# Carbonyl Allenylation/Free Radical Cyclization Sequence as a New Regio- and Stereocontrolled Access to Bi- and Tricyclic β-Lactams

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Received September 4, 2006

i) Ph₃SnH, AIBN, C₆H₆, Δ.
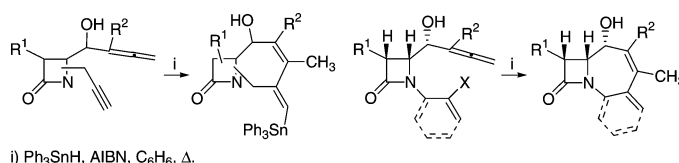
A novel approach to racemic and enantiopure nonconventional fused bi- and tricyclic β-lactams has been developed by using regio- and stereocontrolled intramolecular free radical reactions in monocyclic 2-azetidinone-tethered allenynes and haloallenes. The access to allene cyclization precursors was achieved by metal-mediated carbonyl allenylation of appropriately substituted 4-oxoazetidine-2-carbaldehydes in an aqueous environment. The tin-promoted radical cyclizations of allene-β-lactams are totally regioselective for the central allenic carbon, providing bi- and tricyclic β-lactams containing a seven-membered ring.

Introduction

The extensive use of common β-lactam antibiotics such as penicillins and cephalosporins in medicine has resulted in an increasing number of resistant strains of bacteria through mutation and β-lactamase gene transfer.[1] In order to oppose the destructive action of β-lactamases, one strategy consists of modifying the structure of the β-lactam antibiotic, aiming to render it insensitive to the β-lactamase attack. Among others, the discovery of tricyclic β-lactam antibiotics, which are a new class of synthetic antibacterial agents featuring good resistance to β-lactamases and dehydropeptidases,[2] has triggered a renewed interest in the building of new polycyclic β-lactam systems in an attempt to move away from the classical β-lactam antibiotic structures.[3] In addition, new applications of β-lactams such as

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(4) For a review, see: (a) Veinberg, G.; Vorona, M.; Shestakova, I.; Kanepe, I.; Lukevics, E. *Curr. Med. Chem.* **2003**, *10*, 1741. For selected examples, see: (b) Rothstein, J. D.; Patel, S.; Regan, M. R.; Haenggeli, C.; Huang, Y. H.; Bergles, D. E.; Jin, L.; Hoberg, M. D.; Vidensky, S.; Chung, D. S.; Toan, S. V.; Bruijn, L. I.; Su, Z.-z.; Gupta, P.; Fisher, P. B. *Nature* **2005**, *433*, 73. (c) Hogan, P. C.; Corey, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 15386. (d) Clader, J. W. *J. Med. Chem.* **2004**, *47*, 1. (e) Kvaerno, L.; Ritter, T.; Werder, M.; Hauser, H.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4653. (f) Burnett, D. A. *Curr. Med. Chem.* **2004**, *11*, 1873. (g) Veinberg, G.; Vorona, M.; Shestakova, I.; Kanepe, I.; Lukevics, E. *Curr. Med. Chem.* **2003**, *10*, 1741. (h) Page, M. I.; Laws, A. P. *Tetrahedron* **2000**, *56*, 5631. (i) Haley, T. M.; Angier, S. J.; Borthwick, A. D.; Singh, R.; Micetich, R. G. *Drugs* **2000**, *3*, 512.

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TABLE 1. Allenylation Reaction of 4-Oxoazetidine-2-carbaldehydes 1[a]

aldehyde	R[1]	R[2]	R[3]	product	*syn/anti* ratio[b]	yield (%)[c]
(+)-**1a**	2-propynyl	MeO	Me	(+)-**2a**	98:2	75
(+)-**1a**	2-propynyl	MeO	Ph	(+)-**2b**	95:5	60
(±)-**1b**	PMP	2-propynyl	Me	*anti*-(±)-**2c**	10:90	81[d]
(+)-**1c**	2-Br−2-propenyl	MeO	Me	(+)-**2d**	88:12	63[e]
(+)-**1c**	2-Br−2-propenyl	MeO	Ph	(+)-**2e**	92:8	55[f]
(±)-**1d**	*o*-BrC$_6$H$_4$	MeO	Me	(±)-**2f**	70:30	47[g]
(±)-**1d**	*o*-BrC$_6$H$_4$	MeO	Ph	(±)-**2g**	100:0	57
(±)-**1e**	*o*-IC$_6$H$_4$	MeO	Me	(±)-**2h**	75:25	66[h]
(±)-**1f**	*o*-IC$_6$H$_4$	PhO	Me	(±)-**2i**	85:15	51[e]

