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Intermolecular and Intramolecular α-Amidoalkylation Reactions Using Bismuth Triflate as the Catalyst

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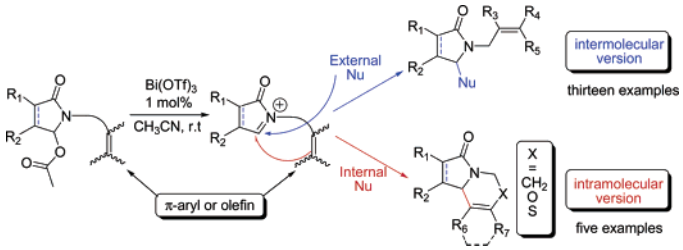

Bismuth(III) triflate was found to promote the formation of stable cyclic *N*-acyliminium species in remarkable catalytic amounts (1 mol %). The α-amidoalkylation process seems to be effective in intermolecular and intramolecular manners leading to α-substituted lactams and heterocyclic systems containing azacycles, respectively. By comparing our results with those obtained with the classical Lewis acids as catalysts, it was evidenced clearly that the use of bismuth(III) triflate had been efficient for nearly all α-acetoxy lactams we used, except for *N*-acyliminium precursors bearing a sulfur atom. Also, the process seems to be easy, general, and clean, having diastereoselectivity comparable to protocols using classical Lewis acids and resulting in the formation of polyheterocyclic systems in good to excellent yields (64−99% in acetonitrile as solvent).

Introduction

N-Acyliminium ions are important intermediates in organic synthesis, especially for the synthesis of various nitrogen-containing natural and unnatural products of biological interest.[1,2] *N*-Acyliminium ions also act as more electron-deficient carbocations[3] toward weak nucleophiles providing exceptionally useful methodologies for carbon−carbon bond formation, both in intermolecular and in intramolecular processes.[1,2] These species have been generated from amides or lactams bearing a good leaving group in the α-position to the nitrogen atom in acidic media. The substrates used for this purpose include *N*,*O*-, *N*,*N*-, and *N*,*S*-acetals as well as α-halo-, α-hydroxy, and α-acetoxy amides, lactames, carbamates, and isomünchnone cycloadducts, and hence, several Brönsted and Lewis acids as catalysts have been used to effect this transformation.

Because of the pivotal role played by these transformations in academic and industrial applications, the search for new rapid protocols to perform these acid-mediated α-amidoalkylation reactions, using particularly a combination of economical

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conditions (cheap reagents with low or no toxicity, catalysts and solvents comparable) and the environmental ones, is still of interest.

In this sense, it has been established now that lanthanide triflates, $Sc(OTf)_3$, $Sn(OTf)_2$, and $Y(OTf)_3$, constitute a type of Lewis acids that are different from classical ones such as $BF_3 \cdot Et_2O$, $AlCl_3$, $TiCl_4$, $SnCl_4$, etc. The former are characterized by their fairly high stability in water and recyclability as well as their higher effectiveness in the case of polynitrogen compounds, exemplified by imines and others,[4] but also by their high cost associated with their difficult preparation, which limits their intensive utilization.

In parallel studies, bismuth(III) compounds have attracted recent attention due to their low toxicity, low cost, good stability, and higher catalytic efficiency rendering them suitable for green chemistry. The use of these salts as catalysts in organic synthesis is well documented, and the results are consigned in two excellent recent reviews.[5] Parenthetically, the preparation of bismuth(III) triflate associated with its applications was patented.[6] According to these reports, bismuth(III) triflate catalyzes various important organic reactions, polymerization, and finally miscellanous reactions. $Bi(OTf)_3$ is particularly attractive because it is commercially available or can be easily prepared under strictly anhydrous conditions from the more accessible $BiPh_3$ or Bi_2O_3 and TfOH or Tf_2O as starting materials, respectively.[7]

Results and discussion

Because few acid-catalyzed carbon−carbon bond-forming reactions through an α-amidoalkylation process catalyzed with bismuth(III) salts have been described in the literature, allied with our interest in the development of new selective and environmentally friendly methodologies toward exploration of these transformations in *N*-acyliminium chemistry,[8] we wish to report herein the preliminary results of our finding on the catalytic activity of $Bi(OTf)_3$ in both intermolecular and intramolecular processes.

To the best of our knowledge, only few applications of the intermolecular α-amidoalkylation process using other triflates such as TBSOTf (from 4.5 to 223 mol %),[9] $Sc(OTf)_3$ (from 10 to 100 mol %),[10] and $Zn(OTf)_2$ (from 120 to 200 mol %)[11] were reported. Also, only two examples of π-cationic cyclization through *N*-acyliminium species were described recently by the Hiemstra group. They concern the formation of piperidine derivatives by π-olefinic-*N*-acyliminium cation cyclization using $Sc(OTf)_2$ (2 mol %)[12] and *N*-sulfonyliminium ion mediated cyclization to α-vinyl-substituted isoquinolines and β-carbolines using $Sc(OTf)_2$ or $Sc(OTf)_3$ in 10 mol % quantities,[13] respectively. As of this date, there have been no reports describing the ability of the nonrare earth-metal triflate, $Bi(OTf)_3$, to promote formation of *N*-acyliminium species and their trapping by nucleophiles either in intermolecular or in intramolecular processes.

