Stereoselective Synthesis of Fused Bicyclic β-Lactams through Radical Cyclization of Enyne-2-azetidinones[1]

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A convenient, stereoselective entry to racemic and enantiomerically pure fused bicyclic β-lactams has been developed that involves the radical-mediated cycloisomerization of easily available monocyclic enyne-β-lactams as the key synthetic step. These compounds are obtained provided that an activated double bond is present as a radical acceptor. In the absence of this condition, new forms of reactivity were observed, including C3−C4 bond cleavage of the β-lactam ring to yield tetrahydropyridine derivatives and 1,5-radical translocation to yield new bicyclic derivatives. Some simple transformations were tested on representative examples of the different types of bicyclic systems prepared to demonstrate their potential as intermediates in the preparation of other differently functionalized systems.

Introduction

Synthetic methodologies based on free radical cyclization reactions have experienced an impressive growth and are the focus of extensive studies. This wide-ranging research has been fostered by the mild, neutral reaction conditions required for radical generation and the fact that, by a combination of stereoelectronic and molecular orbital effects, radical cyclizations occur, in general, with high degrees of both regio- and stereocontrol.[2] Since the pioneering work by Stork,[3] the radical cycloisomerization of doubly unsaturated precursors, especially 1,6-dienes or enynes, promoted by an external radical source, is a powerful entry to complex carbocyclic and heterocyclic systems.[4] The increased interest in the preparation of novel bi- and polycyclic β-lactam systems,[5] a result of the necessity to combat the increasing resistance of bacteria to classical antibiotics,[6] makes these compounds attractive targets for synthetic approaches based on radical cyclization. However, although the radical methodology has been widely used to prepare fused bicyclic β-lactams, radical cyclization of 2-azetidinone-bridged dienes or enynes has been limited to the cyclization of *N*-(2-bromo-2-propen-1-yl)-4-vinyl-2-azetidinone to yield both carbapenam and carbacepham derivatives.[7] Most of the radical routes to fused bicyclic β-lactams make use of halogeno-, thio-, and seleno-derivatives as proradical centers.[8] Generation of the radical by some of the standard methodologies, followed by its intramolecular capture by a radical acceptor attached to the 2-azetidinone nucleus, results in ring closure. There is an isolated example of the use of a terminal alkyne as a proradical center in the synthesis of a bicyclic β-lactam, namely, the elegant preparation of some of these compounds from 4-alkynyl-β-lactams by a one-pot, four step, sequential reaction reported by Bachi.[9]

In our ongoing project directed at the development of efficient routes to prepare bi- and polycyclic β-lactam systems,[10] we recently introduced enyne-2-azetidinones as starting materials for the synthesis of fused bicyclic and tricyclic β-lactams by using radical cyclization[1] and the Pauson−Khand reaction,[11] respectively. We report here a general study into the use of terminal alkynes tethered to a 2-azetidinone ring as proradical centers.[1] The presence of a double bond as a radical acceptor in the appropriate position allows access to different fused bicyclic β-lactams (Scheme 1). Furthermore, different cyclization products, as well as fragmentation com-

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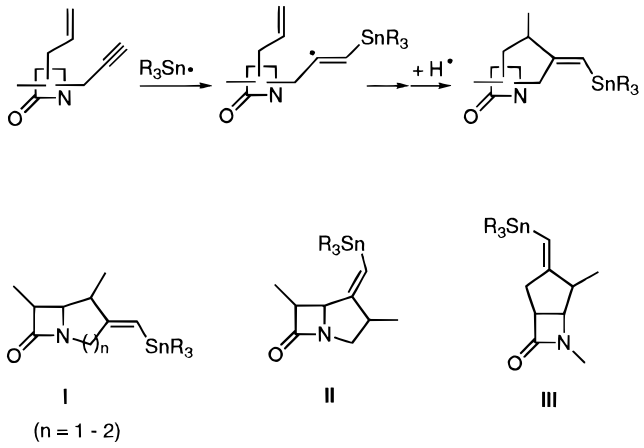
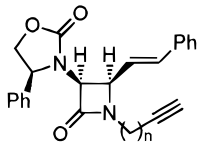
Scheme 1

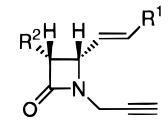


pounds, derived from modes of reaction other than those mentioned above will be also presented. β-Lactams of types I and II have the carbapenam (n = 1) or carbacepham (n = 2) ring systems,[12] whereas compounds of type III have an unusual carbapenam structure, with the lactam group moved out from the point of ring fusion.[13] This structural feature is present in cispentacin, a potent antifungal antibiotic.[14]

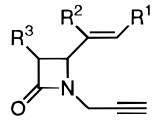
Chart 1



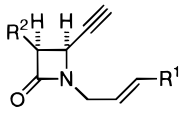
1a: n = 1
1b: n = 2
1c: n = 3



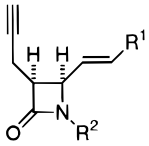
2a: R^1 = Ph, R^2 = OPh
2b: R^1 = Ph, R^2 = OBn
2c: R^1 = CO_2Me, R^2 = OPh
2d: R^1 = CO_2Me, R^2 = OBn
2e: R^1 = Me, R^2 = OPh
2f: R^1 = H, R^2 = OPh
2g: R^1 = H, R^2 = OBn



***cis*-3a**: R^1= Ph, R^2= Me, R^3= OBn
***cis*-3b**: R^1= H, R^2= Me, R^3= OBn
***trans*-3c**: R^1= Ph, R^2= H, R^3= Pr^i
***trans*-3d**: R^1= Ph, R^2= H, R^3= allyl



4a: R^1 = H, R^2 = OPh
4b: R^1 = H, R^2 = OBn
4c: R^1 = H, R^2 = OMe
4d: R^1 = CO_2Me, R^2 = OPh
4e: R^1 = CO_2Me, R^2 = OBn



5a: R^1 = Ph, R^2 = PMP
5b: R^1 = CO_2Me, R^2 = PMP

Results and Discussion

To assess the scope and limitations of the radical cyclization of enyne-β-lactams to access different fused bicyclic β-lactams, a wide variety of substrates was prepared (Chart 1, Scheme 2). In all cases, the four-membered ring was constructed by the standard Staudinger ketene−imine cyclization (Scheme 2).[15] Enyne-β-lactams

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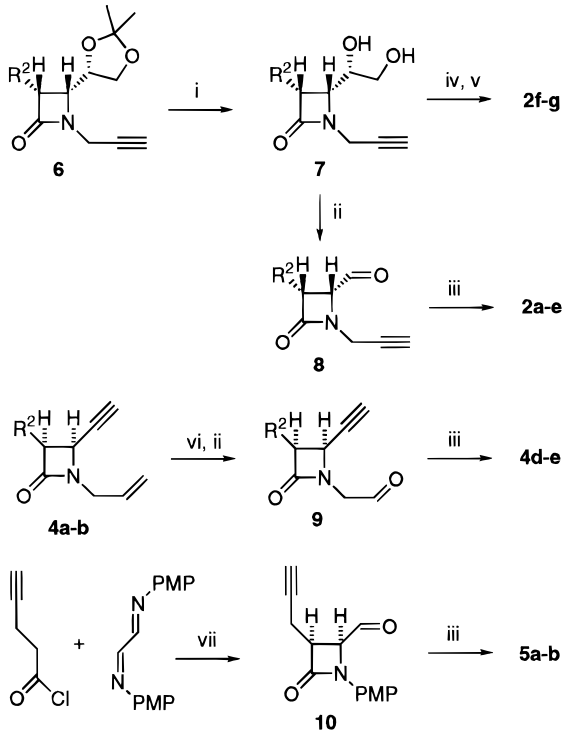
Scheme 2



[a] Key (i): PTSA, THF-H_2O, Δ. (ii): $NaIO_4$, MeOH-H_2O, rt. (iii): $R^1CH{=}PPh_3$, THF, Δ. (iv): TCDI, THF, Δ. (v): Me_3PO_3, Δ (vi): OsO_4, TMO, acetone-water, rt. (vii): TEA, toluene, Δ.

1, **3**, and **4a**−**c** were obtained directly in both the racemic (compounds **3** and **4**) and enantiopure forms (compounds **1**) when enyne imines were used as substrates. 2-Azetidinones **1a**−**c** were obtained as single *cis*-diastereomers (de > 95%) from (+)−(*S*)-(4-phenyl-2-oxo-1,3-oxazolidin-3-yl)acetic acid and the corresponding imine using dichlorophenyl phosphate as the condensating agent.[16] 2-Azetidinones **6**, derived from D-glyceraldehyde acetonide imines, were used as synthetic intermediates to prepare enantiomerically pure enyne β-lactams **2**. Thus, optically pure compounds **2a**−**e** were prepared as *E*/*Z* mixtures in good to excellent yields from enantiomerically pure (+)-(3*R*,4*S*,4′*S*)-2-azetidinones **6**[17] by standard acetonide hydrolysis, followed by cleavage of the diols **7** ($NaIO_4$/MeOH/H_2O),[18] and Wittig olefination of the resulting β-lactam aldehyde **8**.[19] This sequence yielded only moderate yields of 4-vinyl-β-lactams **2f** and **2g**. Good yields of these compounds could be obtained by using the Corey−Hopkins method.[20] Thus, after acetonide hydrolysis, diols **7** were sequentially reacted with thiocarbonyldiimidazole (TCDI) in boiling THF and trimethyl phosphite[21] to form the vinyl derivatives **2f** and **2g**. *N*-Allyl-2-azetidinones **4a** and **4b** were transformed into *E*/*Z* mixtures of enyne-β-lactams **4d** and **4e**, respectively, by dihydroxylation (OsO_4/Me_3NO), diol cleavage ($NaIO_4$/MeOH/H_2O), and Wittig olefination of the aldehyde **9**. Finally, 3-propargyl-4-alkenyl-β-lactams **5** were obtained by Wittig olefination of racemic 4-formyl β-lactams **10**. Aldehydes **10** were prepared according to our previously reported one-pot synthesis for related compounds,[22] by reaction of 4-pentynoyl chloride and the glyoxal diimine derived from *p*-anisidine (Scheme 2).[23]

2-Azetidinones **1**−**5** were reacted with Bu_3SnH (TBTH) or Ph_3SnH (TPTH) in boiling benzene and in the presence of AIBN. Reactions were carried out under standard dilution conditions; syringe pumps or other high dilution techniques were not required. Vinyltin carbapenams **11** and **12** and 3,4-fused bicyclic β-lactams **13** were obtained as the exclusive reaction products when the vinyl group had phenyl or CO_2Me groups attached (Scheme 3, Table 1, entries 1−8, 10−12, 14−19).[24] In these cases, the 5-*exo-trig* products were formed as mixtures of two diastereomers, which are epimers at the newly formed chiral center. Products with a carbacepham structure, arising from 6-*endo-trig* cyclization, or reduced compounds, from hydrostannylation of the triple bond, were not detected in any case. Each diastereoisomer was stereochemically homogeneous at the tin-substituted double bond. The configuration of the double bond is *Z* for compounds **11** and **12** and *E* for compounds **13** (see below). Purification of these compounds was performed easily and efficiently by flash chromatography to give good to excellent yields.

The structure of compounds **11**−**13** was determined by standard NMR techniques. In all cases, the stereochemistry of the 2-azetidinone ring present in the starting material remained unaltered during the cyclization process. It was established by the value of coupling constants of the original H3−H4 protons (J = 3.9−5.4

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(19) β-Lactam aldehydes **8** were obtained and used for Wittig olefination as mixtures with their methoxyhemiacetals. However, these mixtures can be easily transformed to the free aldehydes by azeotropic distillation using a Dean−Stark apparatus.

(20) Corey, E. J.; Snider, D. B. *J. Am. Chem. Soc*. **1972**, *94*, 2459.

(21) Horton, D.; Turner, W. N. *Tetrahedron Lett*. **1964**, *36*, 2531.

(22) Alcaide, B.; Martín-Cantalejo, Y.; Pérez-Castells, J.; Rodríguez-López, J.; Sierra, M. A.; Monge, A.; Pérez-García, V. *J. Org. Chem*. **1992**, *57*, 5921.

