7] we now present a full report on the preparation of functionalized pyrroles from allene-β-lactams.[8]

Results and Discussion

Precursors for pyrrole formation, α-allenols **2a–h** and **5a–i**, were synthesized from 4-oxoazetidine-2-carbaldehydes **1a–f** (Scheme 1, Table 1) and azetidine-2,3-diones **4a–e** (Scheme 2, Table 2) through indium-mediated Barbier-type carbonyl-allenylation reactions in aqueous media by using our previously described methodologies.[9] α-Allenols **2** and **5** were protected as the corresponding methyl ethers **3** and **6** by treatment with dimethyl sulfate under phase-transfer conditions.

With the α-allenol derivatives in hand, the next stage was to carry out the β-lactam ring opening and the subsequent key cyclization reactions. Treatment of allene-β-lactams **3a**



1 2 3

Scheme 1. Indium-mediated Barbier-type carbonyl allenylation of aldehydes **1** followed by protection of α-allenols **2** are precursors for the synthesis of allene-β-lactams **3**. Reagents and conditions: a) In, THF, NH_4Cl (aq. sat.), RT; b) Me_2SO_4, NaOH, TBAI, DCM-H_2O, RT.

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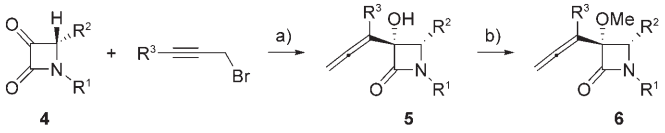
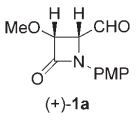
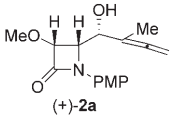
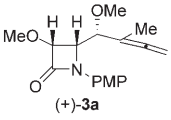
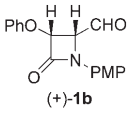
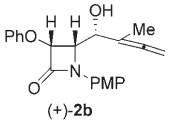
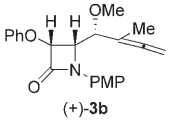
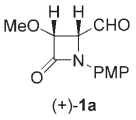
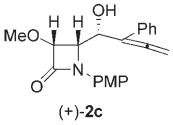
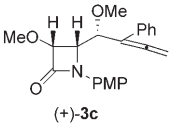
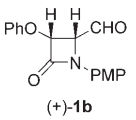
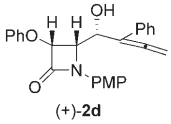
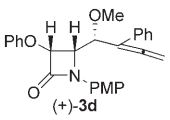
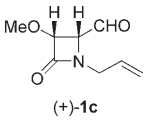
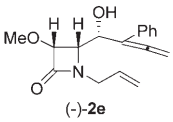
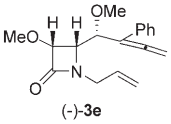
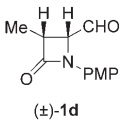
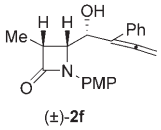
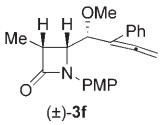
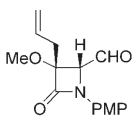
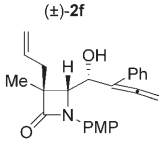
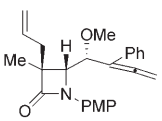
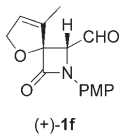
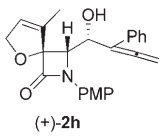
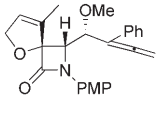


Scheme 2. Indium-mediated Barbier-type carbonyl allenylation of ketones **4** followed by protection of α-allenols **5** are precursors for the synthesis of allene-β-lactams **6**. Reagents and conditions: a) In, THF, NH_4Cl (aq. sat.), RT; b) Me_2SO_4, NaOH, TBAI, DCM-H_2O, RT.