In this context, we report an attractive method using bismuth(III) triflate as a catalyst for the α-amidoalkylation of lactams and a mechanistic aspect of these transformations to access a library of small molecules containing pyrrolidinone or isoindolinone nuclei fused both to simple and complex heterocycles. In fact, as highlighted in retrosynthetic Scheme 1, the selection of different substituents (R_i with $i = 1-7$) in α-acetoxylactam systems **I** allows us to consider the existence of stable *N*-acyliminium cations **II**. This would act as a carbon scavenger in intermolecular and intramolecular processes, furnishing products **III** and **IV**, respectively. Also, the direct heterocyclization process leading to products not represented in this scheme, with heteroatom X (X = O and S) acting as an internal nucleophile, could constitute a serious competing reaction.[8] The requisite intermediates **II** generated from α-acetoxy lactams **I** under $Bi(OTf)_3$ influence in catalytic amounts may indeed be stabilized depending also on the temperature, the solvent, and the quantities of the reactant. At this stage, the measurement of the impact of the nature of the substituent and the required quantities of catalyst poses an important and interesting challenge for the comprehension of the scope and limitations of these processes.

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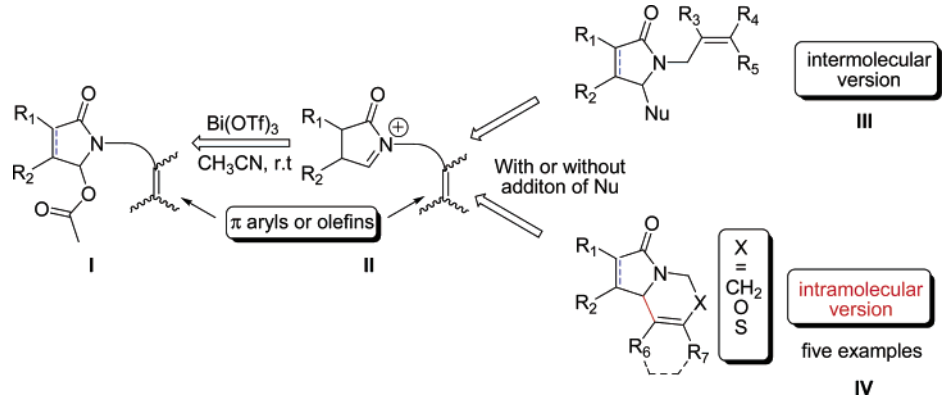
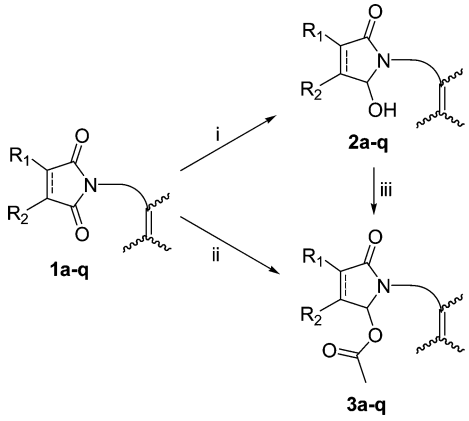
SCHEME 1. Retrosynthetic Scheme Leading to Lactam Targets of Types III and IV



SCHEME 2. Scheme Leading to α-Acetoxy Lactams 3 as *N*-Acyliminium Ion Precursors[a]

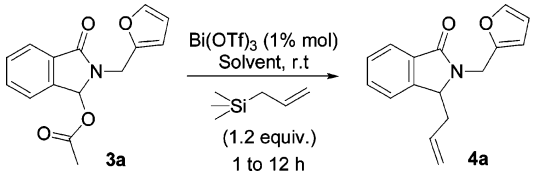


[a] Key: (i) $NaBH_4$ (3−6 equiv), MeOH, −5 to 0 °C, 15−30 min; (ii) in the case of imides **1b**,**i**,**p** (a) $LiBHEt_3$ (1.2 equiv), CH_2Cl_2, −60 °C, 20−40 min, (b) Ac_2O (1.5 equiv), −60 °C to room temperature, 1 h; (iii) Ac_2O (2 equiv), CH_2Cl_2, $DMAP_{cat}$, NEt_3 (2 equiv), room temperature, 12 h.

First, the synthesis of the required α-acetoxy lactams of type **3** was accomplished by a two-step sequence and/or in only one step as outlined in Scheme 2. The N-alkylated imides **1** as starting materials are not commercially available but were prepared according to known procedures from amines and anhydrides by thermal amino−anhydride condensation or by condensation under azeotropic removal of water with the presence of NEt_3 as the catalyst.

Regioselective reduction of imides **1** was performed with a large excess of $NaBH_4$ (3−6 equiv) in dry MeOH at −5 to 0 °C for a short time. To compensate for the poor solubility of starting materials encountered in certain cases, the reaction was performed in a mixture of THF and $CHCl_3$ (v/v) as solvents. Under these conditions, hydroxy lactams **2** were isolated as the sole reaction products in good to excellent yields. Their transformation in the ultimate stage into the corresponding α-acetoxy lactams **3** was accomplished easily by reaction with acetic anhydride (i.e., Ac_2O (2 equiv), CH_2Cl_2, $DMAP_{cat}$, NEt_3 (2 equiv), room temperature, 12 h).[14] The products **3** were isolated in very good yields (>90% in all attempts), and in certain cases, the pure product could be isolated after chromatography on a silica gel column. In the cases of succinimides **1b**,**i**,**p**, the half reduction was brought about with $LiBHEt_3$ (1.15 equiv) in dry CH_2Cl_2 at −60 °C for 20−40 min (monitored by TLC using a silica gel plate and cyclohexane/AcOEt as the eluting mixture). Because the purification of the resulting hydroxy lactams **2b**,**i**,**p** can be somewhat problematic, their in situ conversion into α-acetoxy lactams **3b**,**i**,**p** was accomplished by using 1.3 equiv of Ac_2O.[9d,15]

TABLE 1. $Bi(OTf)_3$-Catalyzed Amidoalkylation of α-Acetoxy Lactam 3a in Different Solvents



entry	solvent	dielectric constant	yield of **4a** (%)
1	1,4-dioxane	2.21	—[a]
2	diethyl ether	4.34	—[b]
3	chloroform	4.81	37
4	tetrahydrofuran	7.60	30
5	dichloromethane	8.93	56
6	nitromethane	35.9	50
7	acetonitrile	37.5	64

[a] Only hydroxy lactam product **2a**, corresponding to the hydrolysis of ester **3a**, was recovered. [b] The starting material **3a** is insoluble.