(23) Other apparently more staightforward methods, i.e., the Staudinger reaction between pentynoyl chloride and the imine derived from *p*-anisidine and cinnamaldehyde, failed to produce the corresponding β-lactam **5a**.

(24) It is notable that radical cyclization to give bicyclic compounds **11**−**13** occurs under standard conditions, whereas related processes developed to prepare bicyclic β-lactams do not occur except in high dilution conditions. See, for example ref 9. In our case, good yields of products were obtained even when working in the absence of solvent (neat conditions).

Scheme 3

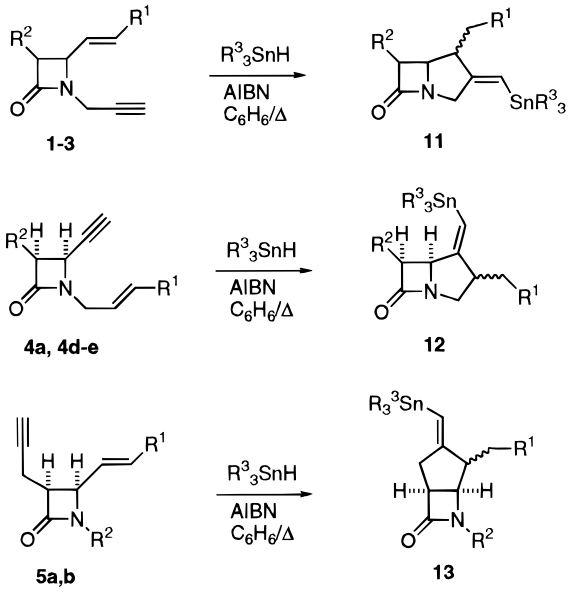


Table 1. Synthesis of Stannyl Bicyclic *β*-Lactams 11−13 from Enyne-2-azetidinones 1−5

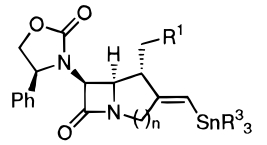
entry	substrate[b,c]	R^1	R^2	R^3	product	*anti*/*syn*[d]	yield, (%)[a] *anti*		*syn*
1	**1a**	Ph	*S*-Ox[e]	Bu	**11a**	88:12	80	(95)	11
2	**1a**	Ph	*S*-Ox[e]	Ph	**11b**	90:10	72	(96)	*f*
3	**2a**	Ph	PhO	Bu	**11c**	81:19	40	(70)	5
4	**2b**	Ph	BnO	Bu	**11d**	82:18	35	(50)	5
5	**2c**	CO_2Me	PhO	Bu	**11e**	85:15	58	(80)	12
6	**2c**	CO_2Me	PhO	Ph	**11f**	85:15	30	(63)	*f*
7	**2d**	CO_{2Me}	BnO	Bu	**11g**	81:19	37	(60)	*f*
8	**2e**	CH_3	PhO	Ph	**11h**	82:18	25	(47)	*f*
9	**2g**	H	BnO	Ph	**11i**	77:23		*g*	
10	***trans*-3c**	Ph	*i*-Pr	Bu	**11j**	90:10	50	(60)	*f*
11	***trans*-3c**	Ph	*i*-Pr	Ph	**11k**	90:10	71	(86)	*f*
12	***trans*-3d**	Ph	allyl	Ph	**11l**	90:10	50	(92)	*f*
13	**4a**	H	PhO	Ph	**12a**	80:20		*g*	
14	**4d**	CO_{2Me}	PhO	Bu	**12b**	68:32	57	(70)	*f*
15	**4e**	CO_{2Me}	BnO	Bu	**12c**	62:38	56	(70)	*f*
16	**5a**	Ph	PMP[h]	Bu	**13a**	78:22		(47)	
17	**5a**	Ph	PMP[h]	Ph	**13b**	88:12		(72)	
18	**5b**	CO_{2Me}	PMP[h]	Bu	**13c**	55:45		(78)	
19	**5b**	CO_{2Me}	PMP[h]	Ph	**13d**	55:45		(64)	

[a] In all cases, complete transformation to the bicyclic products was observed by ^{1}H NMR spectroscopy. Yields without parenthesis are for isolated products purified by column chromatography; those within parentheses are for the chromatographically homogeneous mixture of the two inseparable isomers. With the exception of **2a**, partial destannylation and/or decomposition was observed after chromatographic workup. [b] Compounds **1a** and **2a**−**f** were used as optically pure materials with the configuration indicated in Chart 1. The remaining substrates **3** and **4** were used as racemic mixtures of pure *trans* or *cis* diastereomers. [c] Except for enyne *β*-lactams **1a** and *trans*-**3c**,**d** (*E*-isomers), *E*/*Z* mixtures of isomers were used for the remaining substrates (see Experimental Section). [d] Isomer ratio (epimers at C1) were determined by integration of well-resolved signals in the ^{1}H NMR spectra of crude reaction mixtures. [e] *S*-Ox = (*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl. [f] Attempts to isolate the minor (*syn*) isomer were unsuccessful in this case. [g] The cyclization product was obtained along with a hydrostannylated product as a chromatographically inseparable mixture. [h] PMP = 4-Methoxyphenyl.

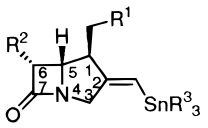
Hz for the *cis*-isomers; J = 0−1.5 Hz for the *trans*-isomers). The stereochemistry of the new chiral center of compounds **11** was determined from an X-ray diffraction analysis carried out on compound *anti*-**29a**, the destannylation product of the major isomer of carbapenam **11a** (see Table 2 and Scheme 10).[25] This analysis allows the assignment of a 1*R*,5*R*,6*S* configuration for this compound. It is therefore reasonable to assume that the configuration at C1 of all major isomers of compounds **11** is 1*R*,5*R*,6*S* for Evans oxazolidine derivatives **11a**,**b** and 1*S*,5*S*,6*R* for carbapenams **11c**−**h** derived from glyceraldehyde acetonide (Chart 2). The slight variation in the diastereomer ratio in the formation of compounds **11**, which is independent of the nature of $R^1$and R^2, supports this hypothesis. It also seems reasonable that the stereocenter determining the configuration of the new chiral center is that at the C4 *β*-lactam carbon of the starting 2-azetidinones.

The relative stereochemistry of racemic compounds **12b**,**c** was determined by NOE experiments carried out on the major isomer of compound **12c**. Irradiation of the vinyl proton at 6.05 ppm resulted in an 11% and 3% enhancement of the signals of the C*H*$_2$CO$_2$Me group and *H*2 respectively, which is in agreement with a *Z* stereochemistry for the double bond. However, no enhancement was observed when H5 was irradiated. This is compatible with an *anti* stereochemistry between H2 and H5. Therefore, a 2*S**,5*S**,6*R** configuration was assigned to the major isomer of compounds **12b**,**c**. Finally, the stereochemistry of compounds **13** was determined from the coupling constants between H4−H5 of the bicyclic system. Thus, coupling between H4−H5 was not observed for the major isomers of compounds **13**, while vicinal coupling constants $J_{4,5}$ were 4.5−4.8 Hz for the minor isomers. These values are in good agreement with a *syn*-stereochemistry for the major isomers and an *anti*-disposition for the minor isomers, as reported for related systems.[18] Chart 2 shows the stereochemistry data for compounds **11**−**13**.

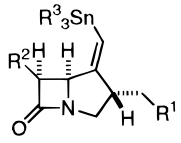
Chart 2



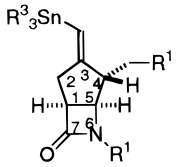
n = 1: **11a-b** (major isomers)
n = 2: **17a-b**



11c-g (major isomers)



12b-c (major isomers)



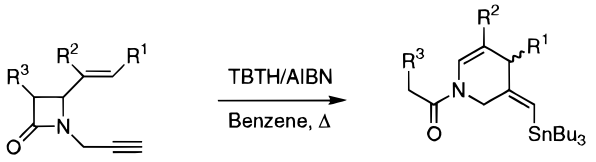
13a-d (major isomers)

The synthesis of carbapenams and related bicyclic *β*-lactams discussed above makes use of α,*β*-unsaturated esters or styryl groups as radical acceptors. This ensures a 5-*exo*-*trig* ring closure and an enhancement of the rate of the radical cyclization due to the electron-withdrawing nature of the acceptor. Furthermore, the diastereomer ratio was remarkably independent of the stereochemistry of the radical acceptor double bond. To confirm this statement, an *E*/*Z* mixture (85:15) of 2-azetidinone **2c** and its pure *Z*-isomer were reacted independently with

(25) Major isomers of carbapenams **11** show a $J_{1,5}$ = 7.4−8.4 Hz, and the minor isomers have a $J_{1,5}$ = 8.0−8.7 Hz. Therefore, the relative configuration at C1 could not be unambiguously established from NMR data.

TBTH/AIBN in refluxing benzene. The diastereomeric ratio of the carbapenam obtained (**11e**) (85:15) was identical in both cases. In contrast, products derived from hydrostannylation of the triple bond were the major components obtained in the reaction of compounds **2e**−**g** and ***cis*-3a,b** with TBTH. However, tetrahydropyridines **14a**,**b** were isolated in the reactions of β-lactams **3a** and **2e**. In fact, compound **14b** was the major product in the reaction of **2e** with TBTH (Scheme 4). Separation and purification of tetrahydropyridines **14** was difficult, and the overall yields were low. In contrast, bicyclic carbapenams **11h**,**i** and **12a** were obtained from compounds **2e**, **2g** and **4a**, respectively (Table 1), albeit in low yields, when TPTH was used instead of TBTH.

Scheme 4

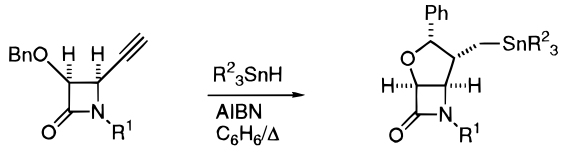


3a R^1 = Ph, R^2 = Me, R^3 = OBn
2e R^1 = Me, R^2 = H, R^3 = OPh

14a
14b

Interestingly, reaction of compound **4b** with both TBTH and TPTH gave new compounds, which were identified as bicyclic β-lactams **15a,b**, in high yield (85% and 62%, respectively, as isolated products) and as single diastereomers. Clearly, this compound represents a new mode of cyclization of enyne-β-lactams in a process that is general for 4-alkynyl-2-azetidinones having a benzyloxy group at C3. This is demonstrated by the preparation of compounds **15a**−**d** in good yields from 3-alkynyl-2-azetidinones **4a** and **16a,b** (Scheme 5). However, this reaction is restricted to this type of substrate, i.e., with a benzyloxy group at C3. Other substituents at this position, such as methoxy and acetoxy, led only to the corresponding hydrostannylated derivatives. The relative stereochemistry of compounds **15a**−**d** was determined from the vicinal coupling constants, as discussed above for compounds **13**. No coupling between H4−H5 was observed, which is indicative of an *anti* relative disposition, whereas a $J_{3,4}$ coupling (4.3−4.8 Hz) arises from a relative *syn* configuration at these centers in compounds **13**. Aza-analogues of bicycles **15** have been reported recently to be active against the class C β-lactamases.[26]

Scheme 5

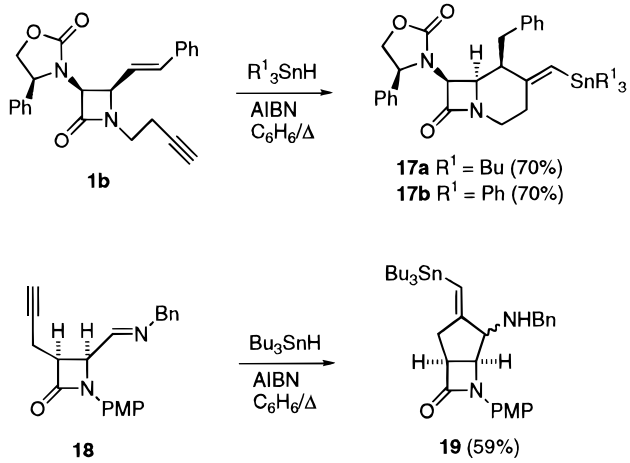


4b R^1 = allyl
16a R^1 = Bn
16b R^1 = *p*-$MeOC_6H_4$

15a R^1 = Allyl, R^2 = Bu (85 %)
15b R^1 = Allyl, R^2 = Ph (64 %)
15c R^1 = Bn, R^2 = Bu (58 %)
15d R^1 = *p*-$MeOC_6H_4$, R^2 = Bu (62 %)

