Metal-Promoted Allylation, Propargylation, or Allenylation of Azetidine-2,3-diones in Aqueous and Anhydrous Media. Application to the Asymmetric Synthesis of Densely Functionalized 3-Substituted 3-Hydroxy-β-lactams

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Metal-mediated carbonyl allylation, allenylation, and propargylation of optically pure azetidine-2,3-diones were investigated in both anhydrous and aqueous environments. Different metals promoters showed varied regioselectivities on product formation during allenylation/propargylation reactions of the keto-β-lactams. The stereochemistry of the new C3-substituted C3-hydroxy quaternary center was controlled by placing a chiral auxiliary at C4. In this way, the coupling of azetidine-2,3-diones with a variety of propenyl-, propynyl-, and allenylmetal reagents offers a convenient asymmetric entry to potentially bioactive 3-substituted 3-hydroxy-β-lactams.

Introduction

The presence of the 2-azetidinone ring in several widely used families of antibiotics has stimulated considerable activity directed at the stereocontrolled synthesis of β-lactams.[1] In recent years, various natural monocyclic β-lactams were shown to exhibit high anti-bacterial activity, suggesting that a suitably substituted monocyclic 2-azetidinone ring might perhaps be the minimum requirement for biological activity. Besides, the ever-growing new applications of azetidine-2-ones in fields ranging from enzyme inhibition,[2] to the use of these products as starting materials to develop new synthetic methodologies, justify a renewed interest in these compounds. In particular, the 3-substituted 3-hydroxy-2-azetidinone moiety, representing an efficient carboxylate mimic,[3] is present in several pharmacologically active monobactams such as sulfazecin and related products[4] and in enzyme inhibitors such as tabtoxin and its analogues.[5] Moreover, these compounds with correct absolute configurations serve as precursors to the corresponding α-hydroxy-β-amino acids (isoserines), which are key components of a large number of therapeutically important compounds. As an example, (2*R*,3*S*)-3-amino-2-hydroxy-5-methylhexanoic acid (norstatine) and (3*R*,4*S*)-4-amino-3-hydroxy-5-methylheptanoic acid (statine) are residues for peptide inhibitors of enzymes, such as renin[6] and HIV-1 protease.[7] In addition, phenylisoserine analogues are used to synthesize new taxoids.[8] However, little attention has been paid to develop methods for the preparation of trisubstituted β-lactams bearing hetero-substituents at a C3 quaternary stereogenic center,[9] despite its importance both as synthons and substrates for studies of biological activity.

On the other hand, the development of new carbon−carbon bond-forming reactions is of particular interest in organic synthesis, especially in the context of creating quaternary chiral centers involving a stereoselective reaction.[10] Among the most fundamental and important reactions for constructing carbon−carbon bonds are the allylation and the propargylation/allenylation of aldehydes and ketones (carbonyls) with organometallic reagents. For example, Sakurai-, Grignard-, and Barbier-type reactions have been widely utilized for the allylation[11] or propargylation/allenylation[12] of carbonyls, in which chemo-, regio-, and stereoselectivities of the desired alcohols are highly dependent on the nature of the metals employed. Although many efforts have been made in

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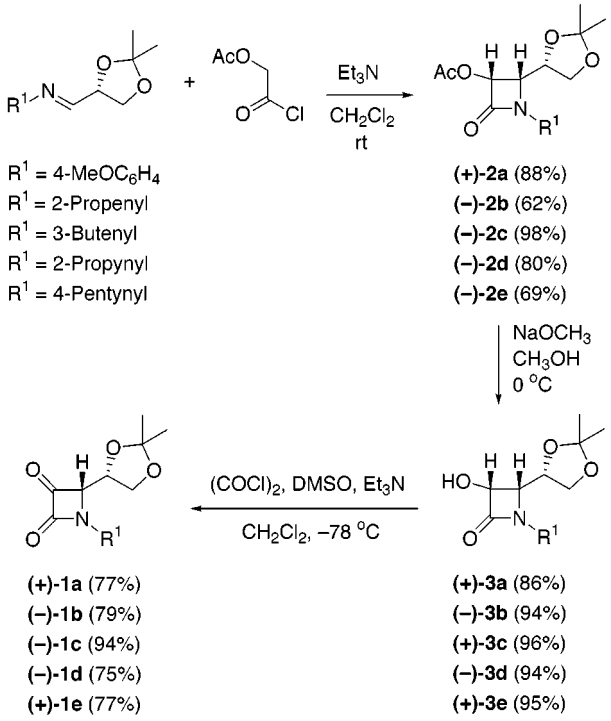
these fields into various types of carbonylic compounds, the allenylation of azetidine-2,3-diones has not been reported yet. Furthermore, the information available on the use of β-lactams as chiral building blocks on the propargylation and allylation reactions is still very scarce; only Cho has recently reported the propargylmetalation of 6-oxopenicillanates in anhydrous and aqueous tetrahydrofuran.[13] Bose[14a] and Paquette[14b] have independently reported the allylindation of azetidine-2,3-diones. However, the asymmetric version was achieved with poor diastereoselectivity on azetidine-2,3-diones bearing a chiral auxiliary at nitrogen.[14b]

Recently, organometallic reactions in aqueous media have elicited considerable interest because of their synthetic advantages (many reactive functional groups, such as hydroxy and carboxylic functions, do not require the protection−deprotection protocol in such reactions, and many water-soluble compounds do not need to be converted into their derivatives and can be reacted directly) as well as its potential as an environmentally benign chemical process (the use of anhydrous inflammable solvents can be avoided and the burden of solvent disposal may be reduced).[15] As part of our research on the synthesis and synthetic applications of chiral, functionalized 2-azetidinones,[16] we decided to pursue a "green chemistry" approach for the stereoselective incorporation of new substituents in the β-lactam ring. In this context, we wish to report now full details of the manner in which enantiomerically pure azetidine-2,3-diones and a variety of allyl, propargyl, or allenyl organometallics undergo coupling.[17]

Results and Discussion

The starting substrates, azetidine-2,3-diones **1**, were prepared in optically pure form using standard methodology. Enantiopure 3-acetoxy-2-azetidinones **2a**−**e** were obtained from imines of (*R*)-2,3-*O*-isopropylideneglyceraldehyde through Staudinger reaction with acetoxyacetyl chloride in the presence of Et_3N as single cis enantiomers,[18] which via transesterification with sodium methoxide in methanol gave 3-hydroxy-2-azetidinones **3a**−**e**. Azetidine-2,3-diones **1a**−**e** were available in high yield and without detectable racemization by Swern oxidation of the corresponding 3-hydroxy-β-lactam **3** (Scheme 1).[19]

Scheme 1



Having obtained the ketones, the next stage was set to carry out the key coupling reactions. We reasoned that by placing a chiral auxiliary at C4 we might be able to control the stereochemistry of the new C3-substituted C3-hydroxy quaternary center. First, the carbonyl allylation of azetidine-2,3-diones **1** was explored in anhydrous conditions. Compounds **1** may be considered similar to N-protected α-amino aldehydes, most of which are relatively unstable both chemically and configurationally in a number of addition reactions.[20] However, the Lewis acid promoted addition of allyltrimethylsilane and allyltributylstannane to enantiopure oxo compounds **1** gave homoallylic alcohols **4a**−**c** as single diastereoisomers (Scheme 2).[21]