Table 1. Preparation of 2-azetidinone-tethered allenes **3**.[a]

Aldehyde	Allenol	Yield [%][b]	Protected allenol	Yield [%][b]
 (+)-**1a**	 (+)-**2a**	77	 (+)-**3a**	66
 (+)-**1b**	 (+)-**2b**	89	 (+)-**3b**	78
 (+)-**1a**	 (+)-**2c**	84	 (+)-**3c**	78
 (+)-**1b**	 (+)-**2d**	53	 (+)-**3d**	84
 (+)-**1c**	 (-)-**2e**	64	 (-)-**3e**	77
 (±)-**1d**	 (±)-**2f**	79	 (±)-**3f**	88
 (+)-**1e**	 (+)-**2g**	78	 (+)-**3g**	80
 (+)-**1f**	 (+)-**2h**	76	 (-)-**3h**	60

[a] PMP = 4-$MeOC_6H_4$. [b] Yield of pure, isolated product with correct analytical and spectral data.

Abstract in Spanish: *Se ha llevado a cabo una síntesis directa de pirroles polisustituídos a partir de (α-alcoxialenil)-β-lactamas por tratamiento con metóxido sódico en metanol, sin necesidad de utilizar metales de transición como catalizadores. Esta reacción puede explicarse a través de un proceso dominó sin precedentes que implica, en primer lugar, la apertura del anillo de 2-azetidinona, seguido de aminociclación con el grupo alénico y aromatización del anillo formado.*

and **3b** with sodium methoxide at room temperature afforded β-allenamines **7a** and **7b** in excellent yields. Most of the previously reported metal-mediated cyclizations of aminoallenes were not suitable for the cyclization of functionalized β-allenamines **7**, which results in a complex mixture of unidentified products.[4] After extensive screening, $AgNO_3$[4d] in the presence of K_2CO_3 was found to be effective at promoting aminocyclization in MeCN at room temperature, to give pyrroles **8a** and **8b**, which have a stereogenic center in the side chain (Scheme 3).[4m] Compounds **8** can be considered as hybrid scaffolds with a combination of the biologically and synthetically relevant pyrrole and α-hydroxy acid cores.[10] However, despite the tendency towards the development of enantiomerically pure drugs, to the best of our knowledge the preparation of optically active substituted (pyrrol-2-yl)acetic acid esters has never been reported.[11] Although complete conversion was observed by TLC and ^1H NMR spectroscopic analysis of the crude reaction mixtures, some decomposition was observed on sensitive pyrroles **8** during purification by flash chromatography, which may be responsible for the moderate isolated yields.

One possible pathway for the synthesis of pyrroles **8** may initially involve the formation of π-complex **9** through coordination of silver nitrate to the 1,2-diene moiety of β-allenamines **7**.[12] Next, regioselective cyclization to form species **10** followed by demetallation and proton transfer afforded intermediates **11**. Pyrrolines **11** were assumed to be unstable and could easily eliminate a methoxy group to yield pyrroles **8** (Scheme 4).

According to the strategy outlined above, 2-azetidinone-tethered phenyl allenes **3c**–**h** were treated with sodium methoxide at room temperature. To our delight, phenyl allenes **3c**–**h** did not give the expected β-allenamines, but instead afforded the corresponding 1,2,3,5-tetrasubstituted pyrroles **12** (Scheme 5). In all cases no other regioisomers were observed. To obtain a reasonable yield of the corresponding pyrrole derivative, the conversion of the allenol precursor into its methyl ether is required. For example,

Table 2. Preparation of 2-azetidinone-tethered allenes **6**.