Extension of this approach to higher homologue bicyclic systems was tested on β-lactams **1b**,**c**. Carbacepham derivatives **17a,b** were obtained from β-lactam **1b** by reaction with TBTH and TPTH, respectively, as single diastereomers in good yields (Scheme 6). However, the analogous reaction of compound **1c** gave a complex reaction mixture with the corresponding hydrostannylated derivative as the main component. In addition, the reaction of azaenyne derivative **18** with TBTH/AIBN behaves in a similar fashion to give the corresponding amino bicyclic β-lactam **19**, in 59% isolated yield, as a mixture of isomers (78:22) (Scheme 6).[27]

Scheme 6



1b

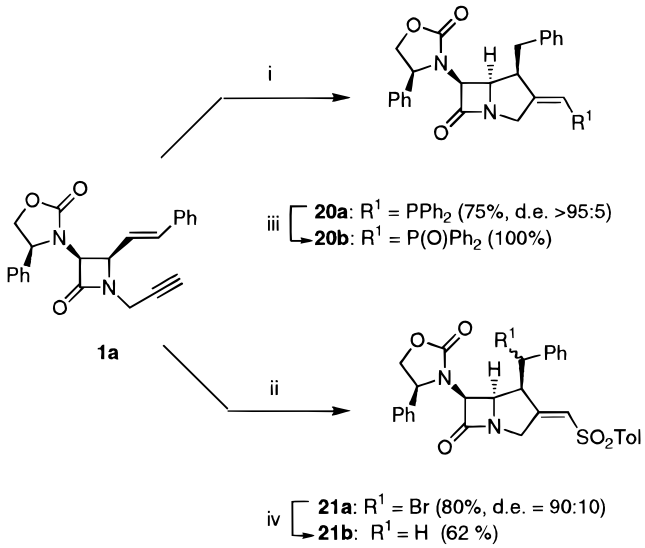
17a R^1 = Bu (70%)
17b R^1 = Ph (70%)

18

19 (59%)

Reaction with other cyclization promoters was also studied. Thus, Ph_2PH and TsBr were reacted with β-lactam **1a** in boiling benzene and in the presence of AIBN.[4k−s] In both cases, a smooth conversion to carbapenams **20** and **21** was observed (Scheme 7). Reaction with Ph_2PH led to the formation of carbapenam **20a** as a single diastereomer and in excellent yield as crude product. Compound **20a** was readily transformed to its phosphine oxide **20b** during the chromatographic purification process. Bromo-sulfone **21a** was obtained as a mixture of isomers (90:10) which are epimers at the newly formed halogenated exocyclic chiral center. Reduction of the bromo-sulfones **19a** (TBTH/AIBN/C_6H_6/Δ) gave bicyclic sulfone **21b**, thus confirming the epimeric nature of isomers of **21a** at the halogenated stereocenter. A

Scheme 7



1a

iii → **20a**: R^1 = PPh_2 (75%, d.e. >95:5); **20b**: R^1 = $P(O)Ph_2$ (100%)

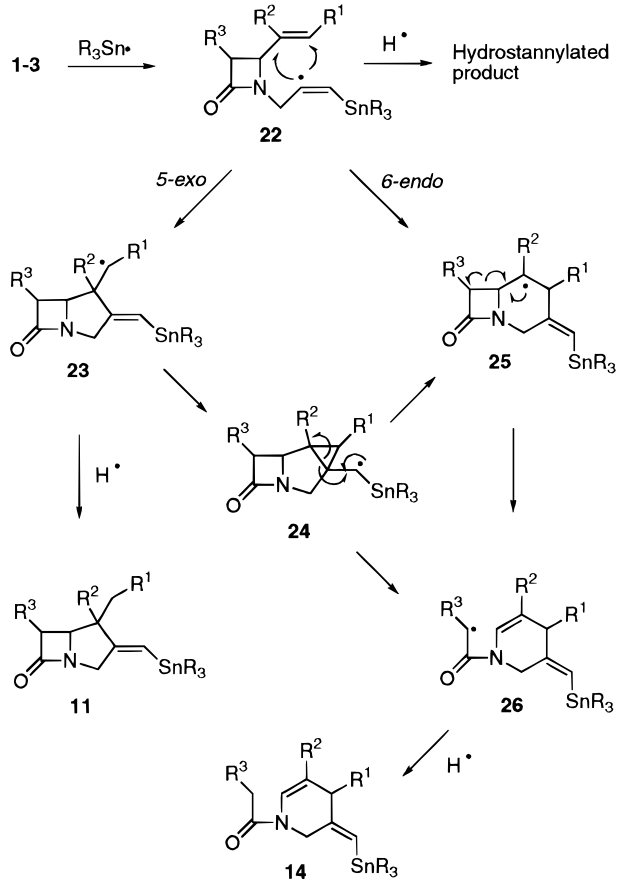
iv → **21a**: R^1 = Br (80%, d.e. = 90:10); **21b**: R^1 = H (62 %)

[a] Key (i): Ph_2PH, AIBN, C_6H_6, Δ. (ii): $TolSO_2Br$, AIBN, C_6H_6, Δ. (iii): SiO_2, air. (iv): TBTH, AIBN, C_6H_6, Δ.

particularly noteworthy aspect of this approach is the total stereoselectivity observed in the formation of the C1 stereocenter in these cases in comparison with that obtained using the tin approach.

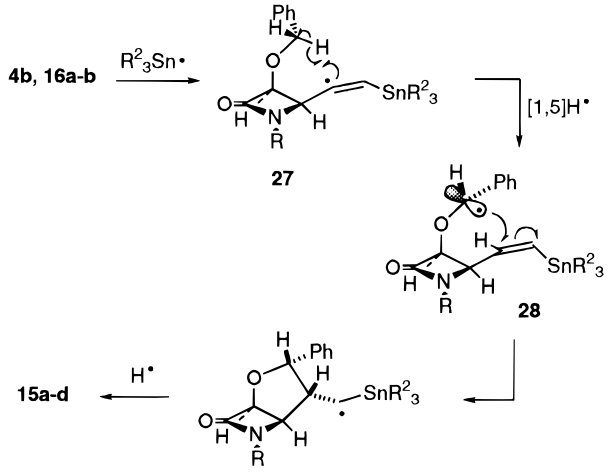
The results discussed above may be understood in terms of the reaction pathway presented in Scheme 8 for the synthesis of bicycles **11**. The first step should be the addition of the in situ-generated stannyl radical to the triple bond to form the key intermediate vinyl radical **22**. For activated double bonds, a 5-*exo*-*trig* ring closure occurs, yielding the expected carbapenam products **11**−**13**. Substitution at the acceptor carbon atom or nonactivated double bonds essentially results in the inhibition of the cyclization process, even for activated double bonds. In these cases, reduction products are obtained as the main components of the reaction mixtures. Furthermore, formation of tetrahydropyridines **14** may be explained by a homolytic C3−C4 bond cleavage in the 2-azetidinone nucleus of intermediates **24** or **25** to form radical intermediates **26**, which are precursors of compounds **14**. This interesting process, which is an example of a radical C3−C4 bond breakage in the β-lactam ring,[28] is closely related to the cyclobutylcarbinyl radical cleavage, a useful methodology for the synthesis of medium-sized rings.[29] In our case, the driving force for the cleavage may be the stability of the captodative radical **26** (Scheme 8, R^3 = PhO) together with the strain in the β-lactam ring.

Scheme 8



Formation of compounds **15a**−**d** from 3-benzyloxy-β-lactams **4b** and **16a,b** may be explained by 1,5-radical translocation of the initially formed vinyl radicals **27**.[9,30] In fact, in the absence of a good radical acceptor, this translocation generates a new, stable, benzyl radical **28**, which evolves to the final products **15** through a 5-*exo*-*trig* cyclization process onto the tin-substituted double bond (Scheme 9). The complete selectivity observed in the formation of compounds **15** should be due to the preference of the radical intermediate **28** for the conformation depicted in Scheme 9 for these cyclizations. This fact is well documented for analogous cyclizations on 1-substituted 5-hexen-1-yl radicals, in which the *cis*-cyclopentane is always obtained.[2,31]

Scheme 9



Finally, some simple transformations were carried out on selected bicyclic β-lactams **11**, **13**, and **17** (Scheme 10, Table 2) to test their viability as intermediates in the synthesis of other differently functionalized fused bicyclic systems. Thus, protiodestannylation ($TsOH/Cl_2CH_2$, rt) of some representative compounds, **11**, **13**, and **17**, afforded the corresponding methylene bicyclic-β-lactams **29**, **30**, and **33**, respectively. Reaction of major isomers of compounds **11a** and **11j** with iodine (I_2/Cl_2CH_2, rt) resulted in the corresponding vinyl iodides **31a,b**, respectively. However, ozonolysis of compound **29a** occurred without problems to give oxo-derivative **32**. Oxo-derivatives related to **32** have been used as advanced intermediates in the synthesis of active carbapenem antibiotics.[12a−f]

(26) (a) Angehrn, P.; Gubernator, K.; Gutknecht, E. M.; Heinze-Krauss, I.; Hubschwerlen, C.; Kania, M.; Page, M. G. P.; Specklin, J. L. *35th Intescience Conference on Antimicrobial Agents and Chemotherapy*; Program and Abstracts, F147, 1995. (b) Charnas, R.; Gubernator, K.; Heinze, I.; Hubschwerlen, C. Eur. Pat. 0508234A2, 1992.

(27) For the related free radical cycloisomerization of alkyne-tethered oxime ethers, see: (a) Marco-Contelles, J. L.; Destabel, Ch.; Gallego, P.; Chiara, J. L.; Bernabé, M. *J. Org. Chem.* **1996**, *61*, 1354. (b) Booth, S. E.; Jenkins, P. R.; Swain, C. J.; Sweeney, J. B. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3499. (c) Enholm, E. J.; Burroff, J. A.; Jaramillo, L. M. *Tetrahedron Lett.* **1990**, *31*, 3927.

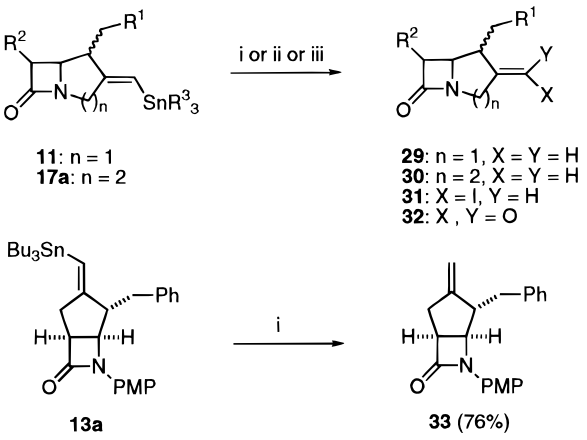
(28) For a related ionic C3−C4 ring fragmentation, see: Alcaide, B.; Martín-Cantalejo, Y.; Rodríguez-López, J.; Sierra, M. A. *J. Org. Chem.* **1993**, *58*, 4767−4770.

(29) See, for example: (a) Crimmings, M. T.; Huang, S.; Guise-Zabacki, L. E. *Tetrahedron Lett.* **1996**, *37*, 6519. (b) Horwell, D. C.; Morrell, A. I.; Roberts, E. *Tetrahedron Lett.* **1995**, *36*, 459−460 and references therein.

(30) For related examples on translocation of radical sites by intramolecular 1,5-hydrogen atom transfer, see: (a) Curran, D. P.; Kim, D.; Liu, H.; Shen, W. *J. Am. Chem. Soc.* **1988**, *110*, 5900. (b) Snieckus, V.; Cuevas, J.-C.; Sloan, C. P.; Liu, H.; Curran, D. *J. Am. Chem. Soc.* **1990**, *112*, 896. (c) Burke, S.; Jung, K. W. *Tetrahedron Lett.* **1994**, *35*, 5837. (d) Parsons, P. J.; Caddick, S. *Tetrahedron* **1994**, *50*, 13523.