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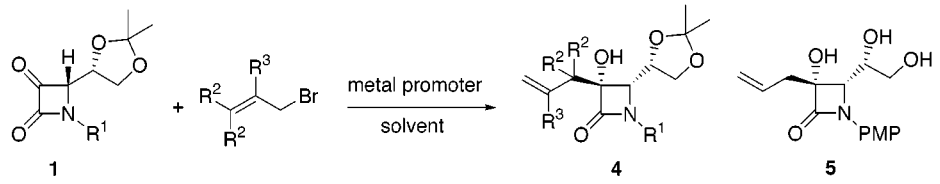
Table 1. Stereoselective Allylation of Azetidine-2,3-diones 1 in Aqueous Media[a]



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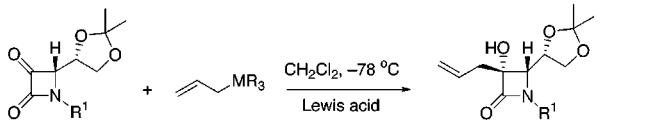
product	R^1	R^2	R^3	promoter	*T* (°C)/t (h)	solvent	yield[b] (%)
(+)-**4a**	PMP	H	H	$Mg/BiCl_3$	20/18	THF/H_2O	72
(+)-**4a**	PMP	H	H	In	20/18	THF/H_2O	73
(+)-**4a**	PMP	H	H	In	0/3	THF/NH_4Cl (aq satd)	73
(+)-**4a**	PMP	H	H	Zn	20/18	THF/H_2O	72
(+)-**4a**	PMP	H	H	Zn	0/3	THF/NH_4Cl (aq satd)	72
(+)-**4a**	PMP	H	H	$In/InCl_3$	20/2	THF/H_2O	73
(+)-**4a**	PMP	H	H	$In/HfCl_4$	20/1.5	THF/H_2O	73
(+)-**4a**	PMP	H	H	$Zn/InCl_3$	20/2	THF/H_2O	75
(+)-**4a**	PMP	H	H	$Zn/HfCl_4$	20/6	THF/H_2O	75
(+)-**4a**	PMP	H	H	Sn	0/1	THF/NH_4Cl (aq satd)	71[c]
(+)-**4d**	PMP	H	COOH	In	0/1.5	THF/NH_4Cl (aq satd)	83
(+)-**4d**	PMP	H	COOH	Zn	0/1.5	THF/NH_4Cl (aq satd)	53
(+)-**4e**	PMP	CH_3	H	Zn	0/1.5	THF/NH_4Cl (aq satd)	85
(−)-**4b**	2-propenyl	H	H	In	20/18	THF/H_2O	70
(−)-**4f**	2-propenyl	CH_3	H	In	0/1	THF/NH_4Cl (aq satd)	80
(−)-**4g**	3-butenyl	H	H	In	0/1	THF/NH_4Cl (aq satd)	100
(−)-**4h**	2-propynyl	H	COOH	In	0/1.5	THF/NH_4Cl (aq satd)	99
(+)-**5**	PMP	H	H	Sn	reflux/1	$MeOH/NH_4Cl$ (aq satd)	71

[a] All reactions were carried out on 1 mmol scale. PMP = $4\text{-}MeOC_6H_4$. Only one isomer was detected in the ^1H NMR spectra of the crude reaction mixtures before purification. [b] Yield of pure, isolated product with correct analytical and spectral data. [c] Some acetonide cleavage was observed.

Scheme 2



(+)-1a	$MR_3 = SiMe_3$	$SnCl_4$	**(+)-4a** R^1 = 4-$MeOC_6H_4$ (75%)
(+)-1a	$MR_3 = SnBu_3$	$SnCl_4$	**(+)-4a** R^1 = 4-$MeOC_6H_4$ (70%)
(+)-1a	$MR_3 = SnBu_3$	$BF_3.Et_2O$	**(+)-4a** R^1 = 4-$MeOC_6H_4$ (55%)
(−)-1b	$MR_3 = SiMe_3$	$SnCl_4$	**(−)-4b** R^1 = 2-Propenyl (66%)
(−)-1d	$MR_3 = SiMe_3$	$SnCl_4$	**(−)-4c** R^1 = 2-Propynyl (64%)

Since we are pursuing addition reactions with different organometallic reagents, we wish to explore further the allylation of α-keto lactams **1** in aqueous media. In the event, different metal mediators showed total diastereoselectivity and good yields (53−100%) on product formation during allylation reactions of azetidine-2,3-diones **1** with allyl bromide, 2-(bromomethyl)acrylic acid, and prenyl bromide, in aqueous environmment (Table 1). Since the main drawbacks of the Barbier-type carbon−carbon bond formation are long reaction times and only reactive halides were found to be effective, we thought that the allylation reaction could proceed with rate enhancement in the presence of some additives. Indeed, the addition of ammonium chloride, indium trichloride, or hafnium chloride to the aqueous medium shortened reactions times, exhibiting the same facial preference (see Table 1). It is to be presumed that the ionic strength enhancement of the reaction solvent provided by the ammonium chloride accelerated the process.[22] Although the role of the indium- and hafnium-derived additives is not completely understood, it may be explained in terms of Lewis acid, which activates the carbonyl group and the softness of these reagents. A transmetalation of the initially formed allylmetal with hafnium(indium) chloride as Lewis acid may be involved.[23] The tin-mediated carbonyl allylation of azetidine-2,3-dione (+)-**1a** in the system solvent methanol/NH_4Cl (aq satd) proceeded with concomitant acetonide cleavage, giving rise to the triol (+)-**5** as single diastereomer.

Once we had established the best reaction conditions to carry out the allylation reaction, our aim was to evaluate the feasibility of other related metal-mediated Barbier-type reactions in enantiomerically pure azetidine-2,3-diones, studying the diastereochemistry (syn vs anti) and the regiochemistry of the connection (e.g., allenylation vs propargylation). However, it is not easy to control selectivity between Barbier-type propargylation and allenylation with propargylic halides. The reaction of propargyl bromide with metals has been proposed to generate an equilibrium between the allenyl and propargyl organometallics. This metallotropic rearrangement often results in poor regioselection in the final organic product, because both organometallic species can react with the carbonyl compounds. Hence, a pertinent synthetic challenge is to tune the regioselectivity toward either acetylenic or allenic products. In this context, the synthesis of homopropargyl alcohols from propargylpalladium reported by Tamaru, using the umpolung approach,[24] and the preparation of homopropargyl and allenyl alcohols from transient allenylindium reagents or propargylic stannanes, respectively, described by Marshall,[25] are noteworthy.

(21) Our results are totally consistent with previously published works on this type of additions to α-amino aldehydes, with no reference to partial racemization. For a recent example, see: Dias, L. C.; Meira, P. R. R. *Synlett* **2000**, 37.

(22) It was reported for related 2-aminoaldehydes that changes in the ionic strength of the solvent can provide modification in the diastereomeric ratio or accelerated the process. See: Chappell, M. D.; Halcomb, R. L. *Org. Lett* **2000**, *2*, 2003.