[a] All reactions were carried out on 1 mmol scale. PMP = 4-MeOC$_6$H$_4$. [b] The ratio was determined by integration of well-resolved signals in the ^{1}H NMR spectra of the crude reaction mixtures before purification. [c] Yield of pure, isolated *syn*-isomer [or *anti*-isomer for (±)-**2c**] with correct analytical and spectral data. [d] Nine percent of pure *syn*-isomer could be isolated. [e] Nine percent of pure *anti*-isomer could be isolated. [f] Five percent of pure *anti*-isomer could be isolated. [g] Twenty percent of pure *anti*-isomer could be isolated. [h] Twenty-two percent of pure *anti*-isomer could be isolated.

enzyme inhibitors[4] as well as building blocks for compounds of biological interest have been discovered.[5] On the other hand, the stereoselective synthesis of complex heterocycles and carbocycles by radical cyclization has now been established as an efficient methodology in organic chemistry.[6] This wide research has been fostered by its operational simplicity and its tolerance to substrate functionalization. In connection with our studies on the preparation and synthetic utility of β-lactams,[7] we report herein full details of an approach to bicyclic β-lactams through radical cyclization of 2-azetidinone-tethered allenynes,[8] as well as the extension to 2-azetidinone-tethered haloallenes for the synthesis (racemic and asymmetric) of fused bi- and tricyclic β-lactams.

Results and Discussion

Starting substrates, 4-oxoazetidine-2-carbaldehydes **1a−f**, were prepared both in the racemic form and in optically pure form using standard methodology. Enantiopure 2-azetidinones (+)-**1a** and (+)-**1c** were obtained as single *cis*-enantiomers from imines of (*R*)-2,3-*O*-isopropylideneglyceraldehyde, through Staudinger reaction with methoxyacetyl chloride in the presence of Et$_3$N, followed by sequential acidic acetonide hydrolysis and oxidative cleavage.[9a] Racemic compound (±)-**1b** was obtained as a single *cis*-diastereoisomer, following our one-pot method

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(7) See, for instance: (a) Alcaide, B.; Almendros, P.; Martínez del Campo, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4501. (b) Alcaide, B.; Almendros, P.; Alonso, J. M. *Chem.−Eur. J.* **2006**, *12*, 2874. (c) Alcaide, B.; Almendros, P.; Luna, A.; Torres, M. R. *J. Org. Chem.* **2006**, *71*, 4818. (d) Alcaide, B.; Almendros, P.; Redondo, M. C. *Chem. Commun.* **2006**, 2616. (e) Alcaide, B.; Almendros, P.; Rodríguez-Acebes, R. *J. Org. Chem.* **2006**, *71*, 2346. (f) Alcaide, B.; Almendros, P.; Aragoncillo, C.; Redondo, M. C.; Torres, M. R. *Chem.−Eur. J.* **2006**, *12*, 1539. (g) Alcaide, B.; Almendros, P.; Rodríguez-Acebes, R. *Chem.−Eur. J.* **2005**, *11*, 5708. (h) Alcaide, B.; Almendros, P.; Cabrero, G.; Ruiz, M. P. *Org. Lett.* **2005**, *7*, 3981. (i) Alcaide, B.; Almendros, P.; Rodríguez-Acebes, R. *J. Org. Chem.* **2005**, *70*, 3198. (j) Alcaide, B.; Almendros, P.; Rodríguez-Acebes, R. *J. Org. Chem.* **2005**, *70*, 2713.

(8) For a preliminary communication of a part of this work, see: Alcaide, B.; Almendros, P.; Aragoncillo, C. *Org. Lett.* **2003**, *5*, 3795.