(31) (a) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959. (b) Reference 2.

Scheme 10



[a] Key : (i) For **29, 30** and **33**: p-TsOH, CH_2Cl_2, rt.
(ii) For **31**: I_2, CH_2Cl_2, rt.
(iii)For **32**: O_3, CH_2Cl_2, -78°C, then Me_2S, rt.

Table 2. Synthesis of Bicyclic β-Lactams 29−32

substrate	R^1	R^2	R^3	X	Y	product	yield, (%)[a]
anti-**11a**	Ph	*S*-Ox[b]	Bu	H	H	*anti*-**29a**	91
syn-**11a**	Ph	*S*-Ox[b]	Bu	H	H	*syn*-**29a**	71
anti-**11b**	Ph	*S*-Ox[b]	Ph	H	H	*anti*-**29a**	90
anti-**11c**	Ph	PhO	Bu	H	H	*anti*-**29b**	35[c]
anti-**11d**	Ph	BnO	Bu	H	H	*anti*-**29c**	46[c]
syn-**11e**	CO_2Me	PhO	Bu	H	H	*syn*-**29d**	98
anti-**11g**	CO_2Me	BnO	Bu	H	H	*anti*-**29e**	25[c]
anti-**11j**	Ph	*i*-Pr	Bu	H	H	*anti*-**29f**	64
anti-**17a**	Ph	*S*-Ox[b]	Bu	H	H	*anti*-**30**	96
anti-**11a**	Ph	*S*-Ox[b]	Bu	I	H	*anti*-**31a**	51[c]
anti-**11j**	Ph	*i*-Pr	Bu	I	H	*anti*-**31b**	45[c]
anti-**29a**	Ph	*S*-Ox[b]		O	O	*anti*-**32**	60

[a] Yields are for pure products purified by column chromatography. [b] *S*-Ox = (*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl. [c] Considerable loss of material was observed in this case after chromatographic purification.

In conclusion, an efficient, stereoselective entry to fused bicyclic β-lactam systems from easily available enyne-β-lactams has been developed. These compounds are obtained if an activated double bond is present as radical acceptor. In the absence of this condition, new forms of reactivity were observed, including C3−C4 bond cleavage of the β-lactam ring to yield tetrahydropyridine derivatives and 1,5-radical translocation to yield new bicyclic derivatives. Some simple transformations were tested on representative examples of the different types of bicyclic systems prepared to demonstrate their potential as intermediates in the preparation of other, differently functionalized systems. Efforts to develop this methodology for the preparation of more elaborate carbapenems and carbacephems are currently underway in our research group.

Experimental Section

General. General experimental data and procedures have been previously reported.[20] NMR spectra were recorded in $CDCl_3$ solutions, except as otherwise stated. Chemical shifts are given in ppm relative to TMS (^{1}H, 0.0 ppm) or $CDCl_3$ (^{13}C, 76.9 ppm). Specific rotation $[\alpha]_D$ is given in degrees per dm at 20 °C, and the concentration (*c*) is expressed in grams per 100 mL in $CHCl_3$. All commercially available compounds were used without further purification. The following chemicals were prepared according to literature procedures: propynal,[32] 4-butynamine,[33] 2,3-*O*-(isopropylidene)-D-glyceraldehyde,[34] (*S*)-phenylglycinol,[35] (*S*)-4-phenyl-2-oxazolidinone,[36] (*S*)-(4-phenyl-2-oxo-oxazolidin-3-yl)-acetic acid,[37] and *N*,*N*-di(*p*-methoxyphenyl)glyoxaldiimine.[38]

General Procedures for the Synthesis of 1-Propargyl-2-azetidinones 1, 3, 4a−c, and 16. Method A. A solution of the corresponding aldehyde (10 mmol) and amine (10 mmol) in CH_2Cl_2 (10 mL) was stirred overnight at room temperature over $MgSO_4$. Then, the $MgSO_4$ was filtered off and washed with an additional 15 mL of CH_2Cl_2, and the resulting solution was cooled at 0 °C under argon. Et_3N (4.16 mL, 30 mmol) and the corresponding acid or acid chloride (15 mmol) (and $PhOP(O)Cl_2$, only when (*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl-acetic acid is used, 2.25 mL, 15 mmol) were successively added, and the mixture was stirred overnight at room temperature. Finally, it was diluted with CH_2Cl_2, washed with 5% HCl (×1), H_2O (×2), and dried ($MgSO_4$). After filtration and evaporation of the solvent under reduced pressure, the crude products were purified by column chromatography (silica gel; hexanes/EtAcO mixtures). **Method B.** A solution of the corresponding aldehyde (30 mmol) and amine (30 mmol) in Et_2O (200 mL) was stirred at room temperature over $MgSO_4$ (35 g). After 6 h, the mixture was filtered, and 100 mL of toluene was added. The resulting solution was concentrated under reduced pressure to 100 mL. To this solution of imine was added Et_3N (90 mmol) and a solution of the corresponding acid chloride (36 mmol) in toluene (25 mL). The resulting mixture was stirred overnight at room temperature and partitioned between H_2O and CH_2Cl_2 (3 × 50 mL). Finally, the organic layer was washed with brine and dried ($MgSO_4$). After filtration and evaporation of the solvent under reduced pressure, the crude products were purified by column chromatography (silica gel; hexanes/EtAcO mixtures). Representative examples for the preparation of enyne-2-azetidinones following both methods follow.[39]

(+)−(3*S*,4*R*)-3-[(*S*)-4-Phenyl-2-oxo-1,3-oxazolidin-3-yl]-1-propargyl-4-(*E*)-styryl-2-azetidinone (1a). Method A. From *E*-cinnamaldehyde (1.32 g, 10 mmol), propargylamine (0.55 g, 10 mmol), (*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl-acetic acid (3.31 g, 15 mmol), and $PhOP(O)Cl_2$ (2.25 mL, 15 mmol), 2.86 g of the title compound was obtained. Flash chromatography (silica gel; hexanes/EtAcO, 2:1). Yield: 77%. White needles. Mp: 183−184 °C. $[\alpha]_D = +107$ (*c* = 2, $CHCl_3$). ^{1}H NMR ($CDCl_3$) *δ*: 2.18 (t, 1H, *J* = 2.7 Hz), 3.70 (dd, 1H, *J* = 2.7, 18.0 Hz), 4.18 (dd, 1H, *J* = 7.2, 8.7 Hz), 4.29 (dd, 1H, *J* = 2.7, 18.0 Hz), 4.47−4.53 (m, 2H), 4.62 (t, 1H, *J* = 8.7 Hz), 4.85 (dd, 1H, *J* = 7.2, 8.7 Hz), 6.05 (dd, 1H, *J* = 8.4, 15.9 Hz), 6.68 (d, 1H, *J* = 15.9 Hz), 7.31−7.44 (m, 10H). ^{13}C NMR ($CDCl_3$) *δ*: 163.1, 157.7, 137.6, 137.0, 135.7, 129.7, 129.6, 128.8, 128.7, 127.8, 127.0, 122.7, 76.4 72.9, 70.8, 63.0, 61.1, 60.3, 30.1. IR (KBr) *ν*: 3250, 1750, 1655. Anal. Calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52. Found: C, 73.84; H, 5.52; N, 7.48.

(±)-*trans*-3-Isopropyl-1-propargyl-4-(*E*)-styryl-2-azetidinone (3c). Method B. From cinnamaldehyde (0.66 g, 5 mmol), propargylamine (0.27 g, 5 mmol), and isovaleryl chloride (0.90 g, 10 mmol), 0.34 g of the title compound was obtained. Flash chromatography (silica gel; hexanes/EtAcO, 5:1). Yield: 27%. Yellowish oil. ^{1}H NMR ($CDCl_3$) *δ*: 0.94 (d, 3H, *J* = 6.6 Hz), 1.02 (d, 3H, *J* = 6.6 Hz), 2.01 (m, 1H), 2.16 (t, 1H, *J* = 2.7 Hz), 2.73 (dd, 1H, *J* = 2.7, 8.4 Hz), 3.65 (dd, 1H, *J* = 2.7, 18.0 Hz), 4.00 (dd, 1H, *J* = 2.4, 8.7 Hz), 4.16 (dd,

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

1H, J = 2.7, 17.7 Hz), 6.10 (dd, 1H, J = 8.4, 15.9 Hz), 6.62 (d, 1H, J = 15.6 Hz), 7.2−7.4 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 169.1, 136.0, 134.1, 128.8, 128.3, 127.0, 126.7, 77.4, 72.2, 64.7, 58.0, 29.7, 28.2, 20.4, 20.2. IR ($CHCl_3$) ν: 3300, 1750. EM (*m*/*e*): 254-(M^+ + 1, 25), 253(M^+, 5), 211(84), 170(83), 129(77), 115(100), 91(45). Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.82; H, 7.41; N, 5.20.

(±)-*cis*-1-Allyl-4-ethynyl-3-phenoxy-2-azetidinone (4a). Method B. From propynaldehyde (1.5 g, 27.8 mmol), allylamine (1.9 g, 33.3 mmol), and phenoxyacetyl chloride (7.10 g, 42 mmol), 4.33 g of the title compound was obtained. Flash chromatography (silica gel; hexanes/EtAcO, 2:1). Yield: 68%. Yellow solid. Mp: 65−66 °C (hexanes/AcOEt). ^{1}H NMR ($CDCl_3$) 2.45 (d, 1H, J = 2.1 Hz), 3.73 (dd, 1H, J = 7.1, 15.5 Hz), 4.0−4.20 (m, 1H), 4.58 (dd, 1H, J = 2.1, 4.3 Hz), 5.2−5.3 (m, 3H), 5.2−5.9 (m, 1H), 6.9−7.0 (m, 3H), 7.2−7.4 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 164.5, 157.3, 130.6, 129.7, 122.6, 119.7, 115.7, 81.2, 77.7, 77.3, 49.5, 43.3. IR (KBr) ν: 3290, 1750, 1590, 1490. Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.86; H, 5.75; N, 6.20.

Preparation of Enyne-2-azetidinones 2 and 4 by Wittig Reaction on Aldehydes 8−10. Representative examples for the preparation of enyne-2-azetidinones by Wittig reaction follow.

(+)-(3*R*,4*S*)-3-Phenoxy-1-propargyl-4-(*E*)-styryl-2-azetidinone (2a). To a stirred solution of diol **7a** (0.93 g, 3.55 mmol) in MeOH/H_2O (5:1, 41 mL), $NaIO_4$ (1.52 g, 7.12 mmol) was added. After 30 min, the mixture was concentrated, diluted with water, extracted with CH_2Cl_2 (×4), and dried ($MgSO_4$). After filtration and evaporation of the solvent, the crude product was used as such in the next step. To a suspension of benzyl triphenylphosphonium chloride (1.9 g, 4.97 mmol) in anhydrous THF (30 mL) under argon, BuLi (1.6 M in hexanes, 2.66 mL, 4.26 mmol) was added dropwise. The red mixture was then stirred for 30 min at room temperature, and a solution of the crude mixture of aldehyde **8** obtained before in THF (20 mL) was then added. After 50 min, the mixture was quenched with brine, extracted with EtAcO (×4), and dried ($MgSO_4$). After filtration and evaporation of the solvent, the crude product was analyzed by ^{1}H NMR, showing a mixture of diastereoisomers, *E*/*Z* ratio 81:19. Purification was performed by column chromatography (silica gel, hexanes/EtAcO 4:1) and afforded 0.85 g of a mixture of isomers. Yield: 80%. An analytical sample of the *E*-isomer was isolated by recrystallization from EtOH. ***E*-Isomer**. White crystals. $[\alpha]_D$ = − 23.5 (c = 0.5, $CHCl_3$). Mp: 110−111 °C (EtOH). ^{1}H NMR ($CDCl_3$) δ: 2.27 (t, 1H, J = 2.7 Hz), 3.78 (dd, 1H, J = 2.7, 17.7 Hz), 4.33 (dd, 1H, J = 2.4, 17.7 Hz), 4.67 (dd, 1H, J = 4.5, 9.0 Hz), 5.37 (d, 1H, J = 4.5 Hz), 6.21 (dd, 1H, J = 9.0, 15.9 Hz), 6.76 (d, 1H, J = 15.9 Hz), 6.95 (m, 3H), 7.20−7.30 (m, 7H). ^{13}C NMR ($CDCl_3$) δ: 164.5, 157.1, 137.3, 135.7, 129.4, 128.5, 128.3, 126.6, 122.2, 121.5, 115.4, 82.1, 76.1, 72.8, 60.4, 29.7. IR (KBr) ν: 3250, 1755. Anal. Calcd for $C_{20}H_{17}NO_2$: C, 79.18; H, 5.65; N, 4.62. Found: C, 79.04; H, 5.55; N, 4.60.

