Stereoselective Synthesis of 3-Substituted 4-(Formyloxy)-2-azetidinones by the Unusual Baeyer−Villiger Reaction of β-Lactam Aldehydes. Scope and Synthetic Applications

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Received September 4, 1996[⊗]

The Baeyer−Villiger oxidation of 4-formyl-β-lactams **1** with *m*-CPBA gave 4-(formyloxy) β-lactams **2** in a simple, efficient, and totally stereoselective process. This reaction is one of the scarce examples of the preferred migration of a carbon moiety in an aliphatic aldehyde. The influence of the substituents at N1 and C3 of the four-membered ring in the Baeyer−Villiger rearrangement has been studied. Thus, alkyl, alkenyl, aryl, and alkyloxy 3-substituted-1-(*p*-anisyl)-2-azetidinones **1** form exclusively 4-(formyloxy) β-lactams **2**. Amide or acetoxy substituents at C3 of the four-membered ring produce mixtures of 4-(formyloxy) β-lactams **2** and 4-carboxy β-lactams **5**. The exclusive formation of carboxy derivatives is observed sometimes for 1-alkyl-substituted-2-azetidinones **1**. 4-(Formyloxy) β-lactams **2** are suitable starting materials to prepare different 4-unsubstituted β-lactams **9** using β-hydroxy amides **8** as isolable intermediates. The overall transformation 4-formyl-2-azetidinone to 4-unsubstituted β-lactam is an easy and convenient stereoselective route to these interesting types of compounds.

Introduction

One of the well established principles in the oxidation of aldehydes with peracids is the formation of carboxylic acids due to the preferential migration of hydrogen over the carbon moiety.[2] Formates, formed by migration of the carbon group, are the alternative reaction products, but this rearrangement seldom occurs. In fact, to the best of our knowledge, electron-rich aromatic[3] and heteroaromatic[4] aldehydes and α-oxygen-substituted aldehydes[5] are the main exceptions to the general rule and are converted to formate esters upon peroxy acid treatment. The bizarre behavior of the 2-azetidinone ring, exemplified by different unique transformations,[6] provides a new example of preferential carbon migration on the Baeyer−Villiger rearrangement of aldehydes. We recently reported[1] that β-lactam aldehydes **1** (Chart 1) exclusively yield 4-(formyloxy) β-lactams **2** after Baeyer−Villiger oxidation. This transformation represents one of the scarce examples of the preferred migration of a carbon group in an aliphatic aldehyde.[3−5]

Chart 1

Total synthesis of mono- and bicyclic β-lactam antibiotics often rests on the modification of monocyclic 2-azetidinones having acyloxy substituents at the C4 of the four-membered ring.[7] Elimination of the ester group promotes the nucleophilic substitution through acyliminium intermediates,[8] and different functionalized nucleophiles are thus attached to the β-lactam ring. Among others, 4-acetoxy-2-azetidinones **3** are recognized as universal key intermediates[7] to obtain biologically active β-lactams. Compounds **3** have been prepared by the classical isocyanate−olefin cycloaddition[9] using chlorosulfonyl isocyanate and different vinyl acetates. However, this approach is often a low yielding, unselective step, incompatible with different functional groups needed for further synthetic steps.[10] Alternative entries to 4-acetoxy-2-azetidinones have been developed, for example, by oxidation of 2-azetidinones lacking substituents at

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[⊗] Abstract published in *Advance ACS Abstracts,* November 15, 1996.

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(2) For recent reviews of Baeyer−Villiger reaction, see: (a) Krow, G. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 7, p 671. (b) Krow, G. R. *Organic Reactions*; Paquette, L. A., Ed.; John Willey and Sons: New York, 1993; Vol. 43, p 251. (c) Krow, G. R. *Tetrahedron* **1981**, *37*, 2697. For recent papers, see: (a) Kaneda, K.; Ueno, S.; Imanaka, T.; Shimotsuma, E.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1994**, *59*, 2915. (b) Chida, N.; Tobe, T.; Ogawa, S. *Tetrahedron Lett.* **1994**, *35*, 7249.

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S0022-3263(96)01268-6 CCC: $12.00

Table 1. Baeyer−Villiger Oxidation of 4-Formyl β-Lactams 1 with *m*-CPBA

entry	substrate[a]	R^1	R^2	R^3 [b]	product(s)	product ratio **2/5**[c]	yield[d,e] (%)
1	**1a**	CH_2=CH	H	PMP	**2a**	100:0	91
2	**1b**	CH_2=C(Me)		PMP	**2b**	100:0	70
3	**1c**	Me_2C=		PMP	**2c**	100:0	90
4	**1d**	Ph	H	PMP	**2d**	100:0	94
5	**1e**	Et	H	PMP	**2e**	100:0	94
6	**1f**	*i*-Pr	H	PMP	**2f**	100:0	72
7	**1g**	H	*i*-Pr	PMP	**2g**	100:0	87
8	**1h**	CH_3	CH_3	PMP	**2h**	100:0	93
9	**1i**	BnO	H	PMP	**2i**	100:0	94
10	(+)-**1i**	BnO	H	PMP	(+)-**2i**	100:0	94
11	**1j**	AcO	H	PMP	**2j/5a**	88:12	80
12	**1k**	Md[f]	H	PMP	**2k/5b**	75:25	73
13	**1l**	Ft[g]	H	PMP	**2l/5c**	65:35	57
14	(+)-**1m**	*S*-Ox[h]	H	PMP	(+)-**2m**/(+)-**5d**	35:65	10
15	**1n**	BnO	H	Bn	**2n/5e**	50:50	45
16	(+)-**1o**	*S*-Ox[h]	H	Bn	(+)-**5f**	0:100	

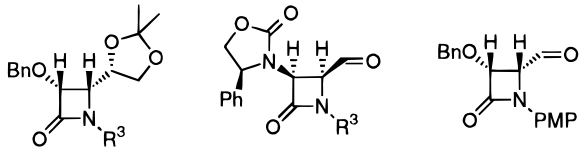
[a] Compounds (+)-**1i**, (+)-**1m**, and (+)-**1o** were used as optically pure materials with the configuration indicated in Chart 2. The remaining compounds **1** were used as racemic mixtures of pure *cis* or *trans* diastereomers. [b] PMP = 4-methoxyphenyl. [c] Determined by integration of well-resolved signals in the ^{1}H NMR spectra of crude reaction mixtures. [d] Yield of pure, isolated compound **2** with correct analytical data. [e] Carboxylic acids **5** are better prepared by oxidation of compounds **1**. See the Experimental Section. [f] Md = Maleimido. [g] Ft = Phthalimido. [h] (*S*)-4-Phenyl-2-oxo-1,3-oxazolidin-3-yl.