SCHEME 1
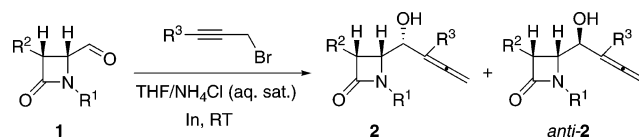
SCHEME 2[a]
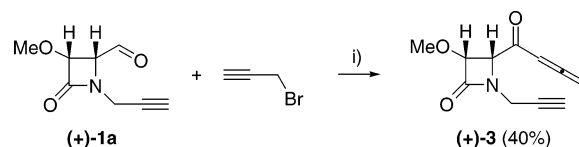
[a] Key: (i) (a) Zn, THF/NH$_4$Cl (aq. sat.), rt; (b) Dess−Martin periodinane, CH$_2$Cl$_2$, rt.

from *N,N*-di(*p*-methoxyphenyl)glyoxal diimine.[9b] Azetidinones **1d−f** bearing a *N*-(*o*-halophenyl) moiety were obtained from styryl imines through Staudinger reaction with the appropriate alkoxyacetyl chloride in the presence of Et$_3$N, followed by ozonolysis.[10] Racemic compounds **1d−f** were obtained as *cis/ trans* mixtures with modest *cis*-selectivity, with the *cis*-isomers being easily separated by column chromatography. 2-Azetidinone-tethered allenols **2a−i** were prepared via indium-mediated Barbier-type carbonyl allenylation reaction of β-lactam aldehydes **1a−f** in aqueous media (Scheme 1 and Table 1).[11]

β-Lactam-tethered allenone (+)-**3** was obtained from 4-oxoazetidine-2-carbaldehyde (+)-**1a** by zinc-mediated carbonyl propargylation followed by Dess−Martin oxidation with concomitant propargyl to allene rearrangement (Scheme 2).

The allene moiety represents a versatile and useful building block in organic synthesis, especially in the area of transition-metal-assisted reactions.[12] Instead of an alkene or an alkyne, an allene component is a fascinating substrate in a free radical cyclization because of its unique reactivity and the synthetic

(9) (a) Rodríguez-Acebes, R. Ph.D. Thesis, Universidad Complutense de Madrid, 2005. (b) Alcaide, B.; Almendros, P.; Salgado, N. R. *J. Org. Chem.* **2000**, *65*, 3310.

(10) (a) Redondo, M. C. Ph.D. Thesis, Universidad Complutense de Madrid, 2006. (b) Alcaide, B.; Almendros, P.; Rodríguez-Vicente, A.; Ruiz, M. P. *Tetrahedron* **2005**, *71*, 2767.

(11) Alcaide, B.; Almendros, P.; Aragoncillo, C. *Chem.−Eur. J.* **2002**, *8*, 1719.