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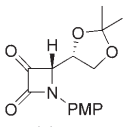
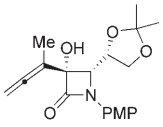
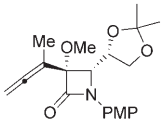
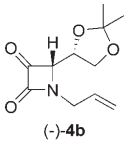
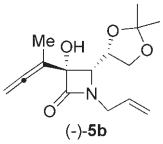
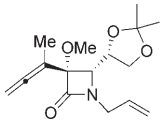
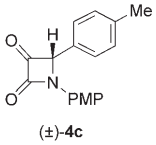
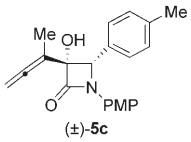
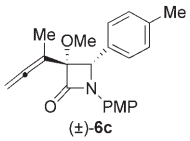
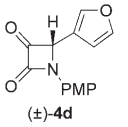
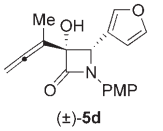
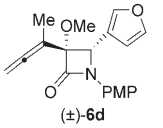
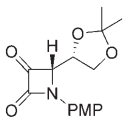
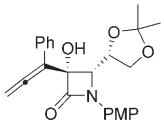
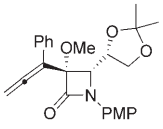
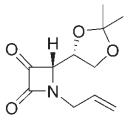
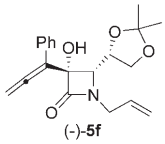
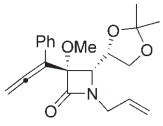
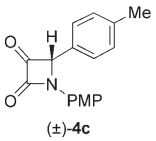
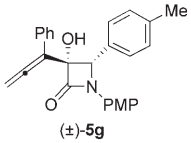
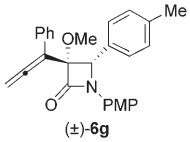
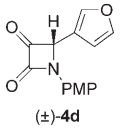
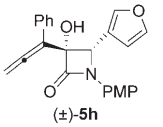
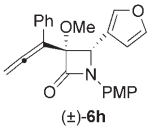
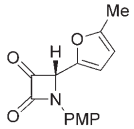
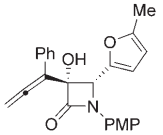
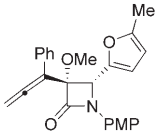
 (+)-**4a**	 (+)-**5a**	74	 (+)-**6a**	97
 (-)-**4b**	 (-)-**5b**	63	 (-)-**6b**	98
 (±)-**4c**	 (±)-**5c**	60	 (±)-**6c**	95
 (±)-**4d**	 (±)-**5d**	91	 (±)-**6d**	99
 (+)-**4a**	 (+)-**5e**	76	 (+)-**6e**	72
 (-)-**4b**	 (-)-**5f**	62	 (+)-**6f**	72
 (±)-**4c**	 (±)-**5g**	62	 (±)-**6g**	80
 (±)-**4d**	 (±)-**5h**	76	 (±)-**6h**	85
 (±)-**4e**	 (±)-**5i**	68	 (±)-**6i**	82

[a] Yield of pure, isolated product with correct analytical and spectral data.

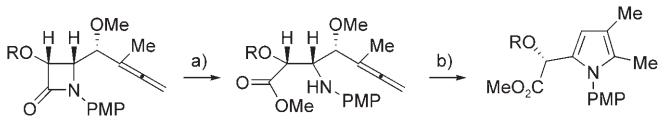
when the reaction was performed on unprotected α-allenol (+)-**2c**, the sequence provided the desired product (−)-**12a**, but in low yield (10%).

From a mechanistic point of view, our domino sequence could be explained through a bond-cleavage process on the four-membered lactam followed by allene cyclization with concomitant aromatization. The selective N1−C2 bond cleavage of the β-lactam nucleus in 2-azetidinone-tethered allenes **3** gave nonisolable allenic-β-amino esters **13**, which yielded pyrroles **12** after a totally regioselective cyclization onto the central carbon atom of the neighboring allene under the reaction conditions, followed by aromatization of pyrrolines **14** (Scheme 6). Pyrrole formation must be driven by forming a more stable five-membered ring, thereby relieving the strain associated with the four-membered ring.

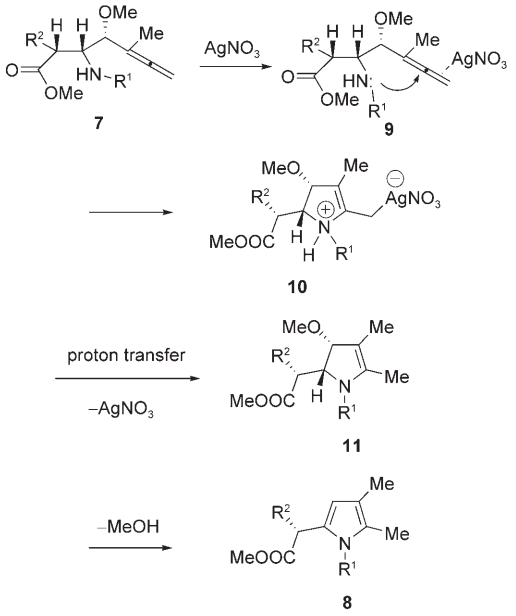
Another possible pathway that involves a 5-*endo* process and leads to an intermediate stabilized benzylic anion may also be considered (see the Supporting Information).