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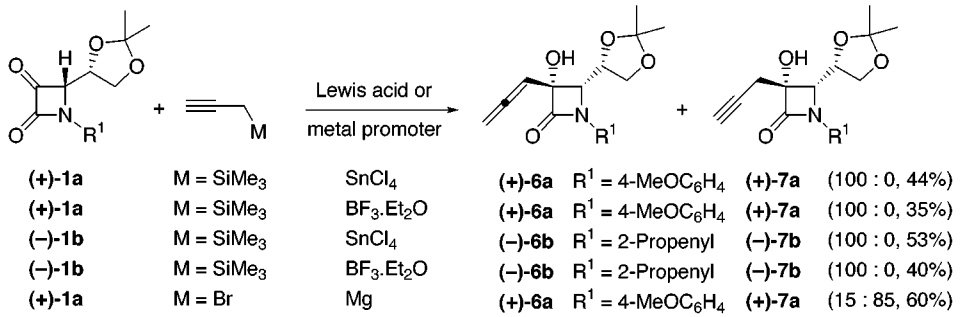
Scheme 3



To achieve the goal of full control of regiochemistry, we have investigated a number of protocols in anhydrous and aqueous environments, with a variety of metal mediators and different prop-2-ynyl systems. First, we examined the Lewis acid-induced reaction of azetidine-2,3-diones with propargylsilane or propargylmagnesium bromide in anhydrous conditions. The reactions of ketones **1a**,**b** with the above organosilane proceeded at −78 °C with total regiocontrol, inducing exclusively the allenic products **6a**,**b** as single diastereoisomers in moderate yields (44−53%). The nature of the acid catalyst had no pronounced influence, showing similar results for both tin tetrachloride and boron trifluoride diethyl etherate (Scheme 3). By contrast, when azetidine-2,3-dione (+)-**1a** was treated with propargyl/allenylmagnesium bromide, the corresponding product was isolated as a mixture (15:85) of allenic and acetylenic products **6a/7a** (Scheme 3).

The aim of a more efficient approach prompted us to seek an aqueous metal-induced propargylation/allenylation reaction. For this purpose, azetidine-2,3-diones **1** were treated with prop-2-ynyl bromides, bearing substituents of varying steric demand at C3, and a broad variety of metals and reaction conditions in aqueous media. Not unexpectedly, the diastereoselectivity was complete in all cases. However, while the chemical yield of the addition was generally good, the regioselectivity of the process was a function of the nature of both the metal reagent and the propargyl bromide and in many cases of the system solvent as well.

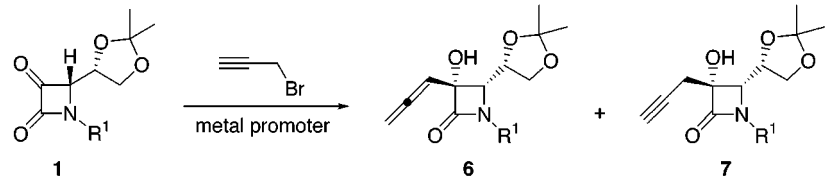
Since indium in aqueous solution has shown considerable promise in the addition of unsaturated halides to the carbonyl groups, the regio- and diastereoselectivity of the carbon−carbon bond formation were initially investigated through the indium-mediated reaction between the azetidine-2,3-dione (+)-**1a** and propargyl bromide in aqueous tetrahydrofuran at room temperature. In the event, the 3-substituted 3-hydroxy-β-lactam moiety was obtained; however, the observed regioselectivity was very poor (58:42) in favor of the allenic product. Surprisingly, the regiochemical preference was reversed on the indium-promoted reaction just by changing the system solvent (a saturated aqueous solution of NH_4Cl in THF was used instead of aqueous tetrahydrofuran), with the expected alcohols (+)-**6a** and (+)-**7a** being obtained as a mixture of regioisomers in a ratio of **6a**:**7a** = 29:71. This preliminary result encouraged us to find a more convenient reagent for this transformation. To our delight, when the above reaction was mediated by zinc and was conducted in a saturated aqueous solution of NH_4Cl in THF at 0 °C, it gave rise to the optically pure homopropargyl alcohol (+)-**7a** as a single regio- and diastereoisomer in a reasonable 70% yield. However, the yield fell dramatically by performing the zinc-mediated coupling of the azetidine-2,3-dione (+)-**1a** and propargyl bromide in anhydrous THF in the presence of solid NH_4Cl. No reaction was observed in anhydrous THF when the NH_4Cl was supressed, and the change of the system solvent from tetrahydrofuran/NH_4Cl (aq satd) to methanol/NH_4Cl (aq satd) resulted in the absence of regioselection. The tin-mediated reaction between ketone (+)-**1a** and propargyl bromide in aqueous tetrahydrofuran resulted in the absence of coupling. By contrast, when the same experiment was carried out in a saturated aqueous solution of NH_4Cl in THF, the allenyl alcohol was formed as major product, together with 25% of the homopropargylic alcohol. Indium trichloride and hafnium chloride were tested as additives in the tin-mediated reaction of propargyl bromide and azetidine-2,3-dione (+)-**1a** in tetrahydrofuran/NH_4Cl (aq satd). Interestingly, the analyses of the crude reaction mixture revealed only the presence of the allenyl alcohol. Manganese, cadmium and bismuth failed to produce any desired propargylation/allenylation compound when they were used as metal promoters. Similar results to those observed for (+)-**1a** were obtained in the metal-mediated Barbier-type reactions of different N-substituted azetidine-2,3-diones **1b**−**d** with propargyl bromide (Table 2).

Our next aim was to find a carbonyl propargylation/allenylation method that proceeds in a highly regioselective fashion by the use of 3-substituted prop-2-ynyl bromides through choice of reaction conditions. Metal-promoted reactions of azetidine-2,3-diones **1** with propargyl bromides bearing an aliphatic or an aromatic substituent at the terminal position, afforded the α-allenic alcohols **8** as essentially regio- and diastereoisomerically pure products. This observation is in sharp contrast to the metal-mediated reaction of propargyl bromide itself. The results are summarized in Table 3.

The different behavior of the organometallic reagents derived from various metals and differently substituted propargyl bromides in a variety of solvents may be due to structural differences in the organometallic species involved in the reaction. It may be reasonable to postulate a metallotropic rearrangement between the propargylmetal and allenylmetal species. Both intermediates from this equilibrium are able to react with the azetidine-2,3-diones **1**, leading to the α-allenic or homopropargylic alcohols. The formation of alcohols **7** and **8** is consistent with participation of the six-membered, cyclic transition

(25) (a) Marshall, J. A.; Maxson, K. *J. Org. Chem.* **2000**, *65*, 630. (b) Marshall, J. A.; Yanik, M. M. *J. Org. Chem.* **1999**, *64*, 3798. (c) Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 696. (d) Marshall, J. A.; Yu, R. H.; Perkins, J. E. *J. Org. Chem.* **1995**, *60*, 5550.

Table 2. Regio- and Stereoselective Propargylation/Allenylation of Azetidine-2,3-diones 1 in Aqueous Media[a]

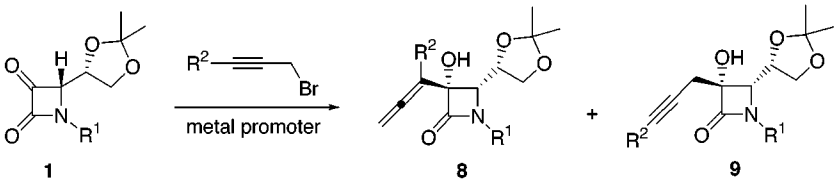


1 6 7

compd	R	metal promoter	system solvent	**6**:**7** ratio[b]	yield[c] (%)
6a/7a	PMP	In	THF/H_2O	58:42	50
6a/7a	PMP	In	THF/NH_4Cl (aq satd)	29:71	67
6a/7a	PMP	Zn	THF/NH_4Cl (aq satd)	0:100	70
6a/7a	PMP	Zn	THF (dry)/NH_4Cl (solid)	0:100	34
6a/7a	PMP	Zn	THF (dry)		
6a/7a	PMP	Zn	MeOH/NH_4Cl (aq satd)	50:50	65
6a/7a	PMP	Sn	THF/NH_4Cl (aq satd)	75:25	65
6a/7a	PMP	$Sn/InCl_3$	THF/NH_4Cl (aq satd)	100:0	33[d]
6a/7a	PMP	$Sn/HfCl_4$	THF/NH_4Cl (aq satd)	100:0	79[d]
6b/7b	2-propenyl	Zn	THF/NH_4Cl (aq satd)	0:100	53
6c/7c	2-propynyl	Zn	THF/NH_4Cl (aq satd)	0:100	56
6d/7d	4-pentynyl	Zn	THF/NH_4Cl (aq satd)	0:100	58

[a] All reactions were carried out on 1 mmol scale. PMP = 4-$MeOC_6H_4$. [b] The ratio was determined by integration of well-resolved signals in the ^1H NMR spectra of the crude reaction mixtures before purification. [c] Yield of pure, isolated product with correct analytical and spectral data. [d] Some acetonide cleavage in the homoallenyl alcohol was detected.