Inspired by the following general observations that (1)-$Bi(OTf)_3$ is tolerant toward C-nucleophiles such as silanes and enoxysilanes and (2) $Bi(OTf)_3$ is an effective catalyst for the nucleophilic addition onto nitrogen functions exemplified by iminium salts in the Michael-type reaction, for example,[16] we began our investigations by screening various solvents for the intermolecular amidoalkylation with allyltrimethylsilane (1.2 equiv) of the *N*-acyliminium cation derived from α-acetoxy lactam **3a** in the presence of 1 mol % of $Bi(OTf)_3$.[17] Out of the various polar solvents tested (Table 1), the reaction failed to operate satisfactorily because it led to hydroxy lactam **2a**, corresponding to hydrolysis of the ester **3a**, and 1,4-dioxane and diethyl ether failed to react altogether because of low

(14) For $LiEt_3BH$ reduction and one-pot reduction/acetylation processes of the imides, see: (a) Takacs, J. M.; Weidner, J. J. *J. Org. Chem.* **1994**, *59*, 6480−6483. (b) Szemes, F., Jr.; Fousse, A.; Othman, R. B.; Bousquet, T.; Othman, M.; Dalla, V. *Synthesis* **2005**, *7*, 875−879.

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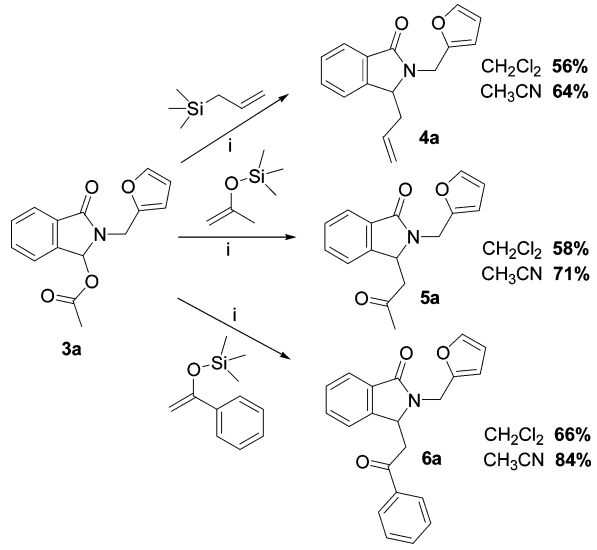
(17) A prescreening of this reaction with, respectively, 10, 5, and 1 mol % of $Bi(OTf)_3$ in CH_2Cl_2 demonstrated the high efficiency of this catalyst, and in addition, only 1 mol % of $Bi(OTf)_3$ was sufficient to catalyze the allylation reaction.

SCHEME 3. Bi(OTf)$_3$-Catalyzed Alkylation of α-Acetoxy Lactam 3a with Different C-Nucleophiles[a]



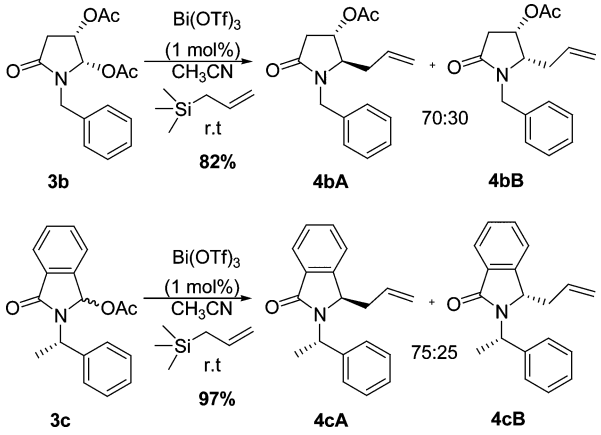
[a] Key: (i) Bi(OTf)$_3$ (1 mol %), solvent, room temperature, 1−12 h, allyltrimethylsilane (1.2 equiv). In the case of enoxysilanes, 1.5 equiv was used.

solubility of the substrate **3a**. Chloroform, THF, and nitromethane gave the expected product **4a** in yields ranging from 30 to 50%, and the best results were obtained with acetonitrile (64% yield). In dichloromethane, the reaction gave rise also to the desired product but only in 56% yield.

Encouraged by the above results, we extended the process to a variety of C-nucleophiles such as enoxysilanes, depicted in Scheme 3. This clearly shows that in the presence of 2-trimethylsiloxypropene (1.5 equiv) as the nucleophile, the reaction under the well-established protocol outlined above is completely selective and the corresponding α-amidoalkylation derivative **5a** constitutes the sole reaction product (71%). Under the same protocol, the reaction with 1-phenyl-1-trimethylsiloxy-ethylene (1.5 equiv) furnished after chromatographic purification α-benzoylmethyl lactam **6a** in a very good yield (84%). In general, the reaction proceeded to completion in 1−12 h and the use of CH_2Cl_2 as solvent instead of acetonitrile led to lower yields because components **5a** and **6a** were isolated in yields of 58 and 66%, respectively. These observations confirm those made above during the formation of α-allyl lactam **4a** (56% in CH_2Cl_2 compared to 64% in acetonitrile; see Scheme 3 and Table 1) and were in accordance with those made during nucleophilic addition of an allyltrimethylsilane reactant onto *N*-acyliminium ion species in the piperidine series.[10a]