Direct cyclization occurred during the treatment of phenyl allenes **3c–h** (Scheme 5), as opposed to the sequential reactions performed with methyl allenes **3a** and **3b** (Scheme 3). The difference in reactivity between both types of allenic-β-lactams can be explained by the electron-withdrawing capacities of phenyl substituents compared with the electron-donating methyl groups. The presence of a Ph substituent in the allene stabilizes intermediate **14**; these conditions favor cyclization over open-chain products.

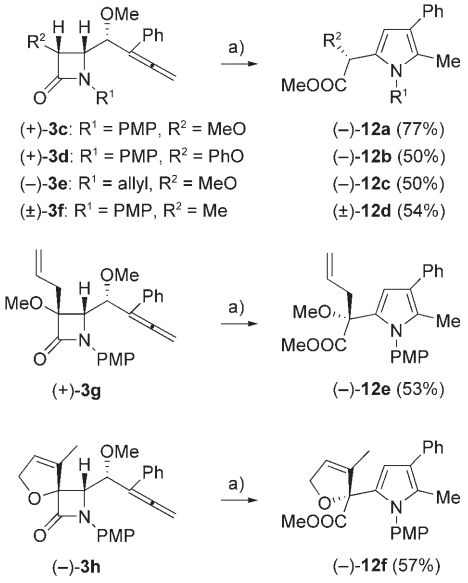
The influence of the position of the allene moiety at the β-lactam ring for the one-pot synthesis of the pyrrole nucleus was investigated by stirring methyl and phenyl quaternary α-allenol derivatives **6** for 48 h in a mixture of MeONa in MeOH at room temperature. After workup, the starting materials were recovered. Only after heating at reflux temperature, β-lactam α-allenic ethers **6a–i** reacted to form the corresponding heterocycles (Scheme 7). New pentasubstituted pyrroles **15a–i** were obtained in fair yields by means of our one-pot procedure,[13] without the concomitant formation of any regioisomer (Scheme 7). Hydroxymethyl functionalities or aryl moieties at the 2-position are structural features that are often associated with pronounced physiological activities of pyr-



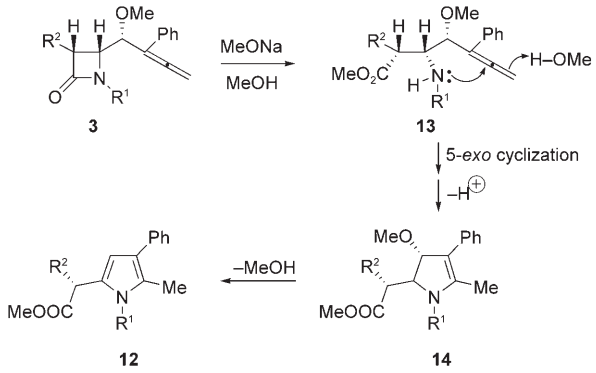
Scheme 3. Ring opening of β-lactams **3** followed by silver-catalyzed aminocyclization reactions leads to the formation of β-allenamines **7** and pyrroles **8**. Reagents and conditions: a) NaOMe, MeOH, RT, 8 h; b) 20 mol% $AgNO_3$, K_2CO_3, MeCN, RT, 12 h.