Table 3. Regio- and Stereoselective Allenylation of Azetidine-2,3-diones 1 in Aqueous Media[a]



1 8 9

compd	R^1	R^2	metal promoter	system solvent	**8**:**9** ratio[b]	yield[c] (%)
8a/9a	PMP	Me	Zn	THF/NH_4Cl (aq satd)	100:0	59
8a/9a	PMP	Me	In	THF/NH_4Cl (aq satd)	100:0	74
8a/9a	PMP	Me	Sn	THF/NH_4Cl (aq satd)	100:0	16
8b/9b	2-propenyl	Me	In	THF/NH_4Cl (aq satd)	100:0	63
8c/9c	PMP	Ph	Zn	THF/NH_4Cl (aq satd)	80:20	71
8c/9c	PMP	Ph	Zn	THF/H_2O	100:0	16
8c/9c	PMP	Ph	In	THF/NH_4Cl (aq satd)	100:0	76
8c/9c	PMP	Ph	In	THF/H_2O	100:0	75
8c/9c	PMP	Ph	Sn	THF/NH_4Cl (aq satd)	100:0	75
8c/9c	PMP	Ph	Sn	THF/H_2O		*d*
8d/9d	2-propenyl	Ph	In	THF/NH_4Cl (aq satd)	100:0	62
8e/9e	2-propynyl	Ph	In	THF/NH_4Cl (aq satd)	100:0	48

[a] All reactions were carried out on 1 mmol scale. PMP = 4-$MeOC_6H_4$. [b] The ratio was determined by integration of well-resolved signals in the ^1H NMR spectra of the crude reaction mixtures before purification. [c] Yield of pure, isolated product with correct analytical and spectral data. [d] Acetonide cleavage and further internal acetal formation was observed.

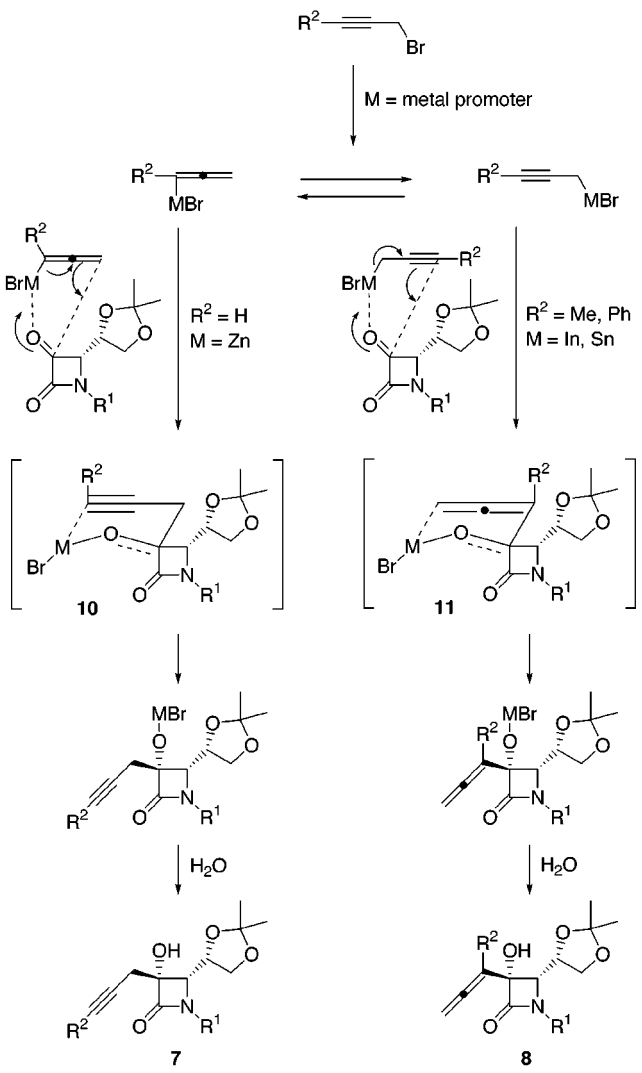
structures **10** and **11**. A plausible mechanism for the propargylation/allenylation process is illustrated in Scheme 4.

It seems reasonable to propose that the different regiochemical preference observed on the metal-promoted reactions of propargyl bromide and substituted propargyl bromides with azetidine-2,3-diones must be controlled by steric effects.[26] Probably, the isomerization of propargylmetal to allenylmetal is restricted by the steric effect of a substituent ($R^2 = CH_3$ or C_6H_5) in the bromopropyne. Thus, allenyl alcohols **8** are produced almost exclusively. Isomerization of the initially formed propargylmetal species to the corresponding allenyl organometallic can be induced by the absence of substituent ($R^2 = H$) at the propargyl bromide. Then, the allenylmetal undergoes nucleophilic addition to afford homopropargylic alcohols **7** selectively. The different regioselectivities observed in various system solvents, should be attributed perhaps to the extent of coordination of the solvent molecules to the reactive organometallic species, stabilizing one of the intermediates involved in the metallotropic equilibrium rather than the other.

Configurational Assignment. The stereochemistry at the C3-heterosubstituted quaternary center for compounds **5**−**8** was assigned by qualitative homonuclear NOE difference spectra. Thus, an anti-relative disposition between the hydroxy group and H4 was established for compound (+)-**4a** by the absence of NOE enhancement in the hydroxylic hydrogen signal when H4 was irradiated. Furthermore, NOE irradiation of the methylenic hydrogens on compound (+)-**4a** resulted in 6% enhancement on the signal corresponding to H4, which is in agreement with the proposed stereochemistry. Com-

(26) For selective formation of propargylmetals and allenylmetals mediated by steric effects, see: (a) Masuyama, Y.; Watabe, A.; Ito, A.; Kurusu, Y. *Chem. Commun.* **2000**, 2009. (b) Kobayashi, S.; Nishio K. *J. Am. Chem. Soc.* **1995**, *117*, 6392. (c) Zhang, L.-J.; Huang, Y.-Z.; Huang, Z.-H. *Tetrahedron Lett.* **1991**, *32*, 6579.

Scheme 4



pounds (+)-**6a** and (+)-**8a** are α-allenic alcohols. A NOE enhancement of 3% on H4 upon irradiation of the allenic proton for compound (+)-**6a** showed a syn stereochemistry for these moieties. Absence of NOE enhancement was observed on the hydroxylic hydrogen when H4 was irradiated. Furthermore, NOE irradiation of the methyl group on compound (+)-**8a** resulted in 2% enhancement of the signal corresponding to H4, which is consistent with the proposed stereochemistry. The syn H4-propargyl moiety stereochemistry for the homopropargylic alcohol (+)-**7a** was obvious on the basis of 8% NOE enhancement in H4 upon irradiation of the methylenic hydrogens. Similar figures were observed when NOE experiments were carried out in related β-lactams **5**−**8**, being the stereochemistry immediately deduced by comparison with the above results (Figure).