(+)-(3*R*,4*S*)-4-(*E* or *Z*)-(2′-Methoxycarbonyl)ethenyl-3-phenoxy-1-propargyl-2-azetidinone (2c). Diol **7a** (1.35 g, 5.17 mmol) was treated with $NaIO_4$ as stated above for **2a**. The crude product obtained before was dissolved in anhydrous THF (50 mL), $Ph_3P{=}CHCO_2Me$ (2.07 g, 6.20 mmol) was added, and the mixture was heated under reflux in an argon atmosphere for 3 h. Then, the solvent was evaporated, and the crude product (^{1}H NMR analysis showed an *E*/*Z* ratio of 86:14) was purified by column chromatography (silica gel, hexanes/EtAcO 3:1) to give, in sequence, 0.18 g (12%) of the *Z*-isomer as a pale yellow oil and 1.20 g (82%) of the *E*-isomer as a white solid. Yield: 94%. ***Z*-Isomer.** Pale yellow oil. $[\alpha]_D$ = +195 (c = 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 2.28 (t, 1H, J = 2.7 Hz), 3.74 (s, 3H), 4.01 (dd, 1H, J = 2.7, 17.7 Hz), 4.19 (dd, 1H, J = 2.7, 17.7 Hz), 5.41 (d, 1H, J = 4.8 Hz), 5.79 (ddd, 1H, J = 1.5, 4.8, 9.0 Hz), 6.05 (dd, 1H, J = 1.5, 11.7 Hz), 6.37 (dd, 1H, J = 9.0, 11.7 Hz), 6.95−7.05 (m, 3H), 7.20−7.30 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 166.0, 164.9, 157.2, 142.0, 129.6, 125.6, 122.5, 115.6, 82.5, 76.3, 73.3, 56.1, 51.8, 30.5. Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.52; H, 5.61; N, 5.02. ***E*-Isomer**. White crystals. $[\alpha]_D$ = +31 (c = 1.2, $CHCl_3$). Mp: 85−86 °C (EtAcO/hexanes). ^{1}H NMR ($CDCl_3$) δ: 2.31 (t, 1H, J = 2.4 Hz), 3.73 (s, 3H), 3.79 (dd, 1H, J = 2.4, 17.7 Hz), 4.35 (dd, 1H, J = 2.4, 17.7 Hz), 4.65 (dd, 1H, J = 4.8, 8.4 Hz), 5.38 (d, 1H, J = 4.8 Hz), 6.17 (dd, 1H, J = 1.2, 15.9 Hz), 6.85−7.05 (m, 4H), 7.20−7.30 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 165.5, 164.4, 157.1, 140.1, 129.7, 127.2, 122.7, 115.7, 82.5, 75.7, 73.7, 58.6, 52.0, 30.2. IR (KBr) ν: 3240, 1760, 1715. Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.24; H, 5.38; N, 4.89.

General Procedure for the Synthesis of 4-Vinyl-2-azetidinones 2f,g. To a solution of the corresponding 4-[(*S*)-1′,2′-dihydroxyethyl]-2-azetidinone **7** (4 mmol) in anhydrous THF (100 mL) was added TCDI (4.84 mmol), and the mixture was stirred until complete disappearance of the starting product (TLC). The crude mixture was extracted with CH_2Cl_2 (4 × 10 mL) to give the corresponding thiocarbonate. A solution of the aforementioned thiocarbonate (4 mmol) in trimethyl phosphite (25 mL) was stirred at reflux until complete disappearance of the starting material (TLC). Then, the solvent was evaporated under vacuum, and the crude product was purified by column chromatography to give the desired 4-vinyl-2-azetidinone. A representative example for the preparation of enyne-2-azetidinone **2f** follows.

(+)-(3*R*,4*S*)-3-Phenoxy-1-propargyl-4-vinyl-2-azetidinone (2f). From compound **7a** (0.17 g, 0.64 mmol), 0.08 g of the title compound was obtained. Flash chromatography (silica gel, hexanes/EtAcO 6:1). Yield: 55%. Colorless oil. $[\alpha]_D$ = +10 (c = 0.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 2.26 (t, 1H, J = 2.7 Hz), 3.73 (dd, 1H, J = 2.7, 17.7 Hz), 4.33 (dd, 1H, J = 2.7, 17.7 Hz), 4.50 (dd, 1H, J = 4.5, 8.7 Hz), 5.29 (d, 1H, J = 4.5 Hz), 5.35−5.51 (m, 2H), 5.81−5.93 (m, 1H), 6.9−7.3 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 164.6, 157.2, 130.9, 129.6, 123.2, 122.3, 115.6, 81.8, 76.2, 73.0, 60.8, 29.6. IR ($CHCl_3$) ν: 3290, 1760. Anal. Calcd for $C_{14}H_{13}NO_2$: C, 74.00; H, 5.77; N, 6.16. Found: C, 74.22; H, 5.99; N, 5.83.

Synthesis of 4-Ethynyl-1-(3′-methoxycarbonyl-2′-propenyl)-2-azetidinones 4d,e. To a solution of the corresponding 1-allyl-2-azetidinone **4a** or **4b** (1 mmol) and trimethylamine-*N*-oxide (2 mmol) in acetone/water (80:10 mL) was added OsO_4 in *tert*-butanol (2.5%, 0.1 mmol). The mixture was stirred at room temperature for 2 h. Then, it was treated with an aqueous solution of $NaHSO_3$ (40%) for 30 min and extracted several times with EtOAc. The organic layer was dried ($MgSO_4$), and the solvent was removed under vacuum to obtain the corresponding diol, which was treated with $NaIO_4$ (2 mmol) and $Ph_3P{=}CHCO_2Me$ (1.4 mmol) as stated for **2a**. A representative example for the preparation of enyne-2-azetidinone **4d** follows.

(±)-*cis*-4-Ethynyl-1-(3′-methoxycarbonyl-2′-propenyl)-3-phenoxy-2-azetidinone (4d) From β-lactam **4a** (0.71 g, 3.12 mmol), 0.51 g of a mixture of diastereoisomers, *E*/*Z* ratio 84:16, was obtained. Yield: 57%. An analytical sample of the *E*-isomer was isolated by recristallization from the mixture. Flash chromatography (silica gel, hexanes/EtAcO 4:1). ***E*-isomer.** White solid. Mp: 95−96 °C (hexane/AcOEt). ^{1}H NMR ($CDCl_3$) δ: 2.50 (d, 1H, J = 2.1 Hz), 3.76 (s, 3H), 3.95 (ddd, 1H, J = 1.4, 6.4, 17.0 Hz), 4.29 (ddd, 1H, J = 1.8, 5.1, 17.0 Hz), 4.63 (dd, 1H, J = 2.1, 4.3 Hz), 5.36 (d, 1H, J = 4.3 Hz), 6.04 (dt, 1H, J = 1.6, 15.6 Hz), 6.87 (ddd, 1H, J = 5.2, 6.4, 15.6 Hz), 7.0−7.1 (m, 2H), 7.3−7.4 (m, 3H). ^{13}C NMR ($CDCl_3$) δ: 166.0, 164.7, 157.2, 140.2, 129.7, 124.2, 122.7, 115.7, 81.6, 78.3, 75.4, 52.0, 50.1, 41.3. IR (KBr) ν: 3300, 1760, 1670. EM (*m*/*e*): 286 ($M - H^{+\cdot}$, 1), 144 (100), 116 (25), 115 (71), 105 (15), 77 (52), 65 (20), 51 (48). Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.54; H, 5.43; N, 4.69.

General Procedure for the Synthesis of Bicycles 11−13, 15, and 17. Method A. A solution of the corresponding monocyclic 2-azetidinone (1 mmol), Bu_3SnH or Ph_3SnH (1.15 mmol), and AIBN (0.1 mmol) in anhydrous benzene (20 mL) under argon was heated under reflux until complete disappearance of starting material (TLC). Then, the solvent was evaporated, and the crude product was analized by ^{1}H NMR. The residue was purified by column chromatography (silica gel; hexanes, then hexanes/EtAcO or hexanes/Et_3N mixtures). **Method B.** A solution of Bu_3SnH or Ph_3SnH (1.15 mmol) and

AIBN (0.1 mmol) in anhydrous benzene (10 mL) was added using a syringe pump (at 2 mL/h rate) over a refluxing solution of the corresponding β-lactam (1 mmol) in anhydrous benzene (15 mL) under argon. Then, the solvent was evaporated, and the crude product was analyzed by ^{1}H NMR. The residue was purified by column chromatography (silica gel; hexanes, then hexanes/EtAcO or hexanes/Et_3N mixtures). In many cases, a second chromatography was performed to isolate both isomers. In these cases, the isolated yield is given for each isomer.

1-Benzyl-2-(*Z*)-tributylstannylmethylene-6-[(*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl]carbapenams 11a. Method A or B. From 0.37 g (1 mmol) of **1a**, a 88:12 isomer mixture was obtained. Flash chromatography (silica gel, hexanes/EtAcO 4:1) afforded in sequence the major isomer (0.53 g, 80%) and the minor isomer (0.070 g, 11%). Total yield: 91%. **Major (1*R*,5*R*,6*S*)-isomer 11a.** Colorless oil. $[\alpha]_D = +187$ (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.7−1.6 (m, 27H), 2.28 (dd, 1H, J = 10.7, 13.0 Hz), 2.82 (dd, 1H, J = 7.7, 8.9 Hz), 3.32 (dd, 1H, J = 3.3, 13.4 Hz), 3.4−3.6 (m, 3H), 3.84 (t, 1H, J = 8.1 Hz), 3.90 (d, 1H, J = 3.9 Hz), 4.16 (t, 1H, J = 8.9 Hz), 4.40 (d, 1H, J = 13.4 Hz), 5.97 (d with satellites, 1H, J = 2.1 Hz), 7.0−7.6 (m, 10H). ^{13}C NMR ($CDCl_3$) δ: 171.8, 160.8, 157.3, 141.6, 137.0, 129.6, 129.4, 129.4, 129.1, 127.2, 126.5, 119.7, 70.9, 65.3, 59.4, 59.3, 52.4, 47.1, 37.9, 29.2, 27.4, 13.8, 10.0. IR ($CHCl_3$) ν: 1780, 1755. Anal. Calcd for $C_{35}H_{48}N_2O_3Sn$: C, 63.36; H, 7.29; N, 4.22. Found: C, 63.45; H, 7.35; N, 4.00. **Minor (1*S*,5*R*,6*S*)-isomer 11a.** Colorless crystals. Mp: 94−95 °C (hexanes/EtAcO). $[\alpha]_D = +49$ (c = 0.52, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.8−1.6 (m, 27H), 2.48 (dd, 1H, J = 11.1, 14.3 Hz), 2.83 (m, 2H), 3.29 (br s, 1H), 3.39 (dd, 1H, J = 4.3, 8.0 Hz), 3.48 (dd, 1H, J = 2.0, 18.1 Hz), 4.01 (dd, 1H, J = 6.2, 8.5 Hz), 4.1−4.3 (m, 2H), 4.33 (t, 1H, J = 8.9 Hz), 5.62 (d with satellites, 1H, J = 2.1 Hz), 7.1−7.5 (m, 10H). ^{13}C NMR ($CDCl_3$) δ: 162.7, 157.5, 140.3, 138.2, 136.7, 135.6, 129.6, 129.5, 129.2, 129.0, 127.4, 126.6, 70.9, 62.4, 58.9, 56.5, 42.4, 41.7, 36.4, 29.1, 27.5, 13.8, 9.3. IR (KBr) ν: 1760. Anal. Calcd for $C_{35}H_{48}N_2O_3Sn$: C, 63.36; H, 7.29; N, 4.22. Found: C, 63.39; H, 7.22; N, 4.19.