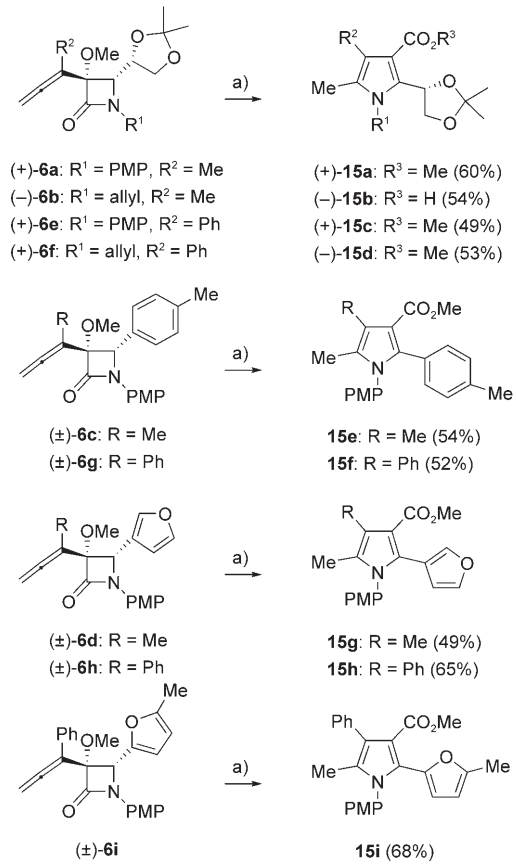
Scheme 4. Mechanistic explanation for the silver-catalyzed aminocyclization of β-allenamines **7**.



Scheme 5. One-pot synthesis of pyrroles **12** through domino β-lactam ring-opening allene cyclization. Reagents and conditions: a) MeONa, MeOH, RT, **12a**: 8 h; **12b**: 24 h; **12c**: 96 h; **12d**: 96 h; **12e**: 24 h; **12f**: 24 h.



Scheme 6. Mechanistic explanation for the direct formation of pyrroles **12** from phenyl allenes **3** through *exo*-cyclization.



Scheme 7. One-pot synthesis of pyrroles **15** through domino β-lactam ring-opening allene cyclization. Reagents and conditions: a) MeONa, MeOH, reflux, **15a**: 2 h; **15b**: 12 h; **15c**: 12 h; **15d**: 6 h; **15e**: 12 h; **15f**: 25 h; **15g**: 34 h; **15h**: 54 h; **15i**: 28 h.

roles.[14,15] Interestingly, compounds **15a–d** are 2-(hydroxyalkyl)pyrroles, whereas compounds **15e–i** are 2-arylpyrroles. More vigorous conditions were required for tertiary allenol derivatives **6**. Nevertheless, a completely regioselective cyclization was still observed in these cases. The reactivity difference between substrates **3** and **6** is striking and indicates a

strong influence of the steric properties of the substrate. Similar behavior for methyl allenes **6a–d** and phenyl allenes **6e–i** occurred during these reactions, compared with the reactions performed with allenic β-lactams **3**, probably because of the higher reaction temperature. The pathway for the formation of products **15** is closely related to the proposed pathway for the formation of pyrroles **12** (see the Supporting Information).

No loss of enantiomeric purity of pyrroles **8**, **12**, and **15** was evident from the ^{1}H NMR spectra of adducts (−)-**8b**, (−)-**12a**, and (+)-**15a**, which were obtained with enantiomeric excess (*ee*) values of >95%, in the presence of a europium(III) chiral shift reagent. Typically, after the addition of the chiral shift reagent the signals for enantiopure pyrroles moved downfield by approximately $\delta = 0.3$ ppm. For racemates, after the addition of the chiral shift reagent, the signals for both enantiomers in the ^{1}H NMR spectra could be differentiated by about $\delta = 0.4$ ppm. In the ^{1}H NMR spectra of the racemates after the addition of the chiral shift reagent, the protons of the enantiomers not prepared in this work were upfield of the analogous protons of our enantiopure pyrrole derivatives.

Conclusion

In conclusion, using a simple reagent we have successfully accomplished an unprecedented domino lactam ring-opening allene cyclization reaction for the construction of the biologically relevant pyrrole frame, which offers clean and synthetically competitive alternatives to existing methodologies.[16]

Experimental Section

General methods: ^{1}H and ^{13}C NMR spectra were recorded by using a Bruker Avance-300, Varian VRX-300S, or Bruker AC-200 spectrometer. NMR spectra were recorded in $CDCl_3$ unless otherwise stated. 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 recorded by using an HP5989A spectrometer in electron impact (EI) or electrospray modes (ES) unless otherwise stated. Specific rotation $[\alpha]_D$ is given in 10^{-1} °cm^{2}g^{-1} at 20 °C, and the concentration (*c*) is expressed in g per 100 mL. All commercially available compounds were used without further purification.