C4[11] or oxidative degradation of 4-carboxy,[12] 4-benzoyl,[13] and 4-acetyl β-lactams.[14] In this context, the Baeyer−Villiger oxidation of ketones has been used to prepare 4-acetoxy- and 4-(benzoyloxy)-2-azetidinones from the corresponding 4-acyl derivatives.[13,14] The close structural relationship of the previously unknown formates **2** and 4-(acyloxy)-2-azetidinones **3** makes those compounds attractive building blocks in β-lactam chemistry. This paper reports in full the scope of this rearrangement, the study of the factors modulating its regioselectivity, and the use of formates **2** to prepare 4-unsubstituted β-lactams.

Results and Discussion

Racemic and enantiomerically pure 4-formyl β-lactams **1** were synthetized by using standard methodology (Table 1). Cycloaddition of the corresponding acid chloride to *N*,*N*-bis(*p*-methoxyphenyl)glyoxal diimine gave *cis*-4-formyl β-lactams **1a**−**f** and **1i**−**m**.[15] Lithium ester enolate−*N*,*N*-bis(*p*-methoxyphenyl)glyoxal diimine reaction formed compounds **1g,h**, with compound **1g** having a *trans*-2-azetidinone ring.[16] Both approaches to 4-formyl-2-azetidinones have been reported previously by us. Compound **1n** and optically pure 4-formyl-2-azetidinone **1o** were prepared by reaction of (benzyloxy)acetyl chloride and the acid chloride derived from Evans' oxazolidinone and *N*-benzylcinnamylideneimine[17] followed by ozonolysis. The remaining optically pure *cis*-4-formyl β-lactam (+)-**1i**[18] was obtained from optically pure 2-azetidinone **4** (Chart 2)[19] by sequential hydrolysis of the ketal and HIO_4 oxidative cleavage. The compounds listed on Table 1 cover a wide range of substituents as well as both *cis* and *trans* stereochemistries on the 2-azetidinone ring. Both benzyl and *p*-anisyl moieties, placed at the lactam nitrogen, are among the most versatile groups in β-lactam chemistry.

Chart 2



(+)-4 **(+)-1m:** R^3 = PMP **(+)-1o:** R^3 = Bn **(+)-1i**

4-Formyl β-lactams **1** were submitted to *m*-chloroperbenzoic (*m*-CPBA) acid treatment in CH_2Cl_2 at rt. The results obtained are best understood by considering first those compounds **1** having a *p*-anisyl group on the lactam nitrogen. Compounds **1a**−**i** gave smoothly the corresponding 4-(formyloxy) β-lactams **2a**−**i** in good to excellent yields (Scheme 1 and Table 1, entries 1−10). 4-(Formyloxy) *N*-(*p*-anisyl)-β-lactams **2** having alkyl,

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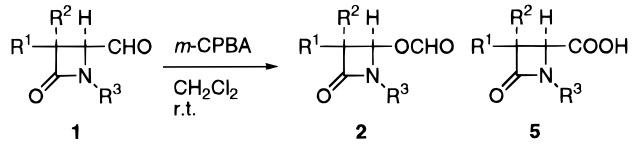
Scheme 1



1 2 5

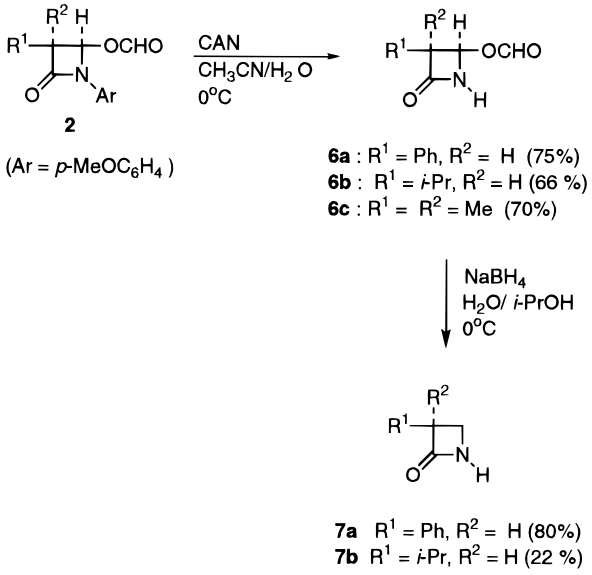
alkenyl, aryl, and alkyloxy substituents on position 3 are formed in excellent yields. The regioisomeric 4-carboxy-2-azetidinones **5** were not formed in any case as established by ^{1}H NMR analysis of the reaction mixtures. The *cis*−*trans* stereochemistry of the starting compound **1** is transferred unaltered to the final products. An attractive feature of this transformation is its high chemoselectivity and the fact that it occurs even in the presence of other oxidizable groups (entries 1−3, Table 1).[20]

The presence of an acyloxy or amide group on C3 of the starting material **1** produces different results. In fact, these compounds yield mixtures of the formates **2** and their regioisomers, 4-carboxy-2-azetidinones **5** (entries 11−14, Table 1). The nature of the substituent determinates the relative ratio of the reaction products, carboxylic acid formation increasing steadly from ester to amide substituents. Interestingly, an oxazolidinone group promoted the migration of hydrogen preferentially over the carbon moiety (entry 14, Table 1). Finally, the influence of the group attached to the lactam nitrogen on the migratory aptitude was studied. 4-Carboxy derivatives **5e,f** were obtained either in equimolar amounts (from **1n**) or exclusively (from **1o**) (entries 15−16, Table 1). Upon comparison of entries 9 and 14 in Table 1 with entries 15 and 16 it is clear that an alkyl group attached to the lactam nitrogen favors the migration of the hydrogen atom. The results obtained in Table 1 may be explained by the preferential migration of the group with higher ability to support a positive charge either by inductive effect or hyperconjugation. Provided that special conformational factors are not present, this fact is well established in the Baeyer−Villiger rearrangement.[2]

To set analogies and differences between 4-(formyloxy)-2-azetidinones **2** and the classical 4-acetoxy β-lactams **3**, some aspects of the chemistry of compounds **2** were studied. Compatibility of the formyloxy substituent with standard manipulations of the group attached at N1 was established by effecting the oxidative cleavage with cerium(IV) ammonium nitrate (CAN)[21] of the *p*-methoxyphenyl group attached to the lactam nitrogen. *N*-Unsubstituted formates **6a**−**c** were obtained in good yields from compounds **2d**, **2f**, and **2h**, respectively. Compounds **6a**, and **6c** underwent also reductive reaction with $NaBH_4$ in aqueous 2-propanol or methanol at 0 °C to give the corresponding C4-unsubstituted *NH*-β-lactams **7a,b**.[22] Thus, standard manipulations can be effected on 4-(formyloxy) β-lactams (Scheme 2).