The stereoselectivity in the addition reaction of these stabilized organometallic reagents with azetidine-2,3-diones **1** is believed to be controlled by the bulky chiral auxiliary at C-4, in which one face of the carbonyl group is blocked preferentially, thus the propenyl-, propynyl-, and allenylmetal species being delivered to the less hindered face.

Conclusions

The present study provides the first insight into the regio- and stereoselective manner in which enantiopure

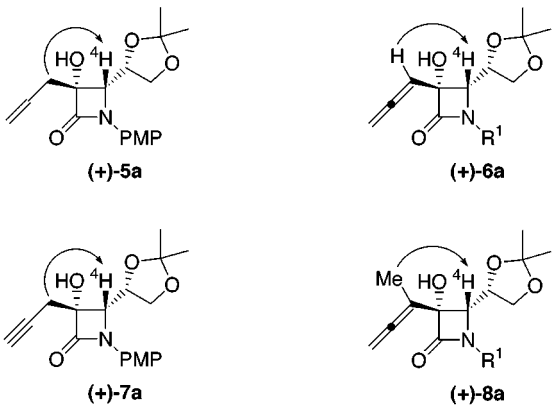


Figure 1. Selected NOE effects and stereochemistry of some 3-substituted 3-hydroxy-β-lactams **5**−**8**.

azetidine-2,3-diones undergo coupling with a variety of propenyl-, propynyl-, and allenylmetal reagents in both anhydrous and aqueous environments. The method of choice to mediate the allylation, propargylation or allenylation should be in the most of the cases one involving aqueous media because of its enviromentally benign properties and atom economy, allied with a high degree of chemo-, regio-, and diastereoselectivity. In view of the simplicity of the present processes for the synthesis of 3-substituted 3-hydroxy-β-lactams, that should be useful in the elaboration of potentially bioactive compounds, these reactions are likely to find considerable applications.

Experimental Section

General Methods. General experimental data and procedures have been previously reported.[16a] NMR spectra were recorded in $CDCl_3$ solutions, except otherwise stated. Chemical shifts are given in ppm relative to TMS (^1H, 0.0 ppm) or $CDCl_3$ (^{13}C, 76.9 ppm). Specific rotation $[\alpha]_D$ is given in deg per dm at 20 °C, and the concentration (*c*) is expressed in g per 100 mL. All commercially available compounds were used without further purification. The following chemicals were prepared according to literature procedures: 3-butenamine,[27] 2,3-*O*-(isopropylidene)-D-glyceraldehyde.[28] 4-Pentynamine was prepared following the procedure of Taylor for 3-butynamine.[29] 2-Azetidinones (+)-**2a** and (+)-**3a** were prepared according to our previously reported procedures.[16d]

Tin(IV) Chloride Promoted Reactions between Allyltrimethylsilane and Azetidine-2,3-diones 1. General Procedure for the Synthesis of Homoallylic Alcohols 4. A solution of the corresponding α-keto lactam (1.0 mmol) in dichloromethane (3.5 mL) was added dropwise to a stirred solution of tin(IV) chloride (1.0 mmol) in dichloromethane (5 mL) at −78 °C. After 5 min, allyltrimethylsilane (1.5 mmol) was added, and the mixture was stirred for 1 h at −78 °C. Saturated aqueous sodium hydrogen carbonate (10 mL) was added, and the mixture was allowed to warm to room temperature before being partitioned between dichloromethane and water. The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for some representative pure forms of **1** follow.[30]

(27) Sato, T.; Nakamura, N.; Ikeda, K.; Okada, M.; Ishibashi, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2399.
(28) Schmid, C.; Bryant, J. D.; Dowlatzedah, M.; Phillips, J.; Prather, D. E.; Schantz, R. D.; Sear, N. L.; Vianco, C. S. *J. Org. Chem.* **1991**, *56*, 4056.
(29) Taylor, E. C.; Macor, J. E.; Pont, J. L. *Tetrahedron*, **1987**, *21*, 5145.

(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolanyl-4-yl]-3-hydroxy-1-(*p*-methoxyphenyl)-3-(2-propenyl)-2-azetidinone, (+)-4a. From 100 mg (0.342 mmol) of azetidine-2,3-dione (+)-**1a** was obtained 86 mg (75%) of compound (+)-**4a** as a colorless oil. $[\alpha]_D = +53.4$ (*c* 1.0, $CHCl_3$). ^1H NMR: δ 1.35 and 1.48 (s, each 3H), 2.58 (dd, 1H, $J = 14.0$, 7.6 Hz), 2.69 (dd, 1H, $J = 14.0$, 7.0 Hz), 3.79 (s, 3H), 3.80 (dd, 1H, $J = 9.0$, 6.8 Hz), 4.02 (d, 1H, $J = 7.6$ Hz), 4.29 (dd, 1H, $J = 9.0$, 6.7 Hz), 4.46 (q, 1H, $J = 7.0$ Hz), 4.59 (brs, 1H), 5.25 (m, 2H), 5.89 (m, 1H), 6.85 and 7.58 (d, each 2H, $J = 9.0$ Hz). ^{13}C NMR: δ 168.4, 156.6, 131.0, 130.6, 120.2, 119.9, 113.9, 109.5, 83.1, 76.6, 66.7, 65.9, 55.3, 40.1, 26.4, 24.9. IR ($CHCl_3$, cm^{-1}): ν 3332, 1748. MS (CI), *m*/*z*: 334 ($M^+ + 1$, 100), 333 (M^+, 25). Anal. Calcd for $C_{18}H_{23}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.96; H, 5.83; N, 4.85.

(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolanyl-4-yl]-3-hydroxy-3-(2-propenyl)-1-(2-propynyl)-2-azetidinone, (−)-4c. From 110 mg (0.492 mmol) of azetidine-2,3-dione (−)-**1d** was obtained 84 mg (64%) of compound (−)-**4c** as a colorless oil. $[\alpha]_D = -33.6$ (*c* 0.7, $CHCl_3$). ^1H NMR: δ 1.35 and 1.46 (s, each 3H), 2.26 (t, 1H, $J = 2.4$ Hz), 2.49 (dd, 1H, $J = 14.1$, 7.6 Hz), 2.51 (dd, 1H, $J = 14.0$, 7.0 Hz), 3.68 (d, 1H, $J = 5.4$ Hz), 3.84 (dd, 1H, $J = 17.6$, 2.4 Hz), 3.89 (dd, 1H, $J = 9.0$, 4.6 Hz), 3.96 (s, 1H), 4.17 (dd, 1H, $J = 9.0$, 6.8 Hz), 4.37 (m, 1H), 4.44 (dd, 1H, $J = 17.6$, 2.7 Hz), 5.24 (m, 2H), 5.89 (m, 1H). ^{13}C NMR: δ 170.3, 131.3, 120.0, 110.1, 84.5, 76.6, 75.4, 72.6, 66.5, 63.8, 39.2, 30.4, 26.5, 24.9. IR ($CHCl_3$, cm^{-1}): ν 3329, 1744. MS (CI), *m*/*z*: 266 ($M^+ + 1$, 100), 265 (M^+, 13). Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.46; H, 7.26; N, 5.25.

Tin(IV) Chloride Promoted Reaction between Allyltributyltin and Azetidine-2,3-dione (+)-1a. A cooled solution of tin(IV) chloride (313 mg, 1.2 mmol) in dichloromethane (1.2 mL) was added dropwise to a stirred solution of allyltributyltin (397 mg, 1.2 mmol) in dichloromethane (4.5 mL) at −78 °C. After 5 min, a solution of the α-keto-*β*-lactam (+)-**1a** (291 mg, 1.0 mmol) in dichloromethane (1 mL) was added dropwise, and the mixture was stirred for 1 h at −78 °C. Saturated aqueous sodium hydrogen carbonate (10 mL) was added, and the mixture was allowed to warm to room temperature before being partitioned between dichloromethane and water. The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes (1:1 containing 1% of triethylamine) as an eluent gave 233 mg (70%) of compound (+)-**4a**. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.94; H, 5.92; N, 4.84.