General procedure for the preparation of β-allenamines 7: Sodium methoxide (0.6 mmol) was added portionwise at 0 °C to a solution of the appropriate allenyl-β-lactam **3** (0.15 mmol) in methanol (3 mL). The reaction was stirred at room temperature under an argon atmosphere for 8 h and then water was added (0.5 mL). The methanol was removed under reduced pressure, the aqueous layer was extracted with ethyl acetate (5× 3 mL), the organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to give β-allenamines **7**. Spectroscopic and analytical data for a representative form of compounds **7** follow.[17]

*β-Allenamine (−)-**7a***: From the starting material β-lactam (+)-**3a** (75 mg, 0.25 mmol), compound (−)-**7a** was obtained as a colorless oil (78 mg, 93%). $[\alpha]_D = -16.0$ ($c = 0.3$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 6.68$ (d, $J = 9.0$ Hz, 2H), 6.50 (d, $J = 9.0$ Hz, 2H), 4.62–4.58 (m, 2H), 4.24 (d, $J = 2.2$ Hz, 1H), 3.88 (dd, $J = 10.0$, 2.9 Hz, 1H), 3.72 (d, $J = 10$ Hz, 1H), 3.70 (s, 3H), 3.54 (s, 3H), 3.49 (s, 3H), 3.29 (s, 3H), 1.49 ppm (t, $J = 3.2$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta =$ 208.7, 172.3, 152.1, 141.4, 115.0, 114.4, 95.2, 82.6, 79.5, 73.7, 59.2, 58.8, 56.1, 55.6, 51.6, 12.8 ppm; IR ($CHCl_3$): $\tilde{\nu} = 1940$, 1735 cm^{-1}; MS (ES): *m*/*z* (%): 336 (100) $[M+H]^+$, 335 (15) $[M]^+$; elemental analysis calcd (%) for $C_{18}H_{25}NO_5$: C 64.46, H 7.51, N 4.18; found: C 64.61, H 7.46, N 4.14.

General procedure for the silver-mediated cyclization of β-allenamines 7—preparation of pyrroles 8: Silver nitrate (68 mg, 0.40 mmol) and potassium carbonate (550 mg, 3.98 mmol) were added to a stirred solution of the corresponding β-allenamine **7** (2.0 mmol) in acetonitrile (10 mL) in the absence of sunlight. The reaction was stirred at room temperature until the starting material had disappeared (typically 12 h). Then, the reaction mixture was filtered though a pad of Celite. Next, brine (2 mL) was added to the filtrate and it was extracted with ethyl acetate (4× 5 mL). The organic extract was washed with brine, dried over $MgSO_4$, and the solvent was removed under reduced pressure. Chromatography of the residue on deactivated silica gel (eluent: ethyl acetate/hexane) gave analytically pure pyrroles **8**.

*Pyrrole (−)-**8a***: From the starting material β-allenamine (−)-**7a** (48 mg, 0.14 mmol), pyrrole (−)-**8a** was obtained as a colorless oil after purification of the residue by column chromatography (hexane/ethyl acetate 2:1) (20 mg, 47%). $[\alpha]_D = -14.1$ ($c = 0.3$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.20$–7.18 (m, 2H), 6.98–6.94 (m, 2H), 6.12 (s, 1H), 4.48 (s, 1H), 3.86 (s, 3H), 3.69 (s, 3H), 3.20 (s, 3H), 2.04 (s, 3H), 1.92 ppm (s, 3H); IR ($CHCl_3$): $\tilde{\nu} = 1740$, 750 cm^{-1}; MS (ES): *m*/*z* (%): 304 (100) $[M+H]^+$, 303 (7) $[M]^+$; elemental analysis calcd (%) for $C_{17}H_{21}NO_4$: C 67.31, H 6.98, N 4.62; found: C 67.44, H 6.93, N 4.66.