These results and observations made during the experimentation deserve some comments. So, the efficacy of the solvent could be related to its dielectric constant (see Table 1). In this sense, acetonitrile contributes, probably concomitantly with the catalyst, to the acceleration of the dissociation of the α-acetoxy lactams **3** into the corresponding *N*-acyliminium cation intermediates. This facilitates the nucleophilic attack of the cation species being stabilized by both the solvent (acetonitrile in this case)[10a] and the counterion. In addition, the grade of solvent was shown to be crucial for the yield of the transformation. Ultimately, the presence of any water traces either in solvents or in reagents decreases dramatically the reaction yields, and in some cases, the reaction failed. In the latter cases, only the

SCHEME 4. Bi(OTf)$_3$-Catalyzed α-Amidoalkylation of Chiral α-Acetoxy Lactams 3b and 3c



α-hydroxy lactams **2** corresponding to reactants **3** were recovered, generally in very good yields.

The ability of Bi(OTf)$_3$ to catalyze diastereoselective α-amidoalkylation of a chiral cyclic *N*-acyliminium cation with C-nucleophiles was examined next. As highlighted in Scheme 4, addition of allyltrimethylsilane to the known enantiopure **3b** according to our protocol effectively provides allylation in 82% yield while providing the desired product as a mixture of two inseparable diastereomers **4bA** and **4bB** in a 70:30 ratio. This stereochemical outcome at C_2 is similar to that reported in the literature for the same reactant **3b** using other Lewis acids such as $BF_3{\cdot}Et_2O$,[18] $InCl_3$,[19a] $NbCl_5$,[19b] as well as TMSOTf,[9d,20] and Sc(OTf)$_3$ for related structures.[10a] Interestingly, it has been reported also that enantiopure *N*-acyliminium derived from **3b** is useful in coupling reactions with silyl enol ethers, obtained from various *β*-ketoesters, ketones, and *β*-diketones,[21] and high stereoselectivity with respect to the lactam ring was obtained for the more sterically demanding nucleophiles. Our results are in line with those cited above and others reported in literature which concern the coupling reaction of chiral *N*-acyliminium cations in the pyrrolidinone series with allyltrimethylsilane.[9b,22,23]

Elsewhere, the 1,3-induction of chirality during the α-amidoalkylation was also examined starting from an α-acetoxy lactam in isoindolinone series **3c** bearing (*S*)-phenylethylamine ((*S*)-PEA) as a chiral auxiliary. Here, the selectivity induced during the *N*-acyliminium trapping of a nucleophile is also similar to that observed above because the reaction products **4cA** and **4cB**, isolated in an excellent yield of 97%, were in a

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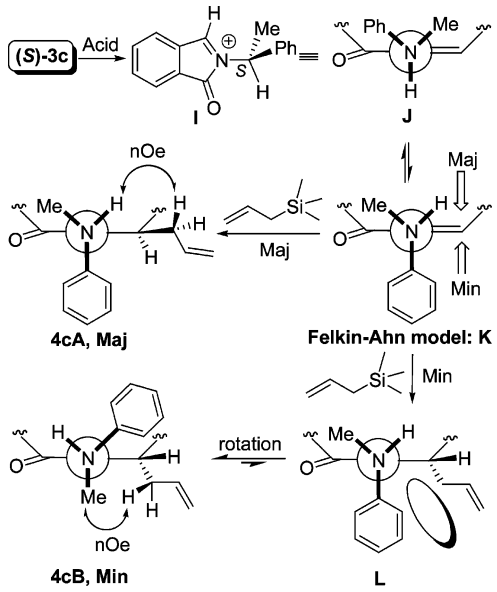
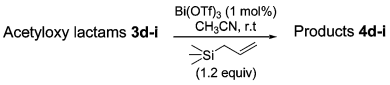
SCHEME 5. Diastereoselective α-Amidoalkylation of Chiral α-Acetoxy Lactam 3c



75:25 ratio. These results are in agreement with those observed for related structures in hydroxy lactams from succinimide[9b,d,22] and phthalimide[23] series. The latter mentioned generally reasonable diastereoselectivity depending on the nature of the acid used, the steric hindrance of the *N*-acyliminium species, and finally the nature of the nucleophiles. On the contrary, high stereoselectivity was obtained, for example, from cyclic *N*,*O*-acetal-trimethyl-silylether or hydroxy imidazolothiazolones and enoxysilanes under the acid influence of both $BF_3{\cdot}Et_2O$ (ee up to 96:4) and TMSOTf (ee up to 98:2)[24] or $BF_3{\cdot}Et_2O$,[25] respectively. Also, an additional study about the total diastereochemistry as well as its reversal of stereoselection was rationalized by a transition state model, using molecular orbital theory and substrate conformational preferences, that was done to clarify the nucleophilic additions to *N*-acyliminium cations.[22] Herein, the determination of the major **4cA** and minor **4cB** diastereomers was based on NOE experiments that involved irradiation of the methylene protons of the allyl group and the proton and methyl residue of the (*S*)-PEA auxiliary of the mixture products **4cA** and **4cB**. In this case, the resulting NMR spectra exhibited a significant NOE enhancement, indicating that the proton of the (*S*)-PEA auxiliary and the methylene allylic protons were spatially proximate in diastereomer **4cA**, but in the case of the minor diastereomer **4cB**, the interaction of the methyl group of the (*S*)-PEA auxiliary and the methylene allylic protons is effective. The stereochemical outcome of the reaction of **3c** with allyltrimethylsilane can be explained as illustrated in Scheme 5. Although the major product **4cA** could be obtained directly by the nucleophilic attack on the opposite side of the phenyl group, the formation of the minor product **4cB** suggests nucleophilic attack occurs from the same side of the phenyl group giving the intermediate **L**, which rotates rapidly about the C−N bond to give the more stable conformer observed in the NOE studies.