Boron Trifluoride Diethyl Etherate Promoted Reaction between Allyltributyltin and Azetidine-2,3-dione (+)-1a. A solution of the α-keto-*β*-lactam (+)-**1a** (291 mg, 1.0 mmol) in dichloromethane (1 mL) was added dropwise to a stirred solution of boron trifluoride diethyl etherate (213 mg, 1.5 mmol) in dichloromethane (4 mL) at −78 °C. After 5 min, allyltributyltin (397 mg, 1.2 mmol) was added, and the mixture was stirred for 1 h at −78 °C. Saturated aqueous sodium hydrogen carbonate (10 mL) was added, and the mixture was allowed to warm to room temperature before being partitioned between dichloromethane and water. The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes (1:1 containing 1% of triethylamine) as an eluent gave 183 mg (55%) of compound (+)-**4a**. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.78; H, 5.84; N, 4.79.

Magnesium/Bismuth(III) Chloride Promoted Reaction between Allyl Bromide and Azetidine-2,3-dione (+)-1a. Allyl bromide (187 mg, 1.54 mmol) was added to a well-stirred suspension of bismuth(III) chloride (501 mg, 1.59 mmol) and metallic magnesium (57 mg, 2.36 mmol) in THF/water (4:1, 4 mL) at room temperature. After 20 min, a solution of the α-keto lactam (+)-**1a** (291 mg, 1.0 mmol) in tetrahydrofuran (1 mL) was added dropwise, and the mixture was stirred for 18 h at room temperature. Hydrochloric acid (1 M, 10 mL) was added at 0 °C, and the mixture was allowed to warm to room temperature, before being extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes (1:1) as an eluent gave 240 mg (72%) of compound (+)-**4a**. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.93; H, 5.91; N, 4.84.

Indium Promoted Reaction between Allyl Bromide and Azetidine-2,3-dione (+)-1a. Allyl bromide (242 mg, 2.0 mmol) was added to a well-stirred suspension of the α-keto lactam (+)-**1a** (291 mg, 1.0 mmol) and indium powder (229 mg, 1.99 mmol) in THF/H_2O (1:1, 5 mL) at room temperature. After 18 h, saturated aqueous sodium hydrogen carbonate (10 mL) was added at 0 °C, and the mixture was allowed to warm to room temperature before being extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes (1:1) as an eluent gave 243 mg (73%) of compound (+)-**4a**. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.92; H, 5.84; N, 4.84.

Indium-Promoted Reaction between Allyl Bromide and Azetidine-2,3-diones 1 in an Aqueous Medium Containing NH_4Cl. General Procedure for the Synthesis of Homoallylic Alcohols 4. Allyl bromide (363 mg, 3.0 mmol) was added to a well-stirred suspension of the corresponding α-keto lactam (1.0 mmol) and indium powder (688 mg, 6.0 mmol) in THF/NH_4Cl (aq satd) (1:5, 5 mL) at 0 °C. After disappearance of the starting material (TLC), the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for some representative pure forms of **4** follow.

From 100 mg (0.342 mmol) of azetidine-2,3-dione (+)-**1a**, 83 mg (73%) of compound (+)-**4a**. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.77; H, 5.91; N, 4.84.

(3*R*,4*S*)-1-(3-Butenyl)-4-[(*S*)-2,2-dimethyl-1,3-dioxolanyl-4-yl]-3-hydroxy-3-(2-propenyl)-2-azetidinone, (−)-4g. From 70 mg (0.293 mmol) of azetidine-2,3-dione (−)-**1c**, 82 mg (100%) of compound (−)-**4g** was obtained as a colorless oil. $[\alpha]_D = -8.1$ (*c* 0.7, $CHCl_3$). ^1H NMR: δ 1.34 and 1.43 (s, each 3H), 2.34 (m, 2H), 2.53 (td, 2H, $J = 14.9$, 7.6 Hz), 3.23 (dt, 1H, $J = 13.7$, 6.3 Hz), 3.45 (d, 1H, $J = 8.3$ Hz), 3.52 (dt, 1H, $J = 13.7$, 6.3 Hz), 4.17 (dd, 1H, $J = 8.5$, 6.6 Hz), 4.31 (m, 1H), 5.13 (m, 4H), 5.80 (m, 2H). ^{13}C NMR: δ 171.2, 135.1, 131.7, 119.6, 117.0, 109.4, 83.4, 76.7, 66.7, 65.0, 40.1, 31.7, 26.7, 25.0. IR ($CHCl_3$, cm^{-1}): ν 3334, 1743. MS (CI), *m*/*z*: 282 ($M^+ + 1$, 100), 281 (M^+, 14). Anal. Calcd for $C_{15}H_{23}NO_4$: C, 64.03; H, 8.24; N, 4.98. Found: C, 64.10; H, 8.21; N, 4.95.

Zinc-Promoted Reaction between Allyl Bromide and Azetidine-2,3-dione (+)-1a. Allyl bromide (242 mg, 2.0 mmol) was added to a well-stirred suspension of the α-keto lactam (+)-**1a** (291 mg, 1.0 mmol) and zinc powder (229 mg, 1.99 mmol) in THF/H_2O (1:1, 5 mL) at room temperature. After 18 h, saturated aqueous sodium hydrogen carbonate (10 mL) was added at 0 °C, and the mixture was allowed to warm to room temperature, before being extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes (1:1) as an eluent gave 240 mg (72%) of compound (+)-**4a**. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.77; H, 5.91; N, 4.83.

Zinc-Promoted Reaction between Allyl Bromide and Azetidine-2,3-dione (+)-1a in an Aqueous Medium Containing NH_4Cl. Allyl bromide (363 mg, 3.0 mmol) was added to a well-stirred suspension of the α-keto lactam (+)-**1a** (291 mg, 1.0 mmol) and zinc powder (392 mg, 6.0 mmol) in THF/NH_4Cl (aq satd) (1:5, 5 mL) at 0 °C. After 3 h at 0 °C, the mixture was allowed to warm to room temperature before

(30) Experimental procedures as well as full spectroscopic and analytical data for compounds not included in this Experimental Section are described in the Supporting Information.

being extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes (1:1) as an eluent gave 240 mg (72%) of compound (+)-**4a**. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.93; H, 5.84; N, 4.78.

Indium/Indium Trichloride Promoted Reaction between Allyl Bromide and Azetidine-2,3-dione (+)-1a. Allyl bromide (242 mg, 2.0 mmol) was added to a well-stirred suspension of the α-keto lactam (+)-**1a** (291 mg, 1.0 mmol), indium powder (229 mg, 1.99 mmol), and indium trichloride (442 mg, 2.0 mmol) in THF/H_2O (1:1, 5 mL) at room temperature. After 2 h, saturated aqueous sodium hydrogen carbonate (10 mL) was added at 0 °C, and the mixture was allowed to warm to room temperature before being extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes (1:1) as an eluent gave 243 mg (73%) of compound (+)-**4a**. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.93; H, 5.91; N, 4.78.