(12) For reviews, see: (a) Ma, S. *Chem. Rev.* **2005**, *105*, 2829. (b) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, Germany, 2004. (c) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701. (d) Alcaide, B.; Almendros, P. *Eur. J. Org. Chem.* **2004**, 3377. (e) Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12. (f) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590. (g) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067.
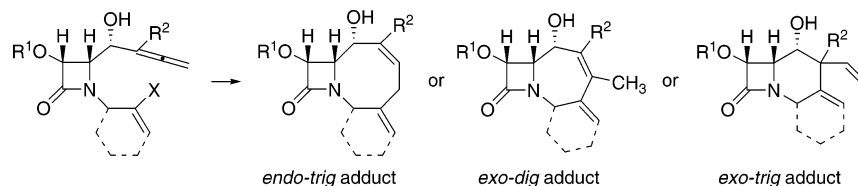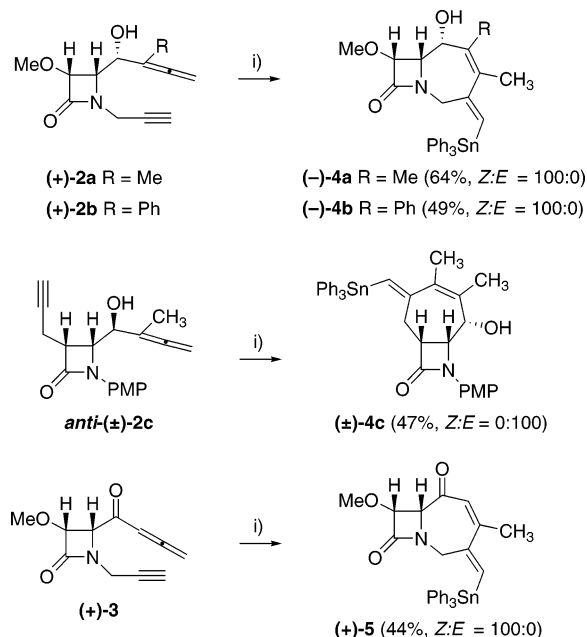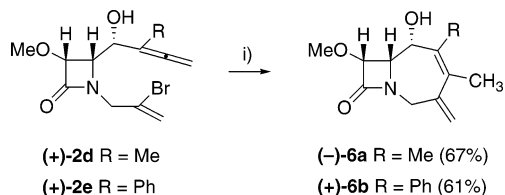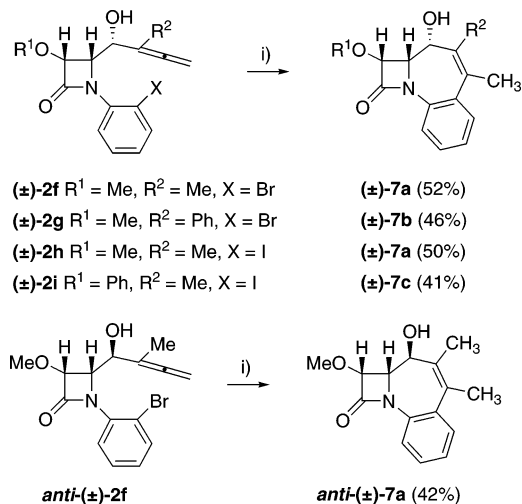
FIGURE 1.

endo-trig adduct   *exo-dig* adduct   *exo-trig* adduct

SCHEME 3[a]

(+)-**2a** R = Me
(+)-**2b** R = Ph

(−)-**4a** R = Me (64%, *Z:E* = 100:0)
(−)-**4b** R = Ph (49%, *Z:E* = 100:0)

anti-(±)-**2c**

(±)-**4c** (47%, *Z:E* = 0:100)

(+)-**3**

(+)-**5** (44%, *Z:E* = 100:0)

[a] Key: (i) Ph₃SnH, AIBN, C₆H₆, 80 °C.

SCHEME 4[a]

(+)-**2d** R = Me
(+)-**2e** R = Ph

(−)-**6a** R = Me (67%)
(+)-**6b** R = Ph (61%)

[a] Key: (i) Ph₃SnH, AIBN, C₆H₆, 80 °C.

SCHEME 5[a]

(±)-**2f** R¹ = Me, R² = Me, X = Br
(±)-**2g** R¹ = Me, R² = Ph, X = Br
(±)-**2h** R¹ = Me, R² = Me, X = I
(±)-**2i** R¹ = Ph, R² = Me, X = I

(±)-**7a** (52%)
(±)-**7b** (46%)
(±)-**7a** (50%)
(±)-**7c** (41%)

anti-(±)-**2f**

anti-(±)-**7a** (42%)

[a] Key: (i) Ph₃SnH, AIBN, C₆H₆, 80 °C.

SCHEME 6[a]

(−)-**6a**, 73%   (−)-**4a**   (−)-**8**, 70%

[a] Key: (i) PTSA, CH₂Cl₂, rt; (ii) NBS, CH₂Cl₂, rt.
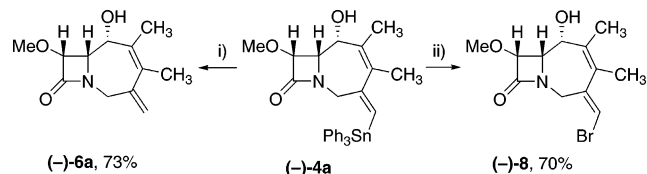
use of the final products.[13] However, regioselectivity problems are significant (*endo-trig* versus *exo-dig* versus *exo-trig* cyclization). The regiochemical possibilities of a radical cyclization using 2-azetidinone-tethered allenes are shown in Figure 1.