The following approaches to β-hydroxy amides **8** and different 4-unsubstituted β-lactams **9** illustrate the potential of 4-(formyloxy)-2-azetidinones **2** as intermediates in more elaborate β-lactam systems. β-Hydroxy amides

Scheme 2



2

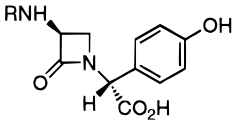
(Ar = *p*-MeOC$_6$H$_4$)

6a : R^1 = Ph, R^2 = H (75%)
6b : R^1 = *i*-Pr, R^2 = H (66 %)
6c : R^1 = R^2 = Me (70%)

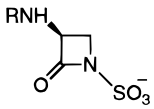
7a R^1 = Ph, R^2 = H (80%)
7b R^1 = *i*-Pr, R^2 = H (22 %)

related to **8** are intermediates in the synthesis of malonamide derivatives as well as useful retroamide isosteres in biologically relevant peptidomimetics.[23] In turn, two important groups of monocyclic β-lactam antibiotics, nocardicins **10**[24] and monobactams **11**,[25] and the glutamine synthetase inhibitor, tabtoxin **12**,[26] are characterized by the presence of a 2-azetidinone nucleus lacking substituents at the 4-position of the β-lactam ring (Chart 3).

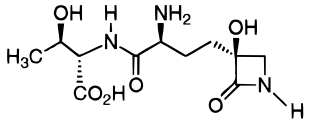
Chart 3



10. Nocardicins



11. Monobactams



12. Tabtoxin

Reduction of 4-(formyloxy) β-lactams **2** with $NaBH_4$ in methanol at 0 °C gave the corresponding α-substituted β-hydroxy amides **8** in high yields.[27] The reduction of the formyloxy group should occur sequentially through α-formyl amides **13**, the open tautomer of 4-hydroxy β-lactams **14**.[28] These intermediates are further reduced to give the final β-hydroxyamides **8** (Scheme 3). Some α-formyl amides **13** can be obtained, independently, by

(20) The sole exception was the 3-(phenylthio)-4-formyl-2-azetidinone. This compound gave the corresponding sulfone after prolongued reaction time. In this case the formyl group remained unaltered.

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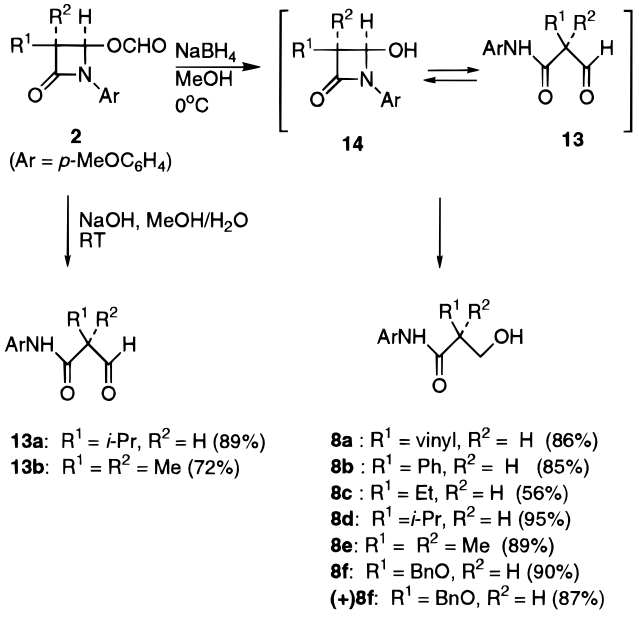
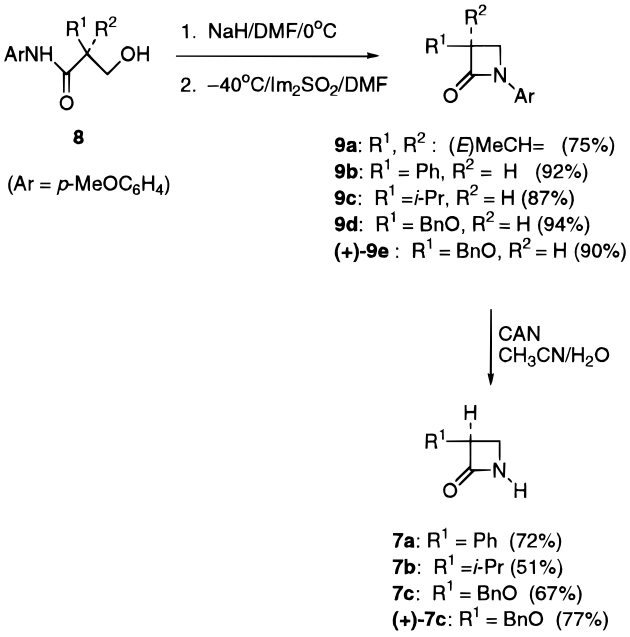
Scheme 3



Scheme 4



NaOH treatment of compounds **2** and are reduced to hydroxy amides **8** by treatment with $NaBH_4$. The synthesis of a 4-hydroxy β-lactam (type **14**) has been reported previously from (3*R*)-4-acetoxy-3-benzyl-3-fluoro-β-lactam.[23] In our hands, when compounds **2f** and **2h** were submitted to analogous reaction conditions, the open-chain aldehyde tautomers **13a** and **13b**, respectively, were obtained in excellent yield.[29] Therefore, 4-formyl β-lactams **1** are efficiently transformed into compounds **8** in two steps following our procedure. The reported method to prepare compounds analogous to **8** starting from a 4-acetoxy-2-azetidinone requires four steps to effect the same overall transformation.

Our intended approach to 4-unsubstituted β-lactams makes use of a ketene−imine cycloaddition to build the starting 4-(formyloxy) β-lactam **2** and an intramolecular C4−N bond formation reaction on α-substituted β-hydroxy amides **8** (Scheme 4). This mixed route employs both general approaches to this class of compounds: the ketene−imine cycloaddition based on unstable, *in situ* generated, formaldehyde imines[30] or formaldehyde imine equivalents[31] and the intramolecular displacement of an activated leaving group attached to the β-position of an acid derivative, usually an amide, under basic conditions.[32] Thus, the hydroxyl group of *N*-(4-methoxyphenyl)amides **8** was activated as its imidosulfonate,[27b] which undegoes the intramolecular displacement by the amide nitrogen upon base treatment to yield the desired compounds **9** (Scheme 4). The overall transformation occurs in good yields and without lost of the stereochemical integrity of the starting material when optically pure starting material was used.[33] Alkyl-, aryl-, and alkoxy groups are tolerated in this transformation. β-Hydroxy amide **8a** having a vinyl group forms 3-ethylidenyl-2-azetidinone **9a**. The isomerization of the double bond should occur upon base treatment.[15b] This sequence, 4-formyl-2-azetidinones **1** to C4-unsubstituted 2-azetidinones **9**, represents a simple, stereoselective, and high-yielding entry to this interesting type of compounds. Finally, CAN dearylation of compounds **9** gives the corresponding *N*-unsubstituted β-lactams **7**.