Indium/Hafnium(IV) Chloride Promoted Reaction between Allyl Bromide and Azetidine-2,3-dione (+)-1a. Allyl bromide (242 mg, 2.0 mmol) was added to a well-stirred suspension of the α-keto lactam (+)-**1a** (291 mg, 1.0 mmol), indium powder (229 mg, 1.99 mmol), and hafnium(IV) chloride (442 mg, 2.0 mmol) in THF/H_2O (1:1, 5 mL) at room temperature. After 1.5 h, saturated aqueous sodium hydrogen carbonate (10 mL) was added at 0 °C, and the mixture was allowed to warm to room temperature before being extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes (1:1) as an eluent gave 243 mg (73%) of compound (+)-**4a**. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.93; H, 5.91; N, 4.78.

Tin(IV) Chloride Promoted Reactions between Propargyltrimethylsilane and Azetidine-2,3-diones 1. General Procedure for the Synthesis of α-Allenic Alcohols 6. A solution of the corresponding α-keto lactam (1.0 mmol) in dichloromethane (3.5 mL) was added dropwise to a stirred solution of tin(IV) chloride (1.5 mmol) in dichloromethane (5 mL) at −78 °C. After 5 min, propargyltrimethylsilane (225 mg, 2 mmol) was added, and the mixture was stirred for 3 h at −78 °C. Saturated aqueous sodium hydrogen carbonate (10 mL) was added, and the mixture was allowed to warm to room temperature before being partitioned between dichloromethane and water. The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for some representative pure forms of **6** follow.

(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolanyl-4-yl]-3-hydroxy-1-(*p*-methoxyphenyl)-3-(1,2-propadienyl)-2-azetidinone, (+)-6a. From 47 mg (0.161 mmol) of azetidine-2,3-dione (+)-**1a** was obtained 23 mg (44%) of compound (+)-**6a** as a colorless oil: $[\alpha]_D = +47.9$ (*c* 0.6, $CHCl_3$). ^1H NMR: δ 1.36 and 1.51 (s, each 3H), 3.80 (s, 3H), 3.82 (dd, 1H, *J* = 9.1, 6.4 Hz), 4.21 (d, 1H, *J* = 7.4 Hz), 4.32 (dd, 1H, *J* = 9.1, 6.7 Hz), 4.51 (q, 1H, *J* = 6.7 Hz), 5.11 (d, 2H, *J* = 6.7 Hz), 5.53 (t, 1H, *J* = 6.7 Hz), 6.87 and 7.63 (d, each 2H, *J* = 9.0 Hz). ^{13}C NMR: δ 207.2, 166.7, 156.7, 130.8, 120.0, 114.0, 109.8, 90.9, 81.5, 80.7, 76.5, 67.4, 66.8, 55.5, 26.5, 25.0. IR ($CHCl_3$, cm^{-1}): ν 3330, 2990, 1939, 1746. MS (CI), *m*/*z*: 332 ($M^+ + 1$, 100), 331 (M^+, 19). Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.32; H, 6.35; N, 4.20.

Zinc-Promoted Reaction between Propargyl Bromide and Azetidine-2,3-diones 1. General Procedure for the Synthesis of Homopropargylic Alcohols 7. Propargyl bromide (3.0 mmol) was added to a well-stirred suspension of the corresponding α-keto lactam (1.0 mmol) and zinc dust (6.0 mmol) in THF/NH_4Cl (aq satd) (1:5, 5 mL) at 0 °C. After disappearance of the starting material (TLC), the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for some representative pure forms of **7** follow.

(+)-(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-hydroxy-1-(*p*-methoxyphenyl)-3-(2-propynyl)-2-azetidinone, (+)-7a. From 43 mg (0.148 mmol) of azetidine-2,3-dione (+)-**1a** was obtained 34 mg (70%) of compound (+)-**7a** as a colorless oil. $[\alpha]_D = +57.4$ (*c* 1.0, $CHCl_3$). ^1H NMR: δ 1.37 and 1.48 (s, each 3H), 2.09 (t, 1H, *J* = 2.4 Hz), 2.80 (t, 2H, *J* = 2.4 Hz), 3.80 (s, 3H), 3.94 (dd, 1H, *J* = 9.3, 6.8 Hz), 4.26 (d, 1H, *J* = 6.8 Hz), 4.28 (dd, 1H, *J* = 8.8, 6.8 Hz), 4.47 (m, 2H), 6.87 and 7.56 (d, 2H, *J* = 9.0 Hz). ^{13}C NMR: δ 166.9, 156.9, 130.3, 120.2, 114.1, 109.9, 82.7, 76.3, 72.1, 72.0, 66.7, 65.7, 55.4, 26.4, 25.7, 25.2. IR ($CHCl_3$, cm^{-1}): ν 3346, 1744. MS (CI), *m*/*z*: 332 ($M^+ + 1$, 100), 331 (M^+, 32). Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.32; H, 6.31; N, 4.19.

(−)-(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-hydroxy-1-(2-propenyl)-3-(2-propynyl)-2-azetidinone, (−)-7b. From 64 mg (0.284 mmol) of azetidine-2,3-dione (−)-**1b** was obtained 40 mg (53%) of compound (−)-**7b** as a colorless oil. $[\alpha]_D = -49.5$ (*c* 1.5, $CHCl_3$). ^1H NMR: δ 1.35 and 1.45 (s, each 3H), 2.09 (t, 1H, *J* = 2.7 Hz), 2.69 (dd, 2H, *J* = 2.7, 1.5 Hz), 3.69 (d, 1H, *J* = 16.1 Hz), 3.75 (d, 1H, *J* = 6.8 Hz), 3.87 (dd, 2H, *J* = 9.0, 5.0 Hz), 4.19 (dd, 1H, *J* = 9.0, 7.0 Hz), 4.24 (ddt, 1H, *J* = 15.1, 4.9, 1.5 Hz), 4.37 (ddd, 2H, *J* = 11.7, 6.6, 4.9 Hz), 4.79 (s, 1H), 5.26 (m, 2H), 5.78 (m, 1H). ^{13}C NMR: δ 169.4, 131.4, 119.1, 109.9, 83.1, 78.1, 75.8, 71.6, 66.6, 64.5, 43.8, 26.6, 25.3, 24.9. IR ($CHCl_3$, cm^{-1}): ν 3343, 1745. MS (CI), *m*/*z*: 266 ($M^+ + 1$, 100), 265 (M^+, 22). Anal. Calcd for $C_{14}H_{19}NO_4$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.32; H, 6.31; N, 4.19.

Zinc-Promoted Reaction between Propargyl Bromide and Azetidine-2,3-dione (+)-1a in an Anhydrous Medium. Propargyl bromide (57 mg, 0.48 mmol, 54 μL of a 80% solution in toluene) was added to a well-stirred suspension of the α-keto lactam (+)-**1a** (92 mg, 0.32 mmol), zinc dust (24.8 mg, 0.38 mmol), and ammonium chloride (20.6 mg, 0.38 mmol) in dry THF (3 mL) at room temperature. After 1.5 h, saturated aqueous ammonium chloride (3 mL) was added at 0 °C, and the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using dichloromethane/ethyl acetate (9:1) as an eluent gave 36 mg (34%) of compound (+)-**7a**. Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.16; H, 6.33; N, 4.25.

Tin/Hafnium(IV) Chloride Promoted Reaction between Propargyl Bromide and Azetidine-2,3-dione (+)-1a. Propargyl bromide (64 mg, 0.538 mmol, 60 μL of a 80% solution in toluene) was added to a well-stirred suspension of the α-keto lactam (+)-**1a** (52 mg, 0.179 mmol), tin powder (43 mg, 0.358 mmol), and hafnium(IV) chloride (57 mg, 0.179 mmol) in THF/NH_4Cl (aq satd) (1:5, 2.0 mL) at 0 °C. After 2 h at room temperature, the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes (1:3) as an eluent gave 47 mg (79%) of compound (+)-**6a**. Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.30; H, 6.41; N, 4.21.