Having obtained the monocyclic precursors, the next stage was set to carry out the key radical cyclization step. In an initial

study, we found that allenynol (+)-**2a** when heated in the presence of triphenyltin hydride and AIBN in benzene solution gave the bicyclic β-lactam (−)-**4a** in 64% yield as a single regio- and *Z*-isomer. Tin-promoted cyclization of allenynol (+)-**2b** afforded the expected 2-azetidinone (−)-**4b** containing a seven-membered ring. Allenynol *anti*-(±)-**2c** having the alkynyl side chain at C3 instead of N1 underwent cyclization to afford the C3−C4 fused β-lactam (±)-**4c**. Similar behavior was observed for the free radical cyclization of allenynone (+)-**3**, which afforded the heterobicyclic ketone (+)-**5**. Interestingly, only bicycles **4** and **5** were found as a consequence of a totally regioselective radical cyclization onto the central carbon (Scheme 3). Neither the *endo-trig*-cyclized product nor the *exo-trig*-cyclized product was detected. Although complete conversion was observed by TLC and ¹H NMR analysis of the crude reaction mixtures, some decomposition was observed on sensitive bicycles **4** and **5** during purification by flash chromatography, which may be responsible for the moderate isolated yields.[14]

Next, we decided to explore the extension of the above radical cyclization of 2-azetidinone-tethered allenynes to the corresponding bromovinyl and haloaryl allenes. The tin-promoted radical reaction was also useful in the conversion of the β-lactam

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SCHEME 7
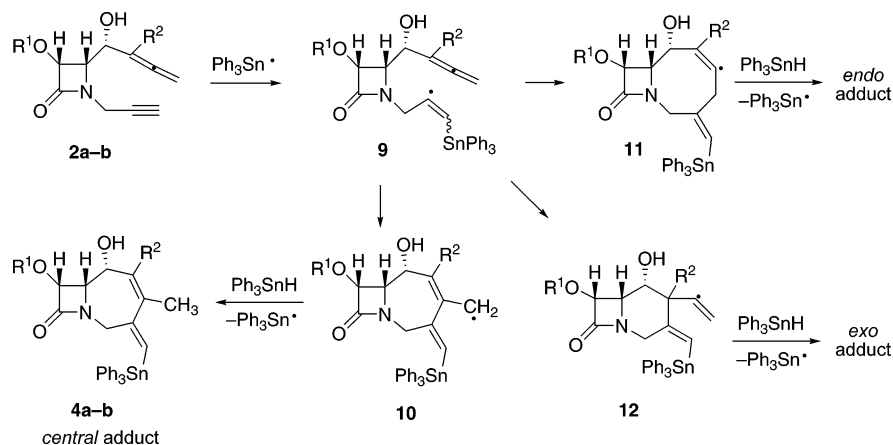
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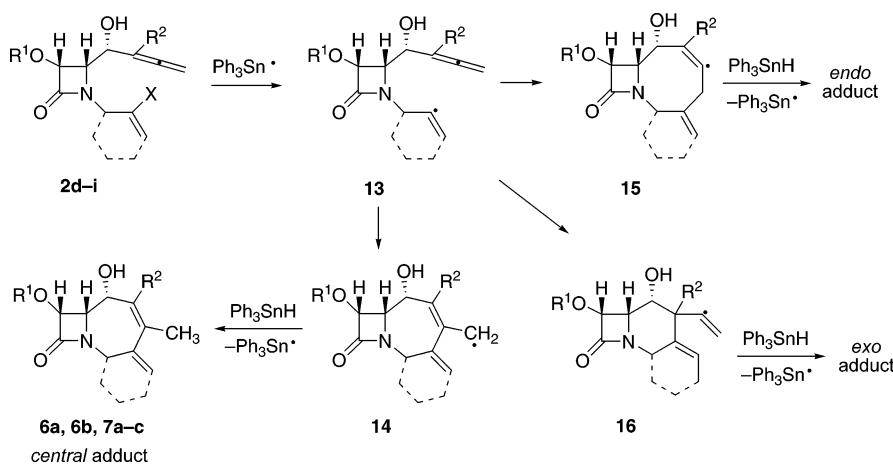
allenes (+)-**2d** and (+)-**2e**, with a bromopropenyl substituted at the nitrogen atom, into the corresponding bicyclic systems (−)-**6a** and (+)-**6b** with similar efficiency and selectivity (Scheme 4).