In conclusion, the Baeyer−Villiger oxidation of 4-formyl β-lactams **1** has been studied. This reaction represents one of the scarce examples of the preferred migration of a carbon moiety in an aliphatic aldehyde and is an efficient and totally stereoselective entry to 4-(formyloxy) β-lactams **2**, which in turn are suitable building blocks for β-lactam antibiotics. The influence of the substituents at N1 and C3 of the four-membered ring in the Baeyer−Villiger rearrangement have been studied. 4-(Formyloxy) β-lactams **2** are suitable starting materials to prepare different 4-unsubstituted β-lactams **9** using β-hydroxy amides **8** as isolable intermediates. The overall transformation of 4-formyl-2-azetidinone **1** to 4-unsubstituted β-lactam **9** is a simple and convenient route to this interesting type of compounds.

Experimental Section[34]

General Procedure. General experimental data and procedures have been reported previously.[15b] 4-Formyl β-lactams **1** were used in all cases as single *cis*- or *trans*-isomers. Except as otherwise stated, spectroscopic data (^{1}H- and ^{13}C-

(27) β-Hydroxy *N*-arylamides related to **6** have been used for the synthesis of relevant C4-unsubstituted-β-lactams. See, for example: (a) Bose, A. K.; Sahu, D. P.; Manhas, M. S. *J. Org. Chem.* **1981**, *46*, 1229. (b) Hanessian, S.; Couture, C.; Wyss, H. *Can. J. Chem.*, **1985**, *63*, 3613.

(28) α-Formylacetanilides related to **13** have been obtained from 4-amino-β-lactams. See, for instance: (a) Perelman, E.; Mizsak, S. A. *J. Am Chem. Soc.* **1962**, *84*, 4988. (b) Opitz, G.; Koch, J. *Angew. Chem.* **1963**, *75*, 167. (c) Bose, A. K.; Kugajevsky, I. *Tetrahedron* **1967**, *23*, 957.

(29) Reduction ($NaBH_4$/Methanol/0 °C) of isolated compound **13a** gave the corresponding β-hydroxy amide **8d** in quantitative yield.

(30) See, for example: (a) Overmann, L. E.; Osawa, T. *J. Am Chem. Soc.* **1985**, *107*, 1698. (b) Nakaguchi, O.; Oku, T.; Takeno, H.; Hashimoto, M.; Kamiya, T. *Chem. Pharm. Bull.* **1987**, *35*, 3985. (c) Hegedus, L. S.; D'Andrea, S. *J. Org. Chem.* **1988**, *53*, 3113.

(31) Selected examples: (a) Kamiya, T.; Hashimoto, M.; Nakaguchi, O.; Oku, T. *Tetrahedron* **1979**, *35*, 323. (b) Curran, W. V.; Sassiver, M. L.; Ross, A. S.; Fields, T. L.; Boothe, J. H. *J. Antibiot.* **1985**, *35*, 329. (c) Narukawa, Y.; Juneau, K.; Snustad, D.; Miller, D. B.; Hegedus *J. Org. Chem.* **1992**, *57*, 5453.

(32) Ternansky, R. J.; Morin, J. M. In *The Organic Chemistry of β-Lactams*; Georg, G. I., Ed.; VCH Publishers, Inc.: New York, 1993; Chapter 5, p 4257.

(33) All enantiomerically pure compounds with a single stereocenter were checked against partial or total racemization by using chiral shift reagents. See the Experimental Section.

NMR) were obtained in $CDCl_3$ solutions. Specific rotation $[\alpha]_D$ is given in deg per dm at the specified temperature, and the concentration (*c*) is expressed in g per 100 mL in the given solvent. The optical purity of those compounds having a single chiral center was checked by ^1H NMR using tris[(3-heptafluoropropyl)hydroxymethylene-*d*-camphorate]europium(III), Eu(hfc)$_3$, as the chiral shift reagent, both in the racemic and optically pure compound. Except as otherwise stated all compounds are racemic.

All commercially available compounds were used without further purification. The following starting materials were prepared according to previously reported procedures: *cis*-1-(*p*-anisyl)-4-formyl-3-vinyl-2-azetidinone,[15b] *cis*-(1-*p*-anisyl)-4-(formy)-3-isopropenyl-2-azetidinone,[15b] *cis*-1-(*p*-anisyl)-4-(formyloxy)-3-isopropylidene-2-azetidinone,[15b] *cis*-1-(*p*-anisyl)-4-formyl-3-phenyl-2-azetidinone,[15b] *cis*-1-(*p*-anisyl)-3-ethyl-4-formyl-2-azetidinone,[15b] *cis*-1-(*p*-anisyl)-3-isopropyl-4-formyl-2-azetidinone,[15b] *trans*-1-(*p*-anisyl)-3-isopropyl-4-formyl-2-azetidinone,[16a] 1-(*p*-anisyl)-3,3-dimethyl-4-formyl-2-azetidinone,[16a] *cis*-1-(*p*-anisyl)-3-(benzyloxy)-4-formyl-2-azetidinone,[15b] *cis*-3-acetyl-1-(*p*-anisyl)-4-formyl-2-azetidinone,[15b] *cis*-1-(*p*-anisyl)-3-maleimido-4-formyl-2-azetidinone,[15b] *cis*-1-(*p*-anisyl)-4-formyl-3-phthalimido-2-azetidinone,[15b] (+)-*cis*-1-(*p*-anisyl)-4-formyl-3-[(*S*)-4-phenyl-2-oxooxazolidin-3-yl)]-2-azetidinone,[15b] *cis*-1-benzyl-3-(benzyloxy)-4-formyl-2-azetidinone,[17] (+)-*cis*-1-benzyl-4-formyl-3-[(*S*)-4-phenyl-2-oxooxazolidin-3-yl)]-2-azetidinone,[17] (+)-(3*R*,4*S*)-*cis*-1-(*p*-anisyl)-3-(benzyloxy)-4-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-azetidinone.[19c]

General Procedure for the Synthesis of *cis*-3-Substituted 4-(Formyloxy)-2-azetidinones 2. A mixture of 4-formyl β-lactam **1** (2 mmol) and *m*-CPBA (calcd 0.414 g, 2.4 mmol, 50−60%) in CH_2Cl_2 (DCM) (40 mL) was stirred at room temperature until total consumption of the starting material (TLC). The reaction mixture was then washed with 5% aqueous $NaHCO_3$ solution (2 × 30 mL) and brine (2 × 30 mL) and finally dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure afforded a residue that was purified by silica gel chromatography with hexane−EtOAc (3:1) to give the corresponding analytically pure product **2**. In those cases in which mixtures of compounds **2** and carboxylic acids **5** were obtained, chromatographic separation afforded analytically pure 2-azetidinones **2**. Compounds **5** were not obtained in pure form by this procedure. Pure compounds **5** were prepared as described below by Jones' oxidation of the corresponding 4-formyl β-lactams **1**. Spectroscopic and analytical data for some representative forms of **2** follow.[34]