1-Benzyl-2-(*Z*)-triphenylstannylmethylene-6-[(*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl]carbapenams 11b. Method A. From 0.15 g (0.40 mmol) of **1a**, a 90:10 mixture of two isomers was obtained. Flash chromatography (silica gel, hexanes/Et_3N, 6:1) afforded the isomer mixture in 96% yield. **Major (1*R*,5*R*,6*S*)-isomer 11b**. Isolated yield: 72%. White solid. Mp: 187−189 °C (hexanes/EtAcO). $[\alpha]_D = +189.1$ (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 2.78 (dd, 1H, J = 10.8, 13.8 Hz), 2.84 (dd, 1H, J = 7.5, 8.7 Hz), 3.36−3.45 (m, 2H), 3.5−3.65 (m, 2H), 3.83 (dd, 1H, J = 8.7, 7.8 Hz), 3.85 (dd, 1H, J = 4.2, 0.9 Hz), 4.15 (t, 1H, J = 8.7 Hz), 4.23 (d, 1H, J = 14.1 Hz), 5.26 (d, 1H, J = 2.1 Hz with satellites), 7.0−7.6 (m, 25H). ^{13}C NMR ($CDCl_3$) δ: 171.4, 165.0, 141.1, 141.1, 137.8, 137.6, 137.0, 136.9, 129.6, 129.4, 129.2, 128.9, 128.9, 127.2, 126.6, 116.2, 70.9, 65.2, 59.4, 59.4 52.5, 47.7, 37.9. IR ($CHCl_3$) ν: 1750, 1780. Anal. Calcd for $C_{41}H_{36}N_2O_3Sn$: C, 68.07; H, 5.01; N, 3.87. Found: C, 68.12; H, 5.04; N, 3.79.

2-(*Z*)-Tributylstannylmethylene-1-methoxycarbonylmethyl-6-phenoxycarbapenams 11e. Method A. From 0.78 g (2.74 mmol) of **2c** (mixture of *E*/*Z* isomers), a 85:15 mixture of two isomers was obtained. Flash chromatography (silica gel, hexanes/EtAcO 4:1) afforded in sequence the major isomer (0.91 g, 58%) and the minor isomer (0.19 g, 12%). Overall yield: 80%. **Major (1*S*,5*S*,6*R*)-isomer 11e.** Colorless oil. $[\alpha]_D = +10$ (c = 1.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.8−1.6 (m, 27H), 2.42 (dd, 1H, J = 7.2, 15.0 Hz), 2.60 (dd, 1H, J = 5.1, 15.0 Hz), 3.1−3.2 (m, 1H), 3.51 (br d, 1H, J = 15.3 Hz), 3.55 (s, 3H), 4.10 (dd, 1H, J = 4.5, 8.4 Hz), 4.28 (br d, 1H, J = 15.3 Hz), 5.48 (dd, 1H, J = 1.2, 4.5 Hz), 5.81 (dd with satellites, 1H, J = 2.7, 5.1 Hz), 6.95−7.05 (m, 3H), 7.25−7.35 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 174.6, 172.2, 159.5, 157.3, 129.7, 122.4, 120.5, 115.4, 79.7, 62.6, 51.8, 51.8, 41.2, 35.3, 29.2, 27.3, 13.8, 9.9. IR ($CHCl_3$) ν: 1770, 1740, 1655. Anal. Calcd for $C_{28}H_{43}NO_4Sn$: C, 58.35; H, 7.52; N, 2.43. Found: C, 58.20; H, 7.25; N, 2.33. **Minor (1*R*,5*S*,6*R*)-isomer 11e:** Colorless oil. $[\alpha]_D = +61$ (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.8−1.6 (m, 27H), 2.32 (m, 2H), 3.1−3.2 (m, 1H), 3.52−3.63 (m, 1H), 3.59 (s, 3H), 3.73 (dd, 1H, J = 4.2, 8.7 Hz), 4.18 (dt, 1H, J = 3.0, 18.3 Hz), 5.37 (dd, 1H, J = 1.8, 4.2 Hz), 5.68 (dd with satellites, 1H, J = 2.4, 4.5 Hz), 6.95−7.10 (m, 3H), 7.25−7.35 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 171.7, 165.4, 157.3, 136.8, 135.5, 129.4, 122.1, 115.5, 81.5, 53.6, 51.6, 42.0, 37.5, 31.4, 28.9, 27.2, 13.6, 9.1. IR ($CHCl_3$) ν: 1750. Anal. Calcd for $C_{28}H_{43}NO_4Sn$: C, 58.35; H, 7.52; N, 2.43. Found: C, 58.05; H, 7.77; N, 2.54.

1-Benzyl-2-(*Z*)-tributylstannylmethylene-6-isopropylcarbapenams 11j. Method A or B. From 0.1 g (0.40 mmol) of ***trans*-3c**, a 90:10 mixture of two isomers was obtained. Flash chromatography (silica gel, hexanes/AcOEt, 4:1) afforded 0.13 g of isomer mixture (60% yield). **Major (1*S**,5*S**,6*S**)-isomer 11j.** Colorless oil. Isolated yield: 50%. ^{1}H NMR ($CDCl_3$) δ: 0.42 (d, 3H, J = 6.6 Hz), 0.6 (d, 3H, J = 6.6 Hz), 0.8−1.4 (m, 27H), 1.6 (m, 1H), 2.28 (dd, 1H, J = 1.5, 7.2 Hz), 2.36 (dd, 1H, J = 11.1, 13.8 Hz), 2.64 (br s, 1H), 3.04 (dd, 1H, J = 1.5, 8.1 Hz), 3.23 (dd 1H, J = 9.8, 13.8 Hz), 3.30 (dt, 1H, J = 1.8, 3.3, 14.7 Hz), 4.16 (dc, 1H, J = 1.2, 2.1, 3.6, 14.7 Hz), 5.86 (d with satellites, 1H, J = 2.1 Hz), 7.2 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 177.5, 162.0, 139.2, 128.7, 128.6, 126.4, 119.3, 64.8, 61.2, 51.5, 51.1, 37.0, 29.1, 27.9, 27.3, 19.9, 19.7, 13.7, 9.8. IR ($CHCl_3$) ν: 1735, 1220. Anal. Calcd for $C_{29}H_{47}NOSn$: C, 63.98; H, 8.70; N, 2.57. Found: C, 63.69; H, 8.89; N, 2.22.

6-Allyl-1-benzyl-2-(*Z*)-triphenylstannylmethylenecarbapenams 11l. Method A or B. From 0.80 g (0.32 mmol) of ***trans*-3d**, a 90:10 mixture of two isomers was obtained. Flash chromatography (silica gel, hexanes/AcOEt, 5:1) afforded 0.18 g of the isomer mixture (92% yield). **Major (1*S**,5*S**,6*S**)-isomer 11l.** Isolated yield: 52%. Colorless oil. ^{1}H NMR ($CDCl_3$) δ: 1.96 (m, 2H), 2.35−2.50 (m, 2H), 2.7 (m, 1H), 3.05 (dd, 1H, J = 1.5, 8.4 Hz), 3.23−3.32 (m, 2H), 4.0 (d, 1H, J = 15 Hz), 4.7−4.8 (m, 2H), 5.2 (m, 1H), 6.19 (d with satellites, 1H, J = 2.1 Hz), 7.1−7.6 (m, 20H). ^{13}C NMR ($CDCl_3$) δ: 176.4, 165.8, 139.2, 137.7, 137.5, 137.4, 134.2, 129.6, 129.2, 129.0, 126.8, 117.2, 116.3, 62.0, 57.1, 52.6, 51.5, 36.8, 32.7. IR ($CHCl_3$) ν: 1750. EM (*m*/*e*): 603(M^+ ^{120}Sn, 2), 602(M^+ ^{119}Sn, 3), 600(M^{+117} Sn, 1), 526(9), 351(50), 197(63), 91(100). Anal. Calcd for $C_{35}H_{33}NOSn$: C, 69.79; H, 5.52; N, 2.32. Found: C, 69.98; H, 5.84; N, 2.10.

1-Tributylstannylmethylene-2-methoxycarbonylmethyl-6-phenoxycarbapenams 12b. Method A. From 0.2 g (0.70 mmol) of **4d**, a 68:32 mixture of two isomers was obtained. Flash chromatography (silica gel, hexanes/AcOEt, 5:1) afforded 0.29 g of isomer mixture (70% yield). **Major (2*S**,5*R**,6*S**)-isomer 12b.** Isolated yield: 57%. White solid. Mp: 51−52 °C (hexanes/AcOEt). ^{1}H NMR ($CDCl_3$) δ: 0.95 (m, 15H), 1.3 (m, 6H), 1.5 (m, 6H), 2.25 and 2.31 (ABX system, 2H, J = 4.1, 9.2, 15.7 Hz), 2.79 (t, 1H, J = 10.9 Hz), 3.15 (m, 1H), 3.68 (s, 3H), 4.2−4.4 (m, 2H), 5.45 (d, 1H, J = 5.1 Hz), 6.16 (t, 1H, J = 2.1 Hz), 7.0−7.1 (m, 3H), 7.3−7.4 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 177.7, 172.4, 157.4, 153.7, 129.5, 125.6, 122.4, 116.0, 82.8, 61.2, 53.3, 51.9, 45.3, 35.9, 29.3, 27.3, 13.7, 10.0. IR (KBr) ν: 1760, 1735. Anal. Calcd for $C_{28}H_{43}NO_4Sn$: C, 58.35; H, 7.52; N, 2.43. Found: C, 58.30; H, 7.34; N, 2.39.

4-Benzyl-3-tributylstannylmethylen-6-*p*-methoxyphenyl-6-azabicycle[3.2.0] heptan-7-one 13a. Method A. From 0.2 g (0.63 mmol) of **5a**, a 78:22 mixture of two isomers was obtained. Flash chromatography (silica gel, hexanes/AcOEt, 4:1) afforded 0.18 g (47% yield) of the isomer mixture. A further purification allow us to isolate the major isomer for characterization. **Major (1*S**,4*S**,5*R**)-isomer 13a.** Colorless oil. ^{1}H NMR ($CDCl_3$) δ: 0.8−1.4 (m, 27H), 2.42−2.60 (m, 3H), 2.71 (dd, 1H, J = 6.9, 13.5 Hz), 2.87 (dd, 1H, J = 6.6, 9.6 Hz), 3.57 (dd, 1H, J = 4.5, 7.5 Hz), 3.70 (s, 3H), 4.02 (d, 1H, J = 3.9 Hz), 5.60 (s with satellites, 1H), 6.70 (d, 2H), 6.90 (d, 2H), 7.1−7.3 (m, 5H) ^{13}C NMR ($CDCl_3$) δ: 165.7, 158.7, 155.9, 139.4, 131.1, 129.3, 128.6, 126.6, 126.6, 117.9, 114.4, 59.6, 55.6, 53.1, 51.4, 39.6, 32.7, 29.3, 27.4, 13.9, 10.1. IR ($CHCl_3$) ν: 1745, 1620, 1510, 1380. EM (*m*/*e*): 552(M^+ − Bu,100), 496(M^+ − 2 × Bu, 2), 438(M^+ − 3 × Bu, 81), 149(38). Anal. Calcd for $C_{33}H_{47}NO_2Sn$: C, 65.14; H, 7.79; N, 2.30. Found: C, 65.26; H, 7.95; N, 2.09.