General procedure for the direct formation of pyrroles 12 or 15 from phenyl allenes 3 or allenes 6: Sodium methoxide (0.6 mmol) was added portionwise at 0 °C to a solution of the appropriate allenyl-β-lactam **3** or **6** (0.15 mmol) in methanol (3 mL). The reaction was stirred at room temperature or at reflux under an argon atmosphere until complete disappearance of the starting material was observed by TLC and then water was added (0.5 mL). The methanol was removed under reduced pressure, the aqueous layer was extracted with ethyl acetate (5×3 mL), the organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. Chromatography of the residue on deactivated silica gel (eluent: ethyl acetate/hexane) gave analytically pure pyrroles **12** or **15**.

*Pyrrole (−)-**12a***: From the starting material allene-β-lactam (+)-**3c** (67 mg, 0.18 mmol), pyrrole (−)-**12a** was obtained as a colorless oil after purification of the residue by column chromatography (eluent: hexane/ethyl acetate 2:1; 52 mg, 77%). $[\alpha]_D = -30.0$ ($c = 0.4$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.44$–7.20 (m, 6H), 7.04–7.00 (m, 3H), 6.45 (s, 1H), 4.52 (s, 1H), 3.88, 3.71 (2s, each 3H), 3.24 (s, 3H), 2.13 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 170.6$, 159.4, 136.7, 130.1, 129.8, 128.3, 128.0, 127.9, 127.5, 125.3, 121.7, 114.2, 114.1, 109.2, 74.7, 56.7, 55.5, 52.2, 12.0 ppm; IR ($CHCl_3$): $\tilde{\nu} = 1742$, 750 cm^{-1}; MS (ES): *m*/*z* (%): 366 (100) $[M+H]^+$, 365 (5) $[M]^+$; elemental analysis calcd (%) for $C_{22}H_{23}NO_4$: C 72.31, H 6.34, N 3.83; found C 72.17, H 6.30, N 3.85.

*Pyrrole (−)-**12f***: From the starting material allene-β-lactam (−)-**3h** (28 mg, 0.07 mmol), pyrrole (−)-**12f** was obtained as a colorless oil after purification of the residue by column chromatography (eluent: hexane/ethyl acetate 3:1; 16 mg, 57%). $[\alpha]_D = -98.8$ ($c = 1.2$ in acetone); ^{1}H NMR (300 MHz, [D$_6$]acetone, 25 °C): $\delta = 7.36$–7.28 (m, 4H), 7.14–7.12 (m, 2H), 6.96–6.90 (m, 3H), 6.18 (s, 1H), 5.69 (d, $J = 1.5$ Hz, 1H), 4.44, 4.28 (2dd, $J = 12.5$, 2.0 Hz, each 1H), 3.81, 3.35 (2s, each 3H), 2.00 (s, 3H), 1.76 ppm (d, $J = 1.7$ Hz, 1H); ^{13}C NMR (75 MHz, [D$_6$]acetone, 25 °C): $\delta = 170.3$, 159.3, 137.1, 135.6, 130.8, 130.7, 130.6, 128.2, 127.7, 127.5, 125.5, 124.9, 120.4, 113.5, 113.1, 108.9, 90.7, 73.4, 54.8, 50.9, 12.7, 11.2 ppm; IR ($CHCl_3$): $\tilde{\nu} = 1750$, 747 cm^{-1}; MS (EI): *m*/*z* (%): 403 (4) $[M]^+$, 344 (100) $[M-59]^+$; elemental analysis calcd (%) for $C_{25}H_{25}NO_4$: C 74.42, H 6.25, N 3.47; found C: 74.56, H 6.30, N 3.43.

*Pyrrole (+)-**15a***: From the starting material allenyl-β-lactam (+)-**6a** (50 mg, 0.14 mmol), compound (+)-**17a** was obtained as a colorless oil after purification of the residue by column chromatography (eluent: hexane/ethyl acetate 5:1; 30 mg, 60%). $[\alpha]_D = +72.0$ ($c = 0.6$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.17$, 7.06 (2d, $J = 9.5$ Hz, each 1H), 6.93 (dd, $J = 7.5$, 1.5 Hz, 2H), 5.81 (dd, $J = 8.9$, 6.7 Hz, 1H), 4.02 (t, $J = 7.0$ Hz, 1H), 3.85, 3.84 (2s, each 3H), 3.70 (dd, $J = 8.9$, 7.5 Hz, 1H),