***cis*-1-(*p*-Anisyl)-4-(formyloxy)-3-vinyl-2-azetidinone, 2a.** Reaction time: 3 h. Yield: 0.45 g (91%). White solid. Mp: 105−107 °C (DCM/hexanes). ^1H NMR: δ 8.15 (s, 1H), 7.36 (d, 2H, J = 9.0 Hz), 6.88 (d, 2H, Ar, J = 9.0 Hz), 6.67 (dd, 1H, J_1 = 4.3 Hz, J_2 = 0.6 Hz), 5.77−5.91 (m, 1H), 5.39−5.45 (m, 2H), 4.24 (dd, 1H, J_1 = 8.0 Hz, J_2 = 4.3 Hz), 3.79 (s, 3H). ^{13}C NMR: δ 163.4, 159.7, 157.1, 129.5, 126.4, 123.0, 118.8, 114.6, 77.6, 58.7, 55.6. IR (KBr): ν 1770, 1730, 1560, 1520. Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.66. Found: C, 62.89; H, 5.31; N, 5.58.

***cis*-1-(*p*-Anisyl)-4-(formyloxy)-3-isopropenyl-2-azetidinone, 2b.** Reaction time: 20 h. Yield: 0.36 g (70%). White solid. Mp: 62−64 °C (DCM/hexanes). ^1H NMR: δ 8.14 (s, 1H), 7.34 (d, 2H, J = 9.0 Hz), 6.86 (d, 2H, J = 9.0 Hz), 6.69 (d, 1H, J = 4.3 Hz), 5.15 (s, 1H), 5.09 (s, 1H), 4.18 (d, 1H, J = 4.3 Hz), 3.75 (s, 3H), 1.81 (s, 3H). ^{13}C NMR: 163.6, 159.9, 156.9, 135.2, 129.5, 118.7, 118.2, 114.5, 77.4, 61.5, 55.5, 21.9. IR (KBr): ν 1770, 1720, 1520. Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.19; H, 5.76; N, 5.17.

***cis*-1-(*p*-Anisyl)-4-(formyloxy)-3-isopropylidene-2-azetidinone, 2c.** Reaction time: 2 h. Yield: 0.47 g (90%). White solid. Mp: 104−106 °C (DCM/hexanes). ^1H NMR: δ 8.24 (d, 1H, J = 0.8 Hz), 7.35 (d, 2H, J = 9.0 Hz), 7.15 (s, 1H), 6.89 (d, 2H, J = 9.0 Hz), 3.79 (s, 3H), 2.14 (s, 3H), 1.84 (s, 3H). ^{13}C NMR: δ 160.8, 160.6, 156.6, 141.0, 131.6, 129.9, 118.2, 114.7, 78.3, 55.6, 21.0, 20.4. IR (KBr): ν 1760, 1720, 1520 cm^{-1}. Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.15; H, 5.72; N, 5.09.

***cis*-1-(*p*-Anisyl)-4-(formyloxy)-3-phenyl-2-azetidinone, 2d.** Reaction time: 18 h. Yield: 0.56 g (94%). White solid. Mp: 98−100 °C. ^1H NMR: δ 7.78 (s, 1H), 7.36 (m , 7H), 6.92 (d, 2H, J = 9.0 Hz), 6.77 (d, 1H, J = 4.3 Hz), 4.86 (d, 1H, J = 4.3 Hz), 3.81 (s, 3H). ^{13}C NMR: δ 163.6, 159.3, 157.1, 130.1, 129.8, 129.7, 128.7, 128.5, 118.8, 114.7, 78.2, 60.9, 55.6. IR (KBr): ν 1755, 1735, 1595, 1515 cm^{-1}. Anal. Calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.39; H, 5.10; N, 4.60.

***cis*-1-(*p*-Anisyl)-3-isopropyl-4-(formyloxy)-2-azetidinone, 2f.** Reaction time: 4 h. Yield: 0.45 g (85%). White solid. Mp: 120−122 °C (DCM/hexanes). ^1H NMR: δ 8.23 (s, 1H), 7.32 (d, 2H, J = 9.0 Hz), 6.87 (d, 2H, J = 9.0 Hz), 6.84 (d, 1H, J = 4.3 Hz), 3.78 (s, 3H), 3.23 (dd, 1H, J_1 = 9.7 Hz, J_2 = 4.3 Hz), 2.21 (m, 1H), 1.22 (d, 3H, J = 6.7 Hz), 0.96 (d, 3H, J = 6.7). ^{13}C NMR: δ 165.3, 160.2, 156.7, 129.3, 118.6, 114.5, 75.77, 61.2, 55.5, 25.3, 21.6, 20.2. IR (KBr): ν 1760, 1725, 1520. Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.78; H, 6.47; N, 5.25.

***trans*-1-(*p*-Anisyl)-3-isopropyl-4-(formyloxy)-2-azetidinone, 2g.** Reaction time: 4 h. Yield: 0.46 g (87%). White solid. Mp: 106−107 °C (DCM/hexanes). ^1H NMR: δ 8.15 (s, 1H), 7.33 (d , 2H, J = 9.3 Hz), 6.87 (d, 2H, J = 9.3 Hz), 6.45 (d, 1H, J = 0.9 Hz), 3.78 (s, 3H), 3.11 (dd, 1H, J_1 = 0.9 Hz, J_2 = 7.5 Hz), 2.17 (m, 1H), 1.13 (d, 3H, J = 6.6 Hz), 1.09 (d, 3H, J = 6.9 Hz). ^{13}C NMR: δ 164.5, 159.8, 156.7, 129.3, 118.5, 114.4, 77.8, 64.9, 55.4, 26.7, 20.2, 19.6. IR (KBr): ν 2960, 1760, 1730, 1530. Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.75; H, 6.74; N, 5.19.

***cis*-(+)-3-(Benzyloxy)-4-(formyloxy)-2-azetidinone, (+)-2i.** Reaction time: 2 h. Yield: 0.62 g (94%). White solid. Mp: 88−90 °C (DCM/hexanes). $[\alpha]^{25}_D$ = +128.26 (*c* 1, $CHCl_3$). ^1H NMR: δ 8.18 (s, 1H), 7.36 (m, 7H), 6.89 (d, 2H, J = 9.0 Hz), 6.61 (d, 1H, J = 3.4 Hz), 4.94 (d, 1H, J = 3.4 Hz), 4.78 (AB, 2H, J = 11.7 Hz), 3.79 (s, 3H). ^{13}C NMR: δ 163.5, 160.0, 157.4, 136.5, 129.1, 128.7, 128.4, 128.2, 119.1, 114.7, 82.1, 79.4, 74.0, 55.6. IR (KBr): ν 1780, 1730, 1520 cm^{-1}. Anal. Calcd for $C_{18}H_{17}NO_5$: C, 65.77; H, 5.27; N, 4.24. Found: C, 66.05; H, 5.23; N, 4.28.