4-Benzyl-6-*p*-methoxyphenyl-3-triphenylstannylmethylen-6-azabicycle[3.2.0] heptan-7-one 13b. Method A. From 0.15 g (0.42 mmol) of **5a**, a 88:12 mixture of two isomers was obtained. Flash chromatography (silica gel, hexanes/AcOEt,

4:1) afforded 0.23 g (72% yield) of the isomer mixture. A further purification allow us to isolate an analytical sample of the major isomer. **Major (1*S**,4*S**,5*R**)-isomer 13b**. White solid. Mp: 172−174 °C (hexane/AcOEt). ^{1}H NMR ($CDCl_3$) δ: 2.39−2.61(m, 2H), 2.69 (dd, 1H, J = 9.9, 13.5 Hz), 2.82 (dd, 1H, J = 6.6, 13.5 Hz), 3.11 (dd, 1H, J = 7.2, 9.6 Hz), 3.55 (dd, 1H, J = 3.9, 8.7 Hz), 3.75 (s, 3H), 4.12 (d, 1H, J = 4.2 Hz), 5.96 (d with satellites, 1H, J = 2.1 Hz), 6.8 (d, 2H), 7.1 (d, 2H), 7.2−7.4 (m, 20H). ^{13}C NMR ($CDCl_3$) δ: 165.0, 162.6, 155.8, 138.8, 138.2, 136.8, 130.8, 129.1, 128.9, 128.9, 128.5, 126.6, 122.3, 117.7, 114.3, 59.4, 55.4, 53.0, 51.7, 39.4, 33.1. IR ($CHCl_3$) ν: 1740, 1510, 1480, 1430. EM (*m*/*e*): 665.10(M^+ ^{116}Sn), 667.05(M^+ ^{118}Sn), 668.10(M^+ ^{119}Sn), 669.10(M^+ ^{120}Sn). Anal. Calcd for $C_{39}H_{35}NO_2Sn$: C, 70.08; H, 5.28; N, 2.10. Found: C, 70.24; H, 5.34; N, 2.41.

[1*R,3*S**,4*R**,5*R**]-6-Allyl-4-tributylestannylmethyl-3-phenyl-2-oxa-6-azabicycle[3.2.0]heptan-7-one (15a).** Method A. From 0.12 g (0.50 mmol) of **4b**, only one diastereomer was obtained. Flash chromatography (silica gel, hexanes/AcOEt, 5:1) afforded 0.2 g of the title compound. Yield: 85%. Yellow oil. ^{1}H NMR ($CDCl_3$) δ: 0.25 (m, 2H), 0.90 (m, 15H), 1.3 (m, 6H), 1.40 (m, 6H), 2.5 (dt, 1H, J = 4.8, 11.1 Hz), 3.83 (m, 2H), 4.05 (dd, 1H, J = 5.8, 15.6 Hz), 5.2−5.3 (m, 4H), 5.83 (m, 1H, J = 2.2 Hz), 7.2−7.4 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 166.1, 137.3, 132.1, 128.2, 127.3, 126.3, 119.0, 86.0, 83.5, 65.7, 43.3, 41.7, 29.3, 27.4, 13.8, 9.2, 5.2. IR ($CHCl_3$) ν: 1710, 1645, 1605. Anal. Calcd for $C_{27}H_{43}NO_2Sn$: C, 60.96; H, 8.14; N, 2.63. Found: C, 60.82; H, 8.16; N, 2.59.

[1*R,3*S**,4*R**,5*R**]-6-(*p*-Anisyl)-4-tributylstannylmethyl-3-phenyl-2-oxa-6-azabicycle[3.2.0]heptan-7-one (15d).** Method A. From 0.2 g (0.65 mmol) of **16b**, a 62:38 mixture of cyclyzation product/reduction was obtained. Flash chromatography (silica gel, hexanes/AcOEt, 7:1) afforded 0.24 g of the title compound**.** Yield: 62%. White solid. Mp: 116−117 °C (hexane/AcOEt). ^{1}H NMR ($CDCl_3$) δ: 0.35 (m, 2H), 0.8−1.4 (m, 27H), 2.71 (dt, 1H, J = 4.5, 11 Hz), 3.8 (s, 3H), 4.22 (d, 1H, J = 3.6 Hz), 5.16 (d, 1H, J = 4.3 Hz), 5.30 (d, 1H, J = 3.6 Hz), 6.90−7.4 (m, 4H), 7.2−7.3 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 163.1, 156.7, 137.1, 130.4, 128.2, 127.4, 126.3, 118.6, 114.7, 84.9, 83.6, 65.3, 55.7, 41.5, 29.2, 27.5, 13.8, 9.5, 5.4. IR (KBr) ν: 2960, 2900, 1730, 1510. Anal. Calcd for $C_{31}H_{45}NO_3Sn$: C, 62.22; H, 7.58; N, 2.34. Found: C, 62.16; H, 7.28; N, 2.27.

(+)-(1*R*,6*R*,7*S*)-1-Benzyl-2-(*Z*)-tributylstannylmethylene-7-[(*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl]carbacefam (17a). Method A. From 0.25 g (0.65 mmol) of **1b**, only one isomer was obtained. Flash chromatography (silica gel, hexanes/Et_3N, 6:1) afforded 0.3 g of the title compound. Yield: 70%. Colorless oil. $[\alpha]_D$ = +21.1 (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: (50 °C) 0.8−1.4 (m, 27H), 1.63 (m, 1H), 2.05 (m, 1H), 2.16 (br s, 1H), 2.63 (dd, 1H, J = 6.0, 14.1 Hz), 2.63 (m, 1H), 2.82 (br s, 1H), 3.05 (dd, 1H, J = 6.6, 14.7 Hz), 3.31 (dd, 1H, J = 4.5, 10.2 Hz), 3.94 (m, 1H), 4.03 (dd, 1H, J = 6.0, 7.8 Hz), 4.25 (br s, 1H), 4.38 (t, 1H, J = 9.0 Hz), 5.77 (s with satellites, 1H), 7.2−7.4 (m, 10H). ^{13}C NMR δ: 163.0, 157.8, 153.6, 140.4, 138.3, 129.3, 129.2, 129.0, 128.6, 127.8, 126.1, 123.9, 77.2, 70.9, 63.2, 62.0, 59.1, 44.3, 41.7, 37.4, 29.3, 27.2, 13.5, 10.5. IR ($CHCl_3$) ν: 1750, 1720, 1220. EM (*m*/*e*): 621(M^+ ^{120}Sn − Bu, 60), 622-(M^+ ^{121}Sn − Bu, 20), 620(M^+ ^{120}Sn − Bu, 31), 619(M^+ ^{120}Sn − Bu, 46), 91(100), 57(18). Anal. Calcd for $C_{36}H_{50}N_2O_3Sn$: C, 63.82; H, 7.44; N, 4.13. Found: C, 63.95; H, 7.26; N, 4.02.

Tetrahydropyridine 14a. From 0.31 g of **3a** and Bu_3SnH, 0.06 g (10%) of tetrahydropyridine **14a** were obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ: 0.8−1.4 (m, 27H), 1.64 (s, 3H), 3.73 (d, 1H, J = 14.5 Hz), 3.92 (s, 1H), 4.30 (s, 2H), 4.39 (d, 1H, J = 14.5 Hz), 4.64 (s, 2H), 5.95 (s, 1H), 6.67 (s, 1H), 7.2−7.4 (m, 10H). ^{13}C NMR ($CDCl_3$) δ: 165.8, 150.2, 142.0, 137.4, 128.5, 128.5, 128.4, 128.2, 128.2, 128.1, 127.9, 127.6, 121.2, 117.6, 73.1, 69.2, 56.3, 45.2, 29.2, 19.7, 13.8, 10.4. IR ($CHCl_3$) ν: 1740. Anal. Calcd for $C_{34}H_{49}NO_2Sn$: C, 65.61; H, 7.93; N, 2.25. Found: C, 65.42; H, 7.82; N, 2.55.

Tetrahydropyridine 14b. From 0.2 g of **2e** and Bu_3SnH, 0.2 g (45%) of hydrostannylation product and 0.06 g (14%) of **14b** were obtained. ^{1}H NMR ($CDCl_3$) δ: 0.8−1.4 (m, 27H), 1.18 (d, 3H, J = 7.2 Hz), 3.0 (m, 1H), 4.08 (d, 1H, J = 14.1 Hz), 4.32 (d, 1H, J = 14.1 Hz), 4.74 (s, 2H), 4.97 (dd, 1H, J = 2.1, 8.4 Hz), 5.81 (s, 1H), 6.66 (dd, 1H, J = 2.1, 8.1 Hz), 6.9−7.3 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 164.5, 151.0, 137.5, 129.5, 125.1, 122.1, 123.0, 121.6, 114.7, 67.2, 54.3, 47.0, 29.1, 27.2, 21.5, 13.7, 10.2. IR ($CHCl_3$) ν: 1740. Anal. Calcd for $C_{27}H_{43}NO_2Sn$: C, 60.92; H, 8.14; N, 2.63. Found: C, 61.11; H, 8.36; N, 2.81.

General Procedure for the Synthesis of Carbapenams 20 and 21a. A solution of the β-lactam **1a** (1 mmol), the corresponding radical promoter (Ph_2PH or BrTs, 1.15 mmol), and AIBN (0.1 mmol) in anhydrous benzene (20 mL) under argon was heated under reflux with the addition of AIBN every 2 h until complete disappearance of starting material (TLC, 7−8 h). Then, the solvent was evaporated, and the crude product was analized by ^{1}H NMR. The residue was purified by column chromatography (silica gel; hexanes, then hexanes/EtAcO).

Compounds 20a and 20b. From 0.3 g of **1a**, only one diastereoisomer of compound **20a** was obtained but could not be isolated as such because of oxidation to **20b** during chromatographic purification. **(1*R*,5*R*,6*S*)-Diphenylphosphine derivative 20a** (from the crude reaction mixture). ^{1}H NMR ($CDCl_3$) δ: 2.41 (dd, 1H, J = 10.8, 12.9 Hz), 2.90 (dd, 1H, J = 7.8, 9.0 Hz), 3.36 (dd, 1H, J = 3.9, 12.9 Hz), 3.60 (m, 2H), 3.87 (dd, 1H, J = 7.8, 9.0 Hz), 3.92 (d, 1H, J = 3.9 Hz), 4.01 (d, 1H, J = 16.2 Hz), 4.19 (t, 1H, J = 9.0 Hz), 4.38 (dd, 1H, J = 1.5, 16.2 Hz), 6.24 (d, 1H, J = 1.5 Hz), 7−7.5 (m, 20H). **(1*R*,5*R*,6*S*)-Diphenylphosphine oxide derivative 20b**. A 0.34 g portion of the phosphine oxide derivative was obtained. Yield: 74%. Yellowish solid. Mp: >230 °C (dec). $[\alpha]_D$ = +100 (c = 2, $CHCl_3$).^{1}H NMR ($CDCl_3$) δ: 2.48 (dd, 1H, J = 11.4, 13.2 Hz), 2.97 (dd, 1H, J = 7.5, 9.0 Hz), 3.27 (dd, 1H, J = 4.2, 13.2 Hz), 3.61 (dd, 1H, J = 4.2, 8.4 Hz), 3.75 (m, 1H), 3.88 (dd, 1H, J = 7.5, 9.0 Hz), 3.93 (d, 1H, J = 4.2 Hz), 4.21 (t, 1H, J = 9.0 Hz), 4.25 (d, 1H, J = 17.7 Hz), 4.5 (d, 1H, J = 17.7 Hz), 6.18 (dd, 1H, J = 2.7, J_{P-H} = 20 Hz), 7−7.5 (m, 20H). ^{13}C NMR ($CDCl_3$) δ: 170.8, 168.3, 157.4, 139.8, 136.7, 132.7, 131.1 (5 peaks), 129.2 (13 peaks), 127.1, 126.8, 70.8, 64.6, 63.8, 59.4, 59.1, 49.5, 37.6. IR (KBr) ν: 1780, 1750, 1420. Anal. Calcd for $C_{35}H_{31}N_2PO_4$: C, 73.16; H, 5.44; N, 4.88. Found: C, 73.48; H, 5.13; N, 4.54.