To measure the influence of the group attached to the nitrogen atom of the lactam function in the intermolecular α-amidoalkylation process, two methyl acetate derivatives **3d** and **3e** as *N*-acyliminium precursors were prepared according to the general sequence described above and evaluated (Table 2). Indeed, when exposed to 1 mol % of $Bi(OTf)_3$ under the reaction protocol described above, they were converted to the products **4d** and **4e** which resulted from the allylation process in excellent yields of 99 and 94%, respectively. The formation of **4d** was described more recently in 73% yield by desulfurization of 3-allyl-2-benzyl-3-phenylsulfanyl-2,3-dihydroisoindol-1-one using SmI_2 in the presence of HMPA in dry THF.[26] The structure of allyl **4e** is identical to that reported in our laboratory using 5 mol % of TMSOTf in CH_2Cl_2 at 0 °C for 30 min (88%).[9d] In our cases, the yields are better than those cited above and better than those obtained for the amidoalkylation in the furan series of acetate **3a** into **4a**, which is only 64% in the best case (see Scheme 3). From these results, the nature of the group attached to the nitrogen lactam did not exert much influence on the course of the reaction, and it only decreased the yield of the reaction in the case of heteroaromatics.

TABLE 2. Influence of the N Group and the *N*-Acyliminium Cation Stability on the $Bi(OTf)_3$-Catalyzed Intermolecular α-Amidoalkylation of Acetates 3d−i



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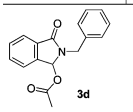
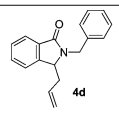
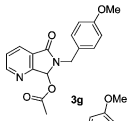
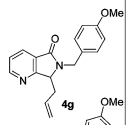
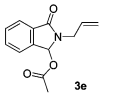
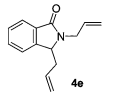
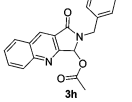
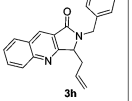
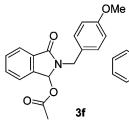
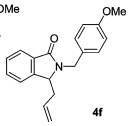
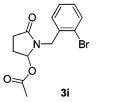
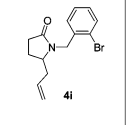
		99			0[a]
		94			92
		82			73

[a] Key: The α-amidoalkylation reaction occurred in 60% yield when the acetate **3g** was treated with allyltrimethylsilane (1.2 equiv) and 300 mol % of $AlCl_3$ (99.99%) in CH_2Cl_2 at room temperature.

Taking into account that *N*-acyliminium ions derived from phthalimide derivatives or equivalents are more stable than those generated from succinimides and related five- and six-membered rings,[2] we decided to investigate the behavior of four α-acetoxy lactams **3f**−**i** as valuable cations for trapping C-nucleophiles (Table 2). These *N*-acyliminium precursors differ essentially by their left parts, which are successively isoindolinone, pyrrolo[3,4-*b*]pyridin-5-one, pyrrolo[3,4-*b*]quinolin-1-one, and pyrrolidin-2-one. The aryl group bears the same substituent to minimize the influence of this block on the alkylation process. Generally, the reaction proceeded cleanly and good to excellent yields (73−95%) of α-allyl lactams **4f**,**h**,**i** were obtained by using our protocol (i.e., 1 mol % of $Bi(OTf)_3$, allyltrimethylsilane (1.2 equiv), CH_3CN, room temperature, 1−12 h) except in the case of **4g**. The relative low yield obtained in the case of pyrrolidinone **4i** (73%) is due to the low stability of the *N*-acyliminium platform intermediate derived from 5-acetoxy-

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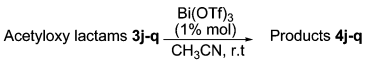
(25) Chavan, S. P.; Chittiboyina, A. G.; Ravindranathan, T.; Kamat, S. K.; Kalkote, U. R. *J. Org. Chem.* **2005**, *70*, 1901−1903.

(26) Hidemi, Y.; Naoki, K.; Kunihiko, T. *Synth. Commun.* **2003**, *33*, 1087−1094.

TABLE 3. Bi(OTf)$_3$-Catalyzed Intramolecular α-Amidoalkylation of Acetoxy Lactams 3j−q



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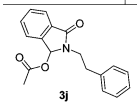
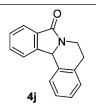
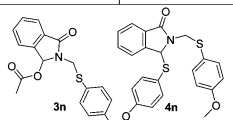
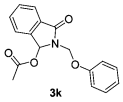
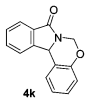
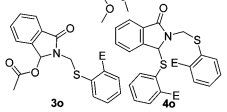
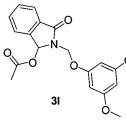
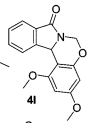
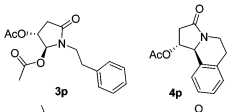
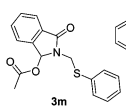
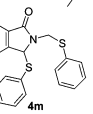
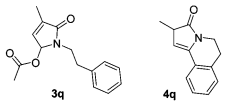
		72			35
		65			43[a]
		65			73
		32			76

[a] E = methoxycarbonyl group (CO_2Me).

pyrrolidin-5-one derivative **3i** compared to those obtained from aromatic and heteroaromatic α-acetoxy lactams **3f**−**h** as mentioned above. Also, in the case of **3i** as the starting material, no byproduct enamide (not presented in the scheme) which would have resulted from the deprotonation of the *N*-acyliminium cation intermediate was observed.