Indium-Promoted Reaction between 1-Bromo-2-butyne and Azetidine-2,3-diones 1. General Procedure for the Synthesis of α-Allenic Alcohols (+)-8a and (−)-8b. 1-Bromo-2-butyne (3.0 mmol) was added to a well-stirred suspension of the corresponding α-keto lactam (1.0 mmol) and indium powder (6.0 mmol) in THF/NH_4Cl (aq satd) (1:5, 5 mL) at 0 °C. After disappearance of the starting material (TLC), the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for some representative pure forms of **8** follow.

(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolanyl-4-yl]-3-hydroxy-1-(*p*-methoxyphenyl)-3-(1-methyl-1,2-propadienyl)-2-azetidinone, (+)-8a. From 50.5 mg (0.173 mmol) of azetidine-2,3-dione (+)-**1a** was obtained 44 mg (74%) of compound (+)-**8a** as a colorless oil. $[\alpha]_D = +75.4$ (*c* 0.7, $CHCl_3$). ^{1}H NMR: δ 1.36 and 1.51 (s, each 3H), 1.85 (t, 3H, $J = 3.0$ Hz), 3.79 (s, 3H), 3.80 (dd, 1H, $J = 8.8$, 6.4 Hz), 4.14 (brs, 1H), 4.24 (d, 1H, $J = 7.7$ Hz), 4.32 (dd, 1H, $J = 8.8$, 6.8 Hz), 4.49 (q, 1H, $J = 7.0$ Hz), 4.98 (dd, 2H, $J = 6.4$, 3.0 Hz), 6.86 and 7.63 (dd, each 2H, $J = 7.0$, 2.5 Hz). ^{13}C NMR: δ 205.2, 166.6, 156.7, 130.7, 120.0, 114.0, 109.7, 98.6, 83.5, 79.4, 76.8, 66.8, 66.5, 55.4, 26.6, 25.0, 13.9. IR ($CHCl_3$, cm^{-1}): ν 3340, 2991, 1940, 1742. MS (CI), *m*/*z*: 346 ($M^+ + 1$, 100), 345 (M^+, 20). Anal. Calcd for $C_{19}H_{23}NO_5$: C, 66.07; H, 6.71; N, 4.06. Found: C, 66.13; H, 6.65; N, 4.00.

(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolanyl-4-yl]-3-hydroxy-3-(1-methyl-1,2-propadienyl)-1-(2-propenyl)-2-azetidinone, (−)-8b. From 61 mg (0.271 mmol) of azetidine-2,3-dione (−)-**1b** was obtained 47 mg (63%) of compound (−)-**8b** as a colorless oil. $[\alpha]_D = -53.4$ (*c* 0.7, $CHCl_3$). ^{1}H NMR: δ 1.34 and 1.42 (s, each 3H), 1.81 (t, 3H, $J = 3.2$ Hz), 3.71 (m, 3H), 4.18 (dd, 1H, $J = 8.8$, 6.8 Hz), 4.20 (ddt, 1H, $J = 15.4$, 4.9, 1.6 Hz), 4.38 (m, 1H), 4.48 (brs, 1H), 4.91 (dd, 2H, $J = 6.1$, 3.1 Hz), 5.23 (m, 2H), 5.76 (m, 1H). ^{13}C NMR: δ 205.1, 169.2, 131.4, 118.6, 109.7, 98.5, 84.2, 78.7, 76.4, 66.7, 64.9, 43.5, 26.7, 25.0, 13.9. IR ($CHCl_3$, cm^{-1}): ν 3336, 2990, 1940, 1744. MS (CI), *m*/*z*: 280 ($M^+ + 1$, 100), 279 (M^+, 17). Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.58; H, 7.55; N, 5.03.

Indium-Promoted Reaction between 1-Bromo-3-phenyl-2-propyne and Azetidine-2,3-diones 1 in an Aqueous Medium Containing NH_4Cl. General Procedure for the Synthesis of α-Allenic Alcohols 8c−e. 1-Bromo-3-phenyl-2-propyne (3.0 mmol) was added to a well-stirred suspension of the corresponding α-keto lactam (1.0 mmol) and indium powder (6.0 mmol) in THF/NH_4Cl (aq satd) (1:5, 5 mL) at 0 °C. After disappearance of the starting material (TLC), the mixture was extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes mixtures gave analytically pure compounds. Spectroscopic and analytical data for some representative pure forms of **8** follow.

(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolanyl-4-yl]-3-hydroxy-1-(*p*-methoxyphenyl)-3-(1-phenyl-1,2-propadienyl)-2-azetidinone, (+)-8c. From 50 mg (0.170 mmol) of azetidine-2,3-dione (+)-**1a** was obtained 53 mg (76%) of compound (+)-**8c** as a colorless oil. $[\alpha]_D = +48.2$ (*c* 0.9, $CHCl_3$). ^{1}H NMR: δ 1.36 and 1.46 (s, each 3H), 3.77 (dd, 1H, $J = 8.8$, 6.8 Hz), 3.79 (s, 3H), 4.00 (brs, 1H), 4.28 (dd, 1H, $J = 8.8$, 6.8 Hz), 4.37 (d, 1H, $J = 6.8$ Hz), 4.55 (q, 1H, $J = 6.8$ Hz), 5.29 (s, 2H), 6.84 and 7.57 (dd, each 2H, $J = 7.0$, 2.5 Hz), 7.28 (m, 1H), 7.35 and 7.64 (m, each 2H). ^{13}C NMR: δ 207.6, 166.1, 156.7, 132.5, 130.7, 128.6, 128.4, 127.8, 120.1, 113.9, 109.8, 105.9, 84.2, 80.9, 76.5, 66.7, 66.3, 55.4, 26.4, 25.2. IR ($CHCl_3$, cm^{-1}): ν 3332, 2988, 1938, 1746. MS (CI), *m*/*z*: 408 ($M^+ + 1$, 100), 407 (M^+, 15). Anal. Calcd for $C_{24}H_{25}NO_5$: C, 70.75; H, 6.18; N, 3.44. Found: C, 70.83; H, 6.16; N, 3.43.

Tin-Promoted Reaction between 1-Bromo-3-phenyl-2-propyne and Azetidine-2,3-dione (+)-1a. 1-Bromo-3-phenyl-2-butyne (99.5 mg, 0.51 mmol) was added to a well-stirred solution of the azetidine-2,3-dione (+)-**1a** (49.7 mg, 0.17 mmol) and tin powder (121.1 mg, 1.02 mmol) in THF/NH_4Cl (aq satd) (1:7, 2.25 mL) at 0 °C. The mixture was allowed to warm to room temperature and was stirred at room temperature for 30 h, before being extracted with ethyl acetate (3 × 5 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes (1:3 containing 1% of triethylamine) as an eluent gave 52 mg (75%) of isomerically pure compound (+)-**8c**. Anal. Calcd for $C_{24}H_{25}NO_5$: C, 70.75; H, 6.18; N, 3.44. Found: C, 70.67; H, 6.15; N, 3.42.

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Supporting Information Available: Spectroscopic and analytical data for compounds **1a**−**e**, **2b**−**e**, **3b**−**e**, (−)-**4b**, (−)-**4g**, (+)-**5**, (−)-**6b**, (−)-**7c**, (+)-**7d**, (−)-**8d**, and (−)-**8e**; as well as general experimental procedures for compounds **1a**−**e**, **2b**−**e**, **3a**−**e**, **4a**−**g**, (+)-**5**, (+)-**6a**, (+)-**7a**, (+)-**8a**, and (+)-**8c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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