The treatment of β-lactam allenes **2f**−**i** having a bromo- or iodophenyl group (N-tethered) under similar conditions for the preparation of bicycles **4**−**6** gave the fused tricyclic β-lactams **7a**−**c** containing a central seven-membered ring (Scheme 5). Benzofused β-lactams **7** can be considered as superior cyclo-homologues of benzocarbapenems and benzocarbacephems, which have been designed as suicide inactivators of β-lacta-mases.[15]

The triphenyltin group in products **4** and **5** represents a very useful handle since it provides an entry into the exceptionally rich chemistry of tin. To illustrate the value of these function-alized substrates, the vinylic stannane (−)-**4a** was transformed into the vinylic bromide (−)-**8** under exposure to *N*-bromosuc-

cinimide, while treatment of cyclized adduct (−)-**4a** with PTSA in CH$_2$Cl$_2$ yielded the destannylated product (−)-**6a** (Scheme 6).

It is presumed that the stannyl radical, by addition to the terminal position of the triple bond in allenynes **2a**−**c** and **3**[16] or through bromine abstraction in bromovinyl and haloaryl allenes **2d**−**i**, gives the vinylic radical intermediates **9** and **13** in the propagation step, followed by cyclization toward the central carbon bond of the allene moiety to give in a total regio- and stereoselective fashion fused cycles **4**−**7** via allylic radical intermediates **10** and **14**. While both *endo-trig* and *exo-trig* cyclizations of radical intermediates **9** and **13** would give vinylic radicals **11**, **15** and **12**, **16**, respectively, 7-*exo-dig* cyclization leads to the energetically more favored allylic radicals **10** and **14** (Schemes 7 and 8).[17] Chemoselectivity of the stannyl radical addition to the triple bond deserved special mention because examples are known where stannyl radicals initiate radical cascade by the addition to the allene bond.[18]

(14) It seems unlikely that *E*-stannylated products, which are susceptible to decomposition, are generated. Nevertheless, the decomposition of *E*-stannylated products possibly generated in the radical cyclization may be responsible as well for the moderate yields. We thank a reviewer for this suggestion.

(15) For selected articles, see: (a) Reference 10. (b) Coulton, S.; Gilchrist, T. L.; Graham, K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1193. (c) Gilchrist, T. L.; Rahmam, A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1203. (d) Joyeau, R.; Yadav, L. D. S.; Wakselman, M. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1899. (e) Ongania, K. H.; Wallnoefer, M. *Arch. Pharm. (Weinheim, Ger.)* **1985**, *318*, 2. (f) Hegedus, L. S.; McGuire, M. A.; Schultze, L. M.; Yijun, C.; Anderson, O. P. *J. Am. Chem. Soc.* **1984**, *106*, 2680. (g) Bachi, M. D.; Klein, J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1925.

(16) (a) Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 2829. (b) Stork, G.; Baine, N. H. *Tetrahedron Lett.* **1985**, *26*, 5927. (c) Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1983**, *105*, 3720. (d) Stork, G.; Baine, N. H. *J. Am. Chem. Soc.* **1982**, *104*, 2321.

(17) At first glance, the allylic radical resulting from radical addition to the central carbon may appear to be a more favorable pathway owing to resonance delocalization. However, the radical intermediate initially gener-ated lacks allylic stabilization because the adjacent π bond is orthogonal to the singly occupied p orbital and a rotation is necessary to realize allylic stabilization. See: (a) Gobbi, A.; Frenking, G. *J. Am. Chem. Soc.* **1994**, *116*, 9275. (b) Mo, Y.; Lin, Z.; Wu, W.; Zhang, Q. *J. Phys. Chem.* **1996**, *100*, 6469.