Even after increasing the reaction temperature, the change of solvent, and the reaction time, the crude product resulted from the reaction of acetate in the pyridine series **3g** with Bi(OTf)$_3$ (1 mol %) and allyltrimethylsilane (1.2 equiv) was identified as the starting acetoxy lactam **3g**. Also, no traces of the required allyl product **4g** were formed as indicated by NMR analysis of the crude reaction mixture. We speculated that the origin of the ineffectiveness of the acid-catalyzed α-amidoalkylation could be due probably to the high basicity of the pyridine heterocycle (pK_a = 5.29) compared to the quinoline (pK_a= 4.94), rendering the catalyst inactive by simple complexation with the nitrogen atom. This fact was corroborated by the results obtained when acetate in furan series **3a** was treated as described in Table 1 but with the addition of traces of NEt_3 or DMAP. In these cases, no α-amidoalkylation took place and only the acetoxy lactam **3a** was recovered as starting material. Here, a thermodynamic argument based on the strength of the N−Bi bond vs the O−Bi bond could be considered.

To perform the transformation of **3g** into corresponding allylated product **4g**, additional Lewis acid screening was necessary. α-Acetoxy derivative **3g** remains unchanged or gives only alcohol **2g** when the reaction was catalyzed by $BF_3.Et_2O$, $HNTf_2$ (10%) or $TiCl_4$ using up to 3 equiv relative to the substrate **3g**, respectively. But the α-amidoalkylation reaction work well when 300 mol % of anhydrous $AlCl_3$ with higher analytical grade (99.99%) was used. In fact, with 1.2 equiv. of allyltrimethylsilane in dry CH_2Cl_2 at ambient temperature, the reaction after 3 h gave the expected **4g** in acceptable yields ranging from 56% to 60%.

Encouraged by the effectiveness of the Bi(OTf)$_3$-catalyzed intermolecular α-amidoalkylation reaction, we then reasoned that a suitably and conveniently substituted *N*-acyliminium precursor of type **II** (Scheme 1) could allow a facile approach to the tricyclic compounds **IV** via an intramolecular catalytic π-cationic cyclization. To the best of our knowledge, utilization of the present application to form a central six-membered ring as a piperidine and 1,3-oxazine rings fused to other systems represents a novel illustration of the chemistry of Bi(OTf)$_3$ in organic synthesis. The two reports using catalytic amounts (2 mol %) of Sc(OTf)$_2$ or Sc(OTf)$_3$ to access intramolecularly fused piperidines constitute pioneering work in this field.[12,13]

As a starting point of this study, three kinds of acetates such as *N*-acyliminium precursors were considered (Table 3). We have chosen α-acetoxy lactam **3j** to allow only the π-cationic cyclization, α-acetoxy lactams **3k**−**o** to test the heterocyclization process (possible intramolecular attack of the *N*-acyliminium cation with a heteroatom such as oxygen and sulfur atoms) as a competing reaction to the π-cyclization one, and finally acetates **3p**,**q** to introduce the possible elimination (dehydration) reaction as well as the measurement of the stereocontrol of the intramoleculer π-cyclization case. We expected to obtain these precursors of cyclization from known α-hydroxy lactams **2j**−**o** by esterification using the protocol outlined above in the general Scheme 2. The enantiopure diacetate **3p** was obtained in one step from the known chiral imide **1p**,[27] and acetate **3q** was prepared by a three-step sequence from the commercially available citraconic anhydride (**7**) and phenylethylamine (**8**) (Table 2). Indeed, they were prepared by successive amino−anhydride condensation in refluxing acetic acid for 12 h (88%) and sodium borohydride reduction of the carbonyl function of the resulting imide under mild conditions in the presence of $CeCl_3{\cdot}7H_2O$, followed in an ultimate step by the acylation of the hydroxylactam **2q**, as a minor regioisomer, with Ac_2O according to the protocol described above in 96% yield. It should be noted that, when the reduction of imide **1q** was performed with a known protocol ($NaBH_4$, $CeCl_3{\cdot}7H_2O$),[28] a mixture of two regioisomers in a 3:1 ratio was obtained in 86% yield. The latter was separated by chromatography on a silica gel column using a mixture of AcOEt/cyclohexane (4:1) as the eluent. The choice of the minor regioisomer hydroxylactam **2qB** as a cycle precursor was due to its high purity and its plausible and easy dehydration process under acidic cyclization conditions to give the conjugated enamidone product **10** as a competing process (Scheme 6).

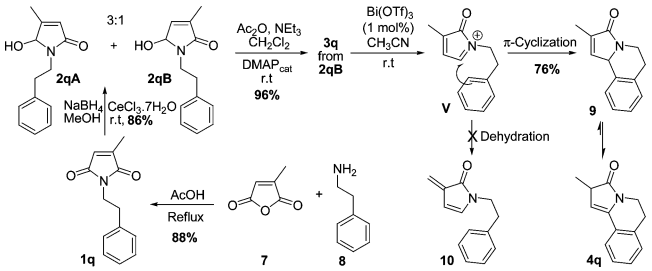
First our attention was directed toward testing the behavior of acetate **3j** toward C-nucleophiles under the catalytic procedure developed above using 1 mol % of Bi(OTf)$_3$. To our surprise, the reaction with 1.2 equiv of allyltrimethylsilane furnished exclusively 5,12*b*-dihydroisoindolo[1,2-*a*]isoquinolin-8(6*H*)-one (**4j**) in 72% yield which was confirmed by spectroscopic assays and comparison with the ^{1}H NMR spectra of an authentic sample.[10b,29] From this result, no allyltrimethylsilane was needed because only the *N*-acyliminium π-cyclization took place exclusively. In fact, when the reaction was conducted without

(27) Lee, Y. S.; Kang, D. W.; Lee, S.-J.; Park, H. *J. Org. Chem.* **1995**, *60*, 7149−7152.