2.19 (s, 3H), 1.80 (s, 3H), 1.26, 0.93 ppm (2s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ = 166.4, 159.4, 131.6, 130.8, 129.3, 128.9, 115.9, 114.2, 113.9, 113.4, 108.6, 70.6, 68.3, 55.5, 50.8, 25.5, 25.0, 11.2, 10.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 1699 cm^{-1}; MS (EI): *m*/*z* (%): 359 (19) $[M]^+$, 152 (100) $[M-207]^+$; elemental analysis calcd (%) for $C_{20}H_{25}NO_5$: C 66.83, H 7.01, N 3.90; found: C 66.97, H 7.05, N 3.86.

*Pyrrole **15e***: From the starting material allenyl-β-lactam (±)-**6c** (86 mg, 0.25 mmol), compound **17e** was obtained as a colorless solid after purification of the residue by column chromatograpy (eluent: dichloromethane; 48 mg, 54%). M.p. 161–162°C; ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 6.99 (d, *J* = 1.5 Hz, 4H), 6.93, 6.77 (2d, *J* = 9.0 Hz, each 2H), 3.78, 3.64 (2s, each 3H), 2.30, 2.27 (2s, each 3H), 1.98 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ = 158.7, 136.7, 131.1, 130.8, 129.6, 129.5, 128.0, 127.3, 116.2, 113.8, 55.3, 50.4, 21.2, 11.1, 10.6 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 1690 cm^{-1}; MS (ES): *m*/*z* (%): 350 (100) $[M+H]^+$, 349 (24) $[M]^+$; elemental analysis calcd (%) for $C_{22}H_{23}NO_3$: C 75.62, H 6.63, N 4.01; found: C 75.74, H 6.60, N 4.03.

*Pyrrole **15i***: From the starting material allenyl-β-lactam (±)-**6i** (72 mg, 0.18 mmol), compound **17i** was obtained as a pale yellow oil after purification of the residue by column chromatography (eluent: hexane/ethyl acetate 5:1; 49 mg, 68%). ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 7.35–7.31 (m, 5H), 7.16, 6.92 (2d, *J* = 9.0 Hz, each 2H), 6.02 (d, *J* = 3.1 Hz, 1H), 5.85 (dd, *J* = 3.1, 1.0 Hz, 1H), 3.85, 3.59 (2s, each 3H), 2.16, 1.98 ppm (2s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ = 165.8, 159.3, 151.7, 143.0, 135.5, 131.1, 130.1, 129.3, 127.7, 126.2, 122.8, 116.2, 114.0, 111.9, 106.6, 55.4, 51.0, 13.4, 11.4 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 1694 cm^{-1}; MS (EI): *m*/*z* (%): 401 (100) $[M]^+$; elemental analysis calcd (%) for $C_{25}H_{23}NO_4$: C 74.79, H 5.77, N 3.49; found: C 74.67, H 5.74, N 3.52.

Acknowledgements

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[13] In contrast with sensitive heterocycles **8**, pyrroles **12** and **15** are stable materials. For example, pyrroles **15e–i** are very stable compounds and can be stored for several months at RT without appreciable decomposition.

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[16] Preliminary studies concerning the oxidative N-deprotection of *N*-PMP pyrroles resulted in a complex process. Further investigations into ruthenium-catalyzed N-allyl cleavage are in progress in our laboratories. All of these results will be reported in due course.

[17] Full spectroscopic and analytical data for compounds not included in the Experimental Section are described in the Supporting Information. It contains compound characterization data, experimental procedures for compounds **2a–h**, (*R*)- and (*S*)-*O*-acetylmandelates of compounds (+)-**2g**, **3a–h**, **5a–h**, **6a–h**, (−)-**7b**, (−)-**8b**, **12b–e**, **15b–d**, and **15f–h**, mechanistic explanation for the direct formation of pyrroles **12** from phenyl allenes **3** through *endo*-cyclization (Scheme S8), and rationalization for the direct formation of pyrroles **15** from allenes **6** (Scheme S9).

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