***cis*-3-Acetoxy-1-(*p*-anisyl)-4-(formyloxy)-2-azetidinone, 2j, and *cis*-3-Acetoxy-1-(*p*-anisyl)-4-carboxy-2-azetidinone, 5a.** Following the standard procedure, after 3 h, a crude reaction mixture containing compounds **2j** and **5a** (88:12) was obtained. From this mixture 0.45 g (80%) of **2j** was obtained as a white solid. Mp: 128−130 °C (DCM/hexanes). **Compound 2j.** ^1H NMR: δ 8.16 (s, 1H), 7.39 (d, 2H, J = 9.0 Hz), 6.90 (d, 2H, J = 9.0 Hz), 6.83 (d, 1H, J = 3.7 Hz), 5.97 (d, 1H, J = 3.7 Hz), 3.80 (s, 3H), 2.19 (s, 3H). ^{13}C NMR: δ 169.1, 161.0, 159.4, 157.6, 128.6, 119.2, 114.7, 77.1, 75.0, 55.6, 20.4. IR (KBr): ν 1770, 1730, 1515. Anal. Calcd for $C_{13}H_{13}NO_6$: C, 55.92; H, 4.69; N, 5.02. Found: C, 55.95; H, 4.74; N, 4.91.

***cis*-1-(*p*-Anisyl)-4-(formyloxy)-3-phthalimido-2-azetidinone, 2l, and *cis*-1-(*p*-Anisyl)-4-carboxy-3-phthalimido-2-azetidinone, 5c.** Following the standard procedure, after 7 h, a crude reaction mixture containing compounds **2l** and **5c** (65:35) was obtained. From this mixture 0.45 g (62%) of **2l** was obtained as a white solid. Mp: 178−180 °C (DCM/hexanes). **Compound 2l.** ^1H NMR: δ 8.04 (s, 1H), 7.80 (m, 2H), 7.46 (m, 2H), 7.46 (d, 2H, J = 9.0 Hz), 6.91 (d, 2H, J = 9.0 Hz), 6.87 (d, 1H, J = 3.9 Hz), 5.72 (d, 1H, J = 3.9 Hz), 3.80 (s, 3H). ^{13}C NMR: δ 166.5, 160.2, 159.5, 157.4, 134.7, 131.6, 128.9, 124.1, 119.4, 114.5, 77.6, 57.6, 55.5. IR (KBr): ν 1790, 1775, 1735, 1715, 1520. Anal. Calcd for $C_{19}H_{14}N_2O_6$: C, 62.30; H, 3.85; N, 7.65. Found: C, 62.08; H, 3.94; N, 7.58.

***cis*-1-Benzyl-3-(benzyloxy)-4-(formyloxy)-2-azetidinone, 2n, and *cis*-1-Benzyl-3-(benzyloxy)-4-carboxy-2-azetidinone, 5e.** Following the standard procedure, after 2.5 h, a crude reaction mixture containing compounds **2n** and **5e** (50:50) was obtained. From this mixture 0.28 g (45%) of **2n** was obtained as a colorless thick oil. **Compound 2n.** ^1H NMR: δ 8.01 (s, 1H), 7.30 (m, 10H), 6.0 (d, 1H, J = 3.4 Hz), 4.77 (d, 1H, J = 3.4 Hz), 4.70 (AB, 2H, J = 14.0 Hz), 4.58 (d, 1H, J = 15.0 Hz), 4.19 (d, 1H, J = 15.0 Hz). ^{13}C NMR: δ 166.7, 160.2, 136.5, 134.8, 129.0, 128.7, 128.5, 128.4, 128.3, 128.2,

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

82.6, 79.9, 73.6, 44.8. IR (KBr): 1750, 1700, 1640. Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.07; H, 5.71; N, 4.47.

General Procedure for the Synthesis of 4-Carboxy-2-azetidinones 5. Jones' reagent was added dropwise to a solution of 4-formyl-2-azetidinone **1** (1 mmol) in acetone (20 mL) cooled to 0 °C (ice bath). The reaction mixture was stirred at 0 °C for 0.5 h; MeOH (1 mL) was added, and stirring was continued for 5 min. The mixture was filtered through Celite, and the solvent was removed under reduced pressure. The residue was taken up in $CHCl_3$ (30 mL), washed with H_2O and brine, and dried ($MgSO_4$). Compound **5** was obtained upon solvent removal under vacuum. Analytically pure compounds were obtained by crystallization of the indicated solvent mixture. Spectroscopic and analytical data for some representative forms of **5** follow.[34]

***cis*-3-Acetoxy-1-(*p*-anisyl)-4-carboxy-2-azetidinone, 5a.** Yield: 85%. White solid. Mp: 214−216 °C (AcOEt/DCM). ^{1}H NMR (DMSO-d_6): δ 7.30 (d, 2H, J = 8.9 Hz), 6.95 (d, Ar, J = 8.9 Hz), 6.16 (d, 1H, J = 5.5 Hz), 5.02 (d, 1H, J = 5.5 Hz), 3.72 (s, 3H), 2.09 (s, 3H). ^{13}C-NMR (DMSO-d_6): δ 168.7, 168.3, 160.7, 156.1, 130.2, 118.1, 114.3, 73.7, 57.8, 55.2, 20.1. IR (KBr): ν 3100−2540, 1770, 1760, 1735, 1515. Anal. Calcd for $C_{13}H_{13}NO_6$: C, 55.92; H, 4.69; N, 5.02. Found: C, 56.08; H, 4.58; N, 4.94.

***cis*-1-(*p*-Anisyl)-4-carboxy-3-phthalimido-2-azetidinone, 5c.** Yield: 87%. White solid. Mp: 260−262 °C (AcOEt/DCM). ^{1}H NMR (DMSO-d_6): δ 7.93 (m, 4H), 7.44 (d, 2H, J = 8.9 Hz), 6.97 (d, 2H, J = 8.9 Hz), 5.85 (d, 1H, J = 6.3 Hz), 5.18 (d, 1H, J = 6.3 Hz), 3.74 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 168.4, 166.5, 160.7, 155.8, 135.2, 131.0, 130.8, 123.7, 118.4, 114.0, 56.8, 55.2, 55.1. IR (KBr): ν 1770, 1720, 1520 cm^{-1}. Anal. Calcd for $C_{19}H_{14}N_2O_6$: C, 62.30; H, 3.85; N, 7.65. Found: C, 62.56; H, 3.54; N, 7.72.