The structure and stereochemistry (by vicinal proton couplings and qualitative homonuclear NOE difference spectra) of compounds **4–8** were assigned by NMR studies (by vicinal proton couplings and qualitative homonuclear NOE difference spectra). Taking into account that isomerically pure allenols **2** could be obtained and cyclized, the stereochemistry at the carbinolic stereogenic center for compounds **2** was immediately deduced by comparison with the NOE results of the bi- and tricyclic systems. Besides, the *cis*-stereochemistry of the four-membered ring is set during the cyclization step to form the 2-azetidinone ring, and it is transferred unaltered during the further synthetic steps.

Conclusions

In conclusion, we have described here radical reactions employing 2-azetidinone allenes. The free radical cyclization of β-lactam-tethered allenynes and haloallenes is totally regioselective for the central carbon in the allenic motif. We have shown that combination of carbonyl allenylation reaction and tin-promoted radical cyclization may lead to a useful preparation of racemic and enantiopure nonconventional fused bi- and tricyclic β-lactams containing a seven-membered ring. Applications to different heterocycles employing these radical cyclizations are underway.

Experimental Section

General. The same experimental techniques were used as previously reported.[7]

General Procedure for the Free Radical Synthesis of Bi- and Tricyclic β-Lactams 4–7. A solution of the appropriate 2-azetidinone-tethered allenyne or haloallene **2** or **3** (0.40 mmol), triphenyltin hydride (0.60 mmol), and AIBN (cat.) in benzene (35 mL) was heated at reflux temperature until complete disappearance (TLC) of starting material. The reaction mixture was allowed to cool to room temperature, the solvent was removed under reduced pressure, and fused adducts **4–7** were obtained after purification by flash chromatography on silica gel using hexanes/ethyl acetate/triethylamine mixtures. Spectroscopic and analytical data for some representative forms of **4–7** follow.[19]

Bicyclic β-Lactam (−)-4a. From 51 mg (0.23 mmol) of allenyne (+)-**2a** and after chromatography of the residue using hexanes/ethyl acetate (1:1 containing 1% of triethylamine) as eluent, compound (−)-**4a** (85 mg, 64%) was obtained as a colorless oil: $[\alpha]_D = -1.3$ (*c* 0.4, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 7.59 (m, 6H), 7.40 (m, 9H), 6.29 (s, 1H), 4.59 (m, 1H), 4.54 (d, 1H, *J* = 5.0 Hz), 4.29 (d, 1H, *J* = 5.0 Hz), 4.23 (d, 1H, *J* = 13.9 Hz), 3.64 (m, 1H), 3.59 (s, 3H), 3.09 (d, 1H, *J* = 6.9 Hz), 2.01 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (CDCl$_3$) δ 166.6, 160.7, 157.5, 138.0, 136.9, 136.8, 128.9, 128.7, 127.9, 83.7, 72.3, 59.3, 55.4, 48.9, 21.6, 16.8; IR (CHCl$_3$, cm^{-1}) ν 1740. MS (CI); *m/z* 572 (M$^+$, 3), 495 (M$^+$ − 77, 100). Anal. Calcd for C$_{30}$H$_{31}$NO$_3$Sn: C, 62.96; H, 5.46; N, 2.45. Found: C, 62.82; H, 5.49; N, 2.42.

Bicyclic β-Lactam (+)-5. From 34 mg (0.16 mmol) of allenynone (+)-**3** and after chromatography of the residue using hexanes/ethyl acetate (6:1 containing 1% of triethylamine) as eluent, compound (+)-**5** (39 mg, 44%) was obtained as a colorless oil: $[\alpha]_D = +60.8$ (*c* 0.2, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 7.39 (m, 15H), 7.00 (dd, 1H, *J* = 15.6, 6.8 Hz), 6.29 (dd, 1H, *J* = 15.6, 1.6 Hz), 4.85 and 4.67 (d, each 1H, *J* = 5.2 Hz), 4.46 and 3.95 (dd, each 1H, *J* = 17.7, 2.6 Hz), 3.49 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (CDCl$_3$) δ 193.6, 165.2, 145.1, 138.2, 137.0, 136.9, 136.7, 129.3, 129.2, 129.0, 128.7, 85.7, 62.0, 59.0, 30.6, 18.6; IR (CHCl$_3$, cm^{-1}) ν 1762, 1635; MS (CI); *m/z* 556 (M$^+$, 5), 479 (M$^+$ − 77, 100). Anal. Calcd for C$_{29}$H$_{27}$NO$_3$Sn: C, 62.62; H, 4.89; N, 2.52. Found: C, 62.78; H, 4.85; N, 2.55.