1-(α-Bromobenzyl)-2-(*Z*-*p*-toluenesulfonylmethylene)-6-[(*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl]carbapenams 21a. From 0.30 g of **1a**, a 90:10 mixture of two isomers was obtained. **Major isomer.** A 0.34 g portion of the title compound was isolated. Yield: 85%. White solid. Mp: >120 °C (dec). $[\alpha]_D$ = +184 (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 2.44 (s, 3H), 4.03 (m, 3H), 4.12−4.22 (m, 2H), 4.32 (d, 1H, J = 4.5 Hz), 4.38 (t, 1H, J = 8.1 Hz), 4.95 (dd, 1H, J = 2.4, 18.6 Hz), 5.14 (d, 1H, J = 5.7 Hz), 5.87 (d, 1H, J = 2.4 Hz), 7.2−7.4 (m, 12H), 7.7 (d, 2H J = 9.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 170.7, 158.3, 144.8, 139.0, 137.6, 136.7, 135.5, 130.0, 129.7, 129.6, 129.3, 129.0, 127.9, 127.3, 127.1, 125.4, 70.9, 61.8, 60.5, 60.1, 55.0, 51.8, 49.4, 21.7. IR (KBr) ν: 1780, 1740. Anal. Calcd for $C_{30}H_{27}N_2O_5SBr$: C, 59.31; H, 4.48; N, 4.61. Found: C, 59.60; H, 4.34; N, 4.89.

(1*R*,5*R*,6*S*)-1-(Benzyl)-2-(*Z*-*p*-toluenesulfonylmethylene)-6-[(*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl]carbapenams 21b. To a refluxing solution of 0.08 g (0.13 mmol) of **21a** and AIBN (1 mg) in benzene (3 mL) under argon was added $HSnBu_3$ (0.02 mL). Analysis of the crude mixture by ^{1}H NMR showed completed transformation. Purification was performed by column chromatography to give 0.04 g of the title compound. Yield: 62%. Colorless oil. $[\alpha]_D$ = +102.8 (c = 3, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 2.45 (s, 3H), 2.96 (t, 1H, J = 7.8 Hz), 3.12 (dd, 1H, J = 3.6, 13.2 Hz), 3.70 (m, 3H), 3.88 (t, 1H, J = 7.5 Hz), 3.94 (d, 1H, J = 3.9 Hz), 4.20 (t, 1H, J = 9.0 Hz), 4.37 (d, 1H, J = 18.3 Hz), 4.76 (dd, 1H, J = 2.4, 18.3 Hz), 6.30 (d, 1H, J = 2.4 Hz), 7.0 (m, 2H), 7.1−7.4 (m, 10H), 7.8 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 170.6, 161.9, 157.4, 144.9, 139.1, 137.8, 136.5, 135.4, 130.1, 129.5, 129.4, 129.1, 127.5, 127.0, 123.8, 111.3, 70.8, 63.7, 59.4, 59.1, 48.8, 46.9, 37.3, 21.6. IR (KBr) ν: 1760, 1740. Anal. Calcd for $C_{30}H_{28}N_2O_5S$: C, 70.02; H, 5.48; N, 2.72. Found: C, 70.20; H, 5.31; N, 2.99.

General Procedure for the Preparation of Carbapenam Derivatives 29 and 30. A mixture of the corresponding tin derivative **11**, **17**, *p*-TsOH·H_2O (1.2 equiv), and CH_2Cl_2 (30 mL/mmol) was stirred at room temperature until complete

disappearance of the starting material (TLC, 15−35 min). After dilution with CH_2Cl_2, the mixture was successively washed with 5% $NaHCO_3$ and H_2O and dried ($MgSO_4$). After filtration and evaporation of the solvent, the crude product was purified by column chromatography (silica gel; hexanes/EtAcO or hexanes/Et_3N mixtures) and/or recrystallization. Representative examples follow.

(+)-(1*R*,5*R*,6*S*)-1-Benzyl-2-methylene-6-[(*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl]-carbapenam (*anti*-29a). From 0.31 g of **major 11a**, 0.16 g of the title compound was obtained. Yield: 91%. White needles. Mp: >197 °C (dec) (hexanes/EtAcO). $[\alpha]_D = +229$ ($c = 0.5$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 2.36 (dd, 1H, $J = 11.0$, 13.2 Hz), 2.86 (dd, 1H, $J = 7.6$, 9.0 Hz), 3.33 (dd, 1H, $J = 3.6$, 13.2 Hz), 3.4−3.6 (m, 1H), 3.55 (d, 1H, $J = 4.3$ Hz), 3.63 (d, 1H, $J = 14.9$ Hz), 3.85 (dd, 1H, $J = 7.7$, 8.5 Hz), 3.90 (d, 1H, $J = 4.7$ Hz), 4.18 (t, 1H, $J = 8.9$ Hz), 4.44 (d, 1H, $J = 14.9$ Hz), 5.13 (d, 2H, $J = 2.1$ Hz), 7.0−7.6 (m, 10H). ^{13}C NMR ($CDCl_3$) δ: 171.9, 157.8, 152.9, 141.1, 137.0, 129.6, 129.4, 129.3, 129.2, 127.2, 126.6, 107.4, 70.9, 65.2, 59.4, 59.1, 50.9, 44.9, 37.5. IR (KBr) ν: 1770, 1750, 1650. Anal. Calcd for $C_{23}H_{22}N_2O_3$: C, 73.78; H, 5.92; N, 7.48. Found: C, 73.73; H, 6.00; N, 7.48.

(+)-(1*S*,5*R*,6*S*)-1-Benzyl-2-methylene-6-[(*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl]-carbapenam (*syn*-29a). From 0.10 g of ***syn*-11a**, 0.04 g of the title compound was obtained. Yield: 71%. White crystals. Mp: 198−199 °C (hexanes/EtAcO). $[\alpha]_D = +43$ ($c = 0.5$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 2.46 (dd, 1H, $J = 11.3$, 14.3 Hz), 2.82 (br d, 2H, $J = 9.9$ Hz), 3.40 (br s, 1H), 3.3−3.5 (m, 2H), 3.9−4.1 (m, 3H), 4.30 (t, 1H, $J = 9.0$ Hz), 5.6−5.7 (m, 2H), 7.1−7.5 (m, 10H). ^{13}C NMR ($CDCl_3$) δ: 163.2, 157.5, 140.1, 138.1, 138.1, 129.5, 129.2, 129.0, 128.8, 127.3, 126.7, 122.2, 71.0, 62.2, 59.0, 56.8, 41.4, 37.5, 34.7. IR (KBr) ν: 1750. Anal. Calcd for $C_{23}H_{22}N_2O_3$: C, 73.78; H, 5.92; N, 7.48. Found: C, 73.41; H, 6.03; N, 7.28.

(+)-(1*R*,5*S*,6*R*)-1-Methoxycarbonylmethyl-2-methylene-6-phenoxycarbapenam (*syn*-29d). From 0.10 g of ***syn*-11e**, 0.05 g of the title compound was obtained. Yield: 98%. Colorless oil. $[\alpha]_D = +189.4$ ($c = 1$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 2.36 (m, 2H), 3.05−3.18 (m, 1H), 3.50 (br d, 1H), 3.60 (s, 3H), 3.73 (dd, 1H, $J = 4.2$, 8.7 Hz), 4.12 (dd, 1H, $J = 3.6$, 18.3 Hz), 5.39 (dd, 1H, $J = 1.8$, 4.2 Hz), 5.7 (s, 2H), 6.95−7.35 (m, 5H). ^{13}C NMR δ: 171.8, 166.1, 157.5, 129.7, 128.1, 122.8, 122.4, 115.7, 81.5, 54.0, 51.9, 37.4, 37.1, 29.9. IR (KBr) ν: 1760. Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.87. Found: C, 66.99; H, 5.88; N, 5.02.

(+)-(1*R*,5*R*,6*S*)-1-Benzyl-2-(*Z*)-iodomethylene-6-[(*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl]-carbapenam (*anti*-31a). To a solution of 0.15 g (0.23 mmol) of ***anti*-11a** in CH_2Cl_2 (10 mL) was added 63 mg (0.25 mmol) of iodine. The mixture was stirred at room temperature until complete disappearance of starting material (TLC). Then, the mixture was successively washed with 10% $NaHSO_3$ and H_2O and dried ($MgSO_4$). After filtration and evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexanes/Et_3N, 6:1). A 0.06 g (51%) portion of **31a** could be obtained by crystallization of one of the purer fractions. White crystals. Mp: >121 (dec, hexane/EtAcO). $[\alpha]_D = +234$ ($c = 0.5$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 2.43 (dd, 1H, $J = 11.1$, 13.2 Hz), 2.92 (dd, 1H, $J = 7.5$, 9.0 Hz), 3.24 (dd, 1H, $J = 3.9$, 13.2 Hz), 3.5−3.6 (m, 1H,), 3.62 (br d, 1H, $J = 15.9$ Hz), 3.69 (dd, 1H, $J = 4.5$, 8.4 Hz), 3.87 (dd, 1H, $J = 7.5$, 8.4 Hz), 3.93 (dd, 1H, $J = 0.9$, 4.2 Hz), 4.19 (t, 1H, $J = 9.0$ Hz), 4.36 (br d, 1H, $J = 15.9$ Hz), 6.23 (dd, 1H, $J = 2.4$, 5.4 Hz), 7.0−7.5 (m, 10H). ^{13}C NMR δ: 171.1, 157.4, 155.7, 140.1, 136.8, 129.6, 129.5, 129.3, 129.3, 127.2, 126.9, 71.1, 70.9, 66.2, 60.0, 59.5, 55.7, 47.7, 37.7. IR ($CHCl_3$) ν: 1760. Anal. Calcd for $C_{23}H_{21}N_2O_3I$: C, 55.21; H, 4.23; N, 5.60. Found: C, 54.91; H, 4.26; N, 5.40.

(+)-(1*R*,5*R*,6*S*)-1-Bencyl-2-oxo-6-[(*S*)-4-phenyl-2-oxo-1,3-oxazolidin-3-yl]-carbapenam (*anti*-32). Ozone was passed through a solution of ***anti*-29a** (0.07 g, 0.19 mmol) in CH_2Cl_2 (10 mL) at −78 °C until blue color was persistent (2 min). Excess Me_2S (1 mL) was then added, and the mixture was stirred overnight at room temperature. Then, it was diluted, washed with water, dried ($MgSO_4$), and evaporated. Crude product was purified by column chromatography (silica gel, EtAcO/hexanes 1:1) to give 0.04 g of the 2-oxocarbapenam **32**. Yield: 60%. White needles. Mp: 194−196 °C (hexanes/EtAcO). $[\alpha]_D = +236$ ($c = 0.5$, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 2.35 (dd, 1H, $J = 11.4$, 13.8 Hz), 3.03 (t, 1H, $J = 8.4$ Hz), 3.28 (dd, 1H, $J = 0.9$, 18.0 Hz), 3.28−3.38 (m, 1H), 3.42 (dd, 1H, $J = 3.6$, 13.5 Hz), 3.77 (dd, 1H, $J = 4.8$, 9.0 Hz), 3.90 (dd, 1H, $J = 7.8$, 8.4 Hz), 4.13 (dd, 1H, $J = 0.9$, 4.8 Hz), 4.19 (t, 1H, $J = 8.9$ Hz), 4.23 (d, 1H, $J = 17.7$ Hz), 7.0−7.5 (m, 10H). ^{13}C NMR ($CDCl_3$) δ: 212.0, 170.2, 157.6, 139.9, 136.2, 129.6, 129.6, 129.3, 128.9, 127.1, 126.8, 71.0, 62.2, 61.2, 59.4, 51.7, 50.6, 34.3. IR (KBr) ν: 1785, 1740. Anal. Calcd for $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.35; N, 7.44. Found: C, 70.35; H, 5.62; N, 7.12.

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Supporting Information Available: Compound characterization data and experimental procedures for products **1b**,**c**, **2b**, **2d**,**e**, **2g**, **3a**,**b**, **3d**, **4b**,**c**, **4e**, **5a**,**b**, **6a**,**b**, **7a**,**b**, **10**, **11c**,**d**, **11f**−**i**, **11k**, **12a**, **12c**, **13c**,**d**, **15b**,**c**, **16a**,**b**, **17b**, **19**, ***anti*-29b**,**c**, ***anti*-29e,f**, ***anti*-30**, ***anti*-31**, and **33**, as well as X-ray data for compound ***anti*-29a**. This material is available free of charge via the Internet at http: //pubs.acs.org.

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