***cis*-1-Benzyl-3-(benzyloxy)-4-carboxy-2-azetidinone, 5e.** Yield: 85%. White solid. Mp: 235−237 °C (DCM/hexanes). ^{1}H NMR ($CDCl_3$): δ 9.46 (br s, 1H), 7.35−7.15 (m, 10 H), 4.91 (d, 1H, J = 15.6 Hz), 4.86 (d, 1H, J = 5.1 Hz), 4.70 (AB, 2H, J = 11.4 Hz), 4.14 (d, 1H, J = 5.1 Hz), 4.12 (d, 1H, J = 15.6 Hz). ^{13}C NMR ($CDCl_3$): δ 172.4, 166.7, 136.4, 134.1, 129.1, 128.7, 128.6, 128.3, 128.3, 128.2, 82.5, 73.4, 58.3, 45.2. IR (KBr): ν 1760, 1530 cm^{-1}. Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.28; H, 5.34; N, 4.65.

***cis*-1-Benzyl-4-carboxy-3-[(*S*)-4-phenyl-2-oxooxazolidin-3-yl)]-2-azetidinone, 5f.** Yield: 86%. White solid. Mp: 145−147 °C (DCM/hexanes). $[\alpha]^{25}_D$ = +190.48 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.74 (br s, 1H), 7.35 (m, 10H), 5.08 (m, 2H), 4.75 (t, 1H, J = 8.7 Hz), 4.38 (d, 1H, J = 14.7 Hz), 4.32 (d, 1H, J = 5.6 Hz), 4.15 (m, 1H), 4.04 (d, 1H, J = 5.6 Hz). ^{13}C-NMR ($CDCl_3$): δ 170.6, 163.9, 158.7, 135.9, 134.6, 129.8, 129.0, 128.9, 128.1, 127.7, 71.6, 61.0, 60.8, 55.4, 45.5. IR (KBr): ν 3280, 1775, 1735. Anal. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.84; H, 4.89; N, 7.75.

General Procedure for the Synthesis of 3-Hydroxy amides 8. Fine granulated $NaBH_4$ (0.46 g, 1.2 mmol) was added to a solution of 4-(formyloxy)-2-azetidinone **2** (1 mmol) in MeOH (40 mL) cooled to 0 °C (ice bath). The resulting mixture was stirred at 0 °C until total consumption of the starting material (TLC). The solvent was removed under reduced pressure, and the residue was dissolved in DCM (30 mL), washed with H_2O (20 mL) and brine (20 mL), and finally dried ($MgSO_4$). The solvent was removed under vacuo, and unless otherwise stated the residue was crystallized from DCM/hexanes mixtures to give analytically pure compounds **8**. Spectroscopic and analytical data for some representative forms of **8** follow.[34]

***N*-(*p*-Anisyl)-3-hydroxy-2-vinylpropanamide, 8a.** Reaction time: 1 h. Yield: 0.19 g (86%). White solid. Mp: 53−55 °C. ^{1}H NMR: δ 7.59 (br s, 1H), 7.40 (d, 2H, J = 9.0 Hz), 6.86 (d, 2H, J = 9.0 Hz), 5.96 (m, 1H), 5.39 (dd, 2H, J_1 = 14.1, J_2 = 2.7 Hz), 3.91 (m, 2H), 3.79 (s, 3H), 3.25 (m, 1H), 3.17 (t, 1H, J = 6.9 Hz). ^{13}C NMR: δ, 171.0, 156.8, 133.3, 130.5, 122.0, 120.8, 114.2, 63.5, 55.6, 53.5. IR (KBr): ν 3280, 1660, 1640, 1520. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 64.85; H, 6.52; N, 6.38.

***N*-(*p*-Anisyl)-3-hydroxy-2-phenylpropanamide, 8b.** Reaction time: 1 h. Yield: 0.23 g (85%). Colorless needles. Mp: 144−146 °C. ^{1}H-NMR: δ 7.37 (m, 7H), 7.16 (br s, 1H), 6.83 (d, 1H, J = 9.0 Hz), 4.22 (m, 1H), 3.85 (m, 2H), 3.78 (s, 3H), 3.32 (t, 1H, J = 8.4 Hz). ^{13}C NMR: δ 171.7, 156.8, 136.4, 130.4, 129.4, 128.6, 128.2, 122.1, 114.2, 65.1, 55.6, 55.2. IR (KBr): ν 3400, 3300, 1660, 1540, 1520. Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.55; H, 6.22; N, 5.04.

***N*-(*p*-Anisyl)-3-hydroxy-2-isopropylpropanamide, 8d.** Reaction time: 0.5 h. Yield: 0.23 g (95%). White solid. Mp: 126−128 °C. ^{1}H NMR: δ 7.64 (br s, 1H), 7.43 (d, 2H, J = 9.0 Hz), 6.85 (d, 2H, J = 9.0 Hz), 3.90 (m, 2H), 3.79 (s, 3H), 2.75 (br s, 1H), 2.13 (m, 2H), 1.03 (d, 3H, J = 6.3 Hz) and 1.01 (d, 3H, J = 6.3 Hz). ^{13}C NMR: δ 173.4, 156.5, 130.6, 122.0, 114.1, 61.7, 56.4, 55.5, 27.7, 21.2, 20.3. IR (KBr): ν 3300, 1665, 1545, 1525. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.94; H, 7.79; N, 5.85.

(+)-*N*-(*p*-Anisyl)-2-(benzyloxy)-3-hydroxypropanamide, (+)-8f. Reaction time: 1 h. Yield: 0.27 g (87%). White solid. Mp: 104−106 °C. $[\alpha]^{25}_D$ = +54.92° (*c* 1, $CHCl_3$). ^{1}H-NMR: δ 8.34 (br s, 1H), 7.43 (m, 7H), 6.86 (d, 2H, J = 9.0 Hz), 4.74 (AB, 2H, J = 11.6 Hz), 4.09 (t, 1H, J = 4.9 Hz), 3.94 (t, 2H, J = 6.0 Hz), 3.79 (s, 3H), 2.50 (t, 1H, J = 6.3 Hz). ^{13}C-NMR: δ 168.9, 156.8, 136.7, 130.1, 129.0, 128.7, 128.3, 121.6, 114.3, 80.1, 73.5, 62.9, 55.6. IR (KBr): ν 3380, 3280, 1660, 1525 cm^{-1}. Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.55; H, 6.35; N, 4.52.