Bicyclic β-Lactam (−)-6a. From 45 mg (0.14 mmol) of haloallene (+)-**2d** and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent, compound (−)-**6a** (21 mg, 67%) was obtained as a colorless oil: $[\alpha]_D = -1.8$ (*c* 1.9, CHCl$_3$); ^{1}H NMR (CDCl$_3$) δ 5.23 and 5.13 (d, each 1H, *J* = 1.0 Hz), 4.52 (dd, 1H, *J* = 4.4, 1.0 Hz), 4.34 (m, 1H), 4.19 (d, 2H, *J* = 12.9 Hz), 3.76 (dd, 1H, *J* = 4.6, 1.9 Hz), 3.63 (s, 3H), 3.06 (t, 1H, *J* = 3.9 Hz), 1.89 (s, 6H); ^{13}C NMR (CDCl$_3$) δ 166.5, 144.3, 131.4, 117.7, 110.6, 83.8, 72.8, 59.5, 56.0, 48.1, 21.5, 19.9; IR (CHCl$_3$, cm^{-1}) ν 3405, 1746; MS (CI); *m/z* 224 (M$^+$ + 1, 100), 223 (M$^+$, 15). Anal. Calcd for C$_{12}$H$_{17}$NO$_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.68; H, 7.63; N, 6.24.

Tricyclic β-Lactam (±)-7a. From 30 mg (0.10 mmol) of haloallene (±)-**2f** and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, compound (±)-**7a** (14 mg, 52%) was obtained as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 7.69 (d, 1H, *J* = 7.9 Hz), 7.38 (m, 2H), 7.15 (m, 1H), 4.77 (dd, 1H, *J* = 5.1, 1.5 Hz), 4.55 (d, 1H, *J* = 5.1 Hz), 4.04 (d, 1H, *J* = 1.3 Hz), 3.70 (s, 3H), 1.65 and 1.58 (s, each 3H); ^{13}C NMR (CDCl$_3$) δ 164.5, 140.4, 131.0, 130.9, 129.6, 125.9, 123.8, 121.0, 120.3, 84.8, 74.1, 59.7, 58.0, 26.9, 26.7; IR (CHCl$_3$, cm^{-1}) ν 3445, 1744; MS (CI), *m/z* 260 (M$^+$ + 1, 100), 259 (M$^+$, 7). Anal. Calcd for C$_{15}$H$_{17}$NO$_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.61; H, 6.65; N, 5.35.

Tricyclic β-Lactam *anti*-(±)-7a. From 26 mg (0.07 mmol) of haloallene *anti*-(±)-**2f** and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, compound *anti*-(±)-**7a** (8 mg, 42%) was obtained as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 8.07 and 7.45 (dd, each 1H, *J* = 8.1, 1.4 Hz), 7.23 (m, 1H), 7.10 (m, 1H), 4.83 (d, 1H, *J* = 4.6 Hz), 4.56 (s, 1H), 4.22 (dd, 1H, *J* = 4.6, 0.9 Hz), 3.71 (s, 3H), 2.16 and 2.07 (d, each 3H, *J* = 0.9 Hz); ^{13}C NMR (CDCl$_3$) δ 167.1, 155.0, 135.6, 130.0, 129.9, 129.0, 128.7, 127.7, 124.5, 86.3, 72.2, 61.7, 60.0, 23.3, 22.5; IR (CHCl$_3$, cm^{-1}) ν 3450, 1748; MS (CI), *m/z* 260 (M$^+$ + 1, 100), 259 (M$^+$, 11). Anal. Calcd for C$_{15}$H$_{17}$NO$_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.35; H, 6.66; N, 5.45.

Supporting Information Available: Compound characterization data and experimental procedures for compounds **2a–i**, (+)-**3**, (−)-**4b**, (±)-**4c**, (+)-**6b**, (±)-**7b**, and (±)-**7c**, and (−)-**8**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO061828S

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(19) Full spectroscopic and analytical data for compounds not included in this Experimental Section are described in the Supporting Information.