(28) (a) Mase, N.; Nishi, T.; Hiyoshi, M.; Ichihara, K.; Bessho, J.; Yoda, H.; Takabe, K. *J. Chem. Soc., Perkin Trans. 1* **2002**, 707−709. (b) Robert, S. Coleman, R. S.; Liu, P.-H. *Org. Lett.* **2004**, *6*, 577−580.

(29) Katritzky, A. R.; Mehta, S.; He, H.-Y. *J. Org. Chem.* **2001**, *66*, 148−152 and references therein.

SCHEME 6. Generation and Intramolecular α-Amidoalkylation of Acetoxy Lactam 3q



adding the silane, the same tricyclic system was obtained in comparable yield.

Having established the capacity of $Bi(OTf)_3$ to promote the capture of an *N*-acyliminium ion in an intramolecular manner, we sought to determine whether this protocol might be extendable to other functionalities such as *N*-aryloxymethylamidals, *N*-arylthiomethylamidals, and *N*-arylethylamidals in chiral or achiral form. Significant structural variation in the π-aromatic system as well as in azacycles as an *N*-acyliminium source can also be realized. More importantly, the $Bi(OTf)_3$-catalyzed intramolecular π-cationic cyclization appears to be quite tolerant toward to the *N*,*O*-acetal functionality in substrates **3k** and **3l**. In these cases, only products 6,12*b*-dihydroisoindolo[1,3-*c*][1,3]-benzoxazin-8-one **4k** and 1,3-dimethoxy derivative **4l** were isolated in 65% yield in each case after chromatographic purification. These structures are identical to that obtained earlier by us through intramolecular arylation of an *N*-acyliminium ion in neat TFA at room temperature for 12 h.[30] The use of $Bi(OTf)_3$ has particularly a beneficial effect on the yield of product **4l**. This may be attributed to a decreased cleavage of the CH_2-O linkage of the methoxy group as a benzene substituent with Lewis acid $Bi(OTf)_3$ instead of TFA. In contrast, substrates bearing the *N*,*S*-acetal function such as that in **3m**−**o** led only to the corresponding *S*,*N*,*S*-diacetals **4m**−**o** in yields of 32,[8c] 35, and 43%, respectively.[31] These products were formed by addition of a thiophenate ion, generated in situ by cleavage of the CH_2-S linkage under $Bi(OTf)_3$ influence, to the not yet cleaved *N*-acyliminium cation. Our group has already observed similar results in sulfur[8c] and oxygen[32] series using TFA as an *N*-acyliminium promoter. Whatever the changes in the experimental conditions, neither the π-cationic cyclization nor the tandem thiocyclization/isomerization/π-cyclization cascade products were detected.

On the other hand, the *N*-acyliminium cyclization of chiral *trans*-diacetate **3p**, derived from L-malic acid in a known three-step sequence, with 1 mol % of $Bi(OTf)_3$ according to our established protocol proceeded cleanly to provide (1*S*,10*bR*)-1-acetoxy-1,2,3,5,6,10*b*-hexahydropyrrolo[2,1-*a*]isoquinolin-3-one (**4p**) in 73% yield as a single diastereomer. Both the yield and stereochemistry of this compound are similar to those reported by the Park group.[27] In the ultimate stage, the behavior of an acetoxy lactam **3q** in a partially reduced pyrrolidinone nucleus was examined under the bismuth triflate catalyzed π-cyclization protocol. Thus, under these conditions, we isolated in 76% yield (Table 2 and Scheme 6) the tricyclic system **4q** in which the double bond of the dihydropyrrole ring is in conjugation with the benzene ring. This is produced with the intermediacy of the azacycle **9** which isomerizes spontaneously into **4q** as the thermodynamic isomer. Also, no traces of **9** and **10** were detected in the reaction mixture.

The structure of all products and intermediates reported herein was confirmed by their ^1H and ^{13}C NMR spectra including DEPT programs as well as NOE measurements and elemental analyses.

Conclusion

In these preliminary studies, intermolecular α-amidoalkylation of various α-acetoxy lactams with C-nucleophiles such as silanes and enoxysilanes have been successfully carried out in the presence of a catalytic amount of bismuth triflate ($Bi(OTf)_3$). The reaction works best with 1 mol % of catalysts and 1.2−1.5 equiv of allyltrimethylsilane in acetonitrile at ambient temperature under strict anhydrous conditions. In contrast to the existing alkylation of *N*-acyliminium ion processes which use many acidic catalysts, our method is very cheap, is characterized by operational simplicity, and uses an easy to handle and nontoxic catalyst. Also, the reaction protocol is high yielding, tolerates structural and substrate diversity, shows no formation of byproducts as well as decomposition products, and more importantly is environmental friendly.

In addition, we have demonstrated also the utility of this methodology in intramolecular arylation of α-acetoxy lactams via the intermediacy of *N*-acyliminium cations which allows construction of polyfunctionalized six-membered fused heterocyclic systems including isoindolinone and pyrrolidinone in chiral form or not. These scaffolds constitute a frequent central core of various alkaloids as well as their heterologues. Thus, we anticipate that the high catalytic properties of bismuth triflate developed in this project will find further applications in organic synthesis using an *N*-acyliminium template to access mainly extremely large libraries of small molecules with significant potential in biological and pharmacological areas. Finally, further explorations of the scope, selectivity, stereocontrol, and related mechanistic considerations are now under investigation in our group, and the results will be published soon as a full account.