General Procedure for the Preparation of 4-Unsubstituted 2-azetidinones 9. A solution of 3-hydroxy amide **8** (1 mmol) in DMF (15 mL) was added dropwise to a solution of NaH (previously washed in hexanes) (0.05 g, 2 mmol) in DMF (2.5 mL) cooled to 0 °C (ice bath). The resulting mixture was cooled to −40 °C, and a solution of diimidazolyl sulfone (0.396 g, 2 mmol) in DMF (7.5 mL) was added dropwise over a 10 min period. After being stirred at −40 °C for 0.5 h the mixture was allowed to reach room temperature. Methanol (0.5 mL) and $CHCl_3$ (125 mL) were successfully added to the reaction mixture and then washed with brine and H_2O and finally dried over $MgSO_4$. The organic solvent was removed under vacuum to yield a residue whose ^{1}H-NMR spectrum of the crude reaction mixture showed a quantitative yield of the expected product **9**. Column chromatography (DCM/AcOEt/hexanes 12:2:1) afforded analytically pure compounds **9**. Spectroscopic and analytical data for some representative forms of **9** follow.[34]

1-(*p*-Anisyl)-3(*E*)-ethylidenyl-2-azetidinone, 9a. Yield: 75%. White solid. Mp: 115−117 °C (DCM/hexanes). ^{1}H NMR: δ 7.32 (d, 2H, J = 9.0 Hz), 6.88 (d, 2H, J = 9.0 Hz), 6.28 (dq, 1H, J_1 = 6.9 Hz, J_2 = 0.7 Hz), 4.05 (d, 2H, J = 0.6 Hz), 3.78 (s, 3H), 1.81 (d, 3H, J = 7.0 Hz). ^{13}C NMR: δ 160.2, 156.0, 136.8, 132.4, 122.9, 117.5, 114.5, 55.6, 46.6, 14.6. IR (KBr): ν 1735, 1520. Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.72; H, 6.19; N, 6.83.

1-(*p*-Anisyl)-3-phenyl-2-azetidinone, 9b. Yield: 92%. White solid. Mp: 124−126 °C (DCM/hexanes). ^{1}H NMR: δ 7.33 (m, 7H), 6.90 (d, 2H, J = 9.0 Hz), 4.50 (dd, 1H, J_1 = 5.8, J_2 = 2.7 Hz), 4.03 (t, 1H, J = 5.8 Hz), 3.80 (s, 3H), 3.64 (dd, 1H, J_1 = 5.7 Hz, J_2 = 2.8 Hz). ^{13}C NMR: δ 164.9, 156.3, 135.6, 132.1, 129.0, 127.8, 127.5, 117.8, 114.5, 55.6, 35.7, 27.0. IR (KBr): ν 1740, 1510. Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.63; H, 5.73; N, 5.51.

1-(*p*-Anisyl)-3-isopropyl-2-azetidinone, 9c. Yield: 87%. White solid. Mp: 80−82 °C (DCM/hexanes). ^{1}H NMR: δ 7.31 (d, 2H, J = 9.0 Hz), 6.87 (d, 2H, J = 9.0 Hz), 3.78 (s, 3H), 3.62 (t, 1H, J = 5.6 Hz), 3.32 (dd, 1H, J_1 = 5.7 Hz, J_2 = 2.7 Hz), 3.11 (m, 1H), 2.07 (m, 1H) 1.12 (d, 3H, J = 6.7 Hz), 1.01 (d, 3H, J = 6.7 Hz). ^{13}C NMR: δ 166.7, 156.0, 132.4, 117.5, 114.4, 55.8, 55.6, 42.5, 28.4, 20.2, 20.1. IR (KBr): ν 1720, 1510. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.24; H, 7.69; N, 6.37.

(+)-1-(*p*-Anisyl)-3-(benzyloxy)-2-azetidinone, (+)-9d. Yield: 90%. White solid. Mp: 102−104 °C (DCM/hexanes). $[\alpha]^{25}_D$ = +33.1 (*c* 1, $CHCl_3$). ^{1}H NMR: δ 7.37 (m, 7H), 7.30 (d, 2H, J = 9.0 Hz), 6.87 (d, 2H, J = 9.0 Hz), 4.91 (d, 1H, J = 11.4 Hz), 4.87 (dd, 1H, J_1 = 4.9 Hz, J_2 = 2.1 Hz), 4.70 (d, 1H, J = 11.5 Hz), 3.79 (s, 3H), 3.75 (dd, 1H, J_1 = 6.0 Hz, J_2 = 4.9

Hz), 3.52 (dd, 1H, J_1 = 6.0 Hz, J_2 = 2.1 Hz). ^{13}C-NMR: δ 163.8, 156.5, 137.0, 131.5, 128.7, 128.4, 118.1, 114.5, 80.0, 72.6, 55.6, 47.5. IR (KBr): ν 1745, 1520. Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.98; H, 6.19; N, 4.77.

General Procedure for the synthesis of 3-Oxopropanamides 13. NaOH (0.05 g, 1.25 mmol) in H_2O (1 mL) was added in a single portion to a solution of 2-azetidinone **2** (1 mmol) in MeOH (8 mL). The mixture was stirred at rt for 1 h, and DCM (17 mL) was added. The resulting heterogeneous mixture was stirred for an additional period of 10 min. The organic layer was separated, washed with brine, and dried ($MgSO_4$). The corresponding α-formyl amide **13** was obtained upon solvent elimination under vacuo.

***N*-(*p*-Anisyl)-2-isopropyl-3-oxopropanamide, 13a.** Yield: 89%. White solid. Mp: 132−134 °C (DCM/hexanes). ^{1}H NMR: δ 9.79 (d, 1H, J = 3.5 Hz), 7.95 (br s, 1H), 7.42 (d, 2H, J = 9.0 Hz), 6.86 (d, 2H, J = 9.0 Hz), 3.79 (s, 3H), 3.00 (dd, 1H, J_1 = 3.5, J_2 = 8.5 Hz), 2.60 (m, 1H), 1.11 (d, 3H, J = 6.76 Hz), 1.04 (d, 3H, J = 6.8 Hz). ^{13}C NMR: δ 201.5, 165.9, 156.9, 130.3, 122.2, 114.3, 67.6, 55.6, 29.5, 20.6, 20.3. IR (KBr): ν 3290, 1730, 1650. Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.35; H, 7.16; N, 6.26.

***N*-(*p*-Anisyl)-2,2-dimethyl-3-oxopropanamide, 13b.** Yield: 72%. Compound **13b** was unstable, and correct analytical data could not be obtained. ^{1}H-NMR: δ 9.63 (s, 1H), 8.05 (br s, 1H), 7.33 (d, 2H, J = 9.0 Hz), 6.77 (d, 2H, J = 9.0 Hz), 3.70 (s, 3H), 1.39 (s, 6H). ^{13}C-NMR: δ 203.3, 169.4, 156.8, 130.5, 122.3, 114.2, 55.5, 53.8, 21.2. IR (KBr): ν 3340, 1740, 1655, 1520.

Acknowledgment. Support for this work by the DGICYT (Project PB93-0442) is gratefully acknowledged. One of us (M.F.A.) acknowledges the receipt of a postdoctoral fellowship by the Ministerio de Educación y Ciencia (Spain). We also thank Alberto Rodríguez-Vicente for his colaboration in the preparation of this manuscript.

Supporting Information Available: Full spectral and analytical data for compounds **(+)-1i**, **2e, 2h,i,k, (+)-2m, 5b, (+)-5d, 6a−c, 7a−c, (+)-7c, 8c, 8e−f,** and **9d** (6 pages). This material is contained in libraries on microfiche, inmediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9612685