Experimental Section

General Procedure for the One-Pot Reduction/Acetylation Process of the Imides 1b,i,p. To a solution of imides **1a**−**q** (3 mmol) in 16 mL of anhydrous dichloromethane was added dropwise at −60 °C a commercially available solution of $LiEt_3BH$ (1 M) in THF (3.6 mL, 3.6 mmol, 1.2 equiv). The solution was stirred for 15−30 min at the same temperature, and acetic anhydride (0.43 mL, 4.5 mmol, 1.5 equiv) was added dropwise at −60 °C. The solution was quenched by addition of an aqueous solution of $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (20 mL), and organic layers were combined, washed with water, dried over $MgSO_4$, and evaporated to dryness. The acetate derivative **3b**,**i**,**p** was obtained in yields ranging from 65 to 95%. In certain cases, additional chromatographic purification on a silica gel column, eluting with cyclohexane/AcOEt (1:1), was necessary.

General Procedure for the Acetylation of Hydroxy Lactams 2a-q. Acetic anhydride (2 equiv) was added dropwise to a solution

(30) Hucher, N.; Daïch, A.; Decroix, B. *J. Heterocycl. Chem.* **1998**, *35*, 1477−1483.

(31) Taking into account that 2 equiv of starting materials **3m**−**o** was necessary for the formation of the disulfurs **4m**−**o**, these products may be obtained at maximum efficiency in 50% yields.

(32) Cul, A.; Chihab-Eddine, A.; Pesquet, A.; Marchalín, Š.; Daïch, A. *J. Heterocycl. Chem.* **2003**, *40*, 499−505.

of the hydroxy lactam (1 equiv), NEt_3 (2 equiv), and DMAP (0.1 equiv) in CH_2Cl_2 (10 mL per 1 mmol of hydroxy lactam **2**). The mixture was stirred at room temperature overnight and quenched by addition of a saturated aqueous solution of $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (20 mL), and organic layers were combined, dried over $MgSO_4$, and evaporated. The acetate derivative **3** was then obtained after purification of the residue by chromatography on a silica gel column.

3-Acetoxy-2-(furan-2-ylmethyl)-isoindolin-1-one (3a). This product was isolated as a brown solid: 86% yield; R_f 0.61 (cyclohexane/AcOEt 1:1); mp 103 °C; IR (KBr) ν 3690, 1741, 1717, 1470, 1618 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.09 (s, 3H, CH_3), 4.48 (d, 1H, J = 15.6 Hz, CH_2N), 4.91 (d, 1H, J = 15.6 Hz, CH_2N), 6.27−6.29 (m, 2H, H_{fur}), 6.96 (s, 1H, CH), 7.32 (s broad, 1H, H_{fur}), 7.45−7.58 (m, 3H, H_{aro}), 7.79−7.83 (m, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3), 37.1 (CH_2), 81.2 (CH), 108.8 (CH_{aro}), 110.6 (CH_{aro}), 123.9 (CH_{aro}), 124.1 (CH_{aro}), 130.4 (CH_{aro}), 131.8 (C_q), 132.7 (CH_{aro}), 141.2 (C_q), 142.8 (CH_{aro}), 150.0 (C_q), 167.6 (C═O), 171.2 (C═O). Anal. Calcd for $C_{15}H_{13}NO_4$ (271.08): C, 66.41; H, 4.83; N, 5.16. Found: C, 66.33; H, 4.73; N, 5.09.

3(*S*)- and 3(*R*)-Acetoxy-2-(1(*S*)-phenylethyl)isoindolin-1-one (3c). This mixture was isolated as an inseparable brown oil in a 60:40 ratio: 97% yield; R_f 0.72 (cyclohexane/AcOEt 1:1); IR (KBr) ν 1739, 1709, 1470, 1401, 1374 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (s, 1.6H, CH_3), 1.64 (d, 3H, J = 7.0 Hz, CH_3), 2.00 (s, 1.4H, CH_3-CO), 5.44−5.61 (m, 1H, CHN), 6.57 (s, 0.4H, CH−OAc), 7.11 (s, 0.6H, CH−OAc), 7.14−7.26 (m, 3H, H_{aro}), 7.29−7.46 (m, 5H, H_{aro}), 7.65−7.77 (m, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 16.9 (CH_3 maj.), 18.3 (CH_3 min.), 20.5 (CH_3 min.), 21.4 (CH_3 maj.), 49.2 (CH maj.), 50.9 (CH min.), 79.1 (CH maj.), 81.4 (CH min.), 123.6 (CH_{aro} maj.), 123.7 (CH_{aro} min.), 123.9 (CH_{aro} maj.), 124.0 (CH_{aro} min.), 127.5 (CH_{aro}), 127.5 ($2CH_{aro}$ maj.), 127.6 ($2CH_{aro}$ min.), 128.4 ($2CH_{aro}$ maj.), 129.0 ($2CH_{aro}$ min.), 130.3 (CH_{aro} min.), 130.4 (CH_{aro} maj.), 132.7 (CH_{aro}), 139.7 (C_q), 140.8 (C_q), 141.4 (C_q maj.), 141.5 (C_q min.), 168.0 (C═O min.), 168.2 (C═O maj.), 170.7 (C═O min.), 170.8 (C═O maj.). Anal. Calcd for $C_{18}H_{17}NO_3$ (295.12): C, 73.20; H, 5.80; N, 4.74. Found: C, 73.13; H, 5.69; N, 4.61.

3-Acetoxy-2-benzylisoindolin-1-one (3d). This product was isolated as a white solid: 94% yield; R_f 0.59 (cyclohexane/AcOEt 1:1); mp 95 °C; IR (KBr) ν 1711, 1687, 1471, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.88 (s, 3H, CH_3), 4.48 (d, 1H, J = 14.9 Hz, CH_2N), 4.85 (d, 1H, J = 14.9 Hz, CH_2N), 6.86 (s, 1H, CH), 7.19−7.24 (m, 5H, H_{aro}), 7.44−7.52 (m, 3H, H_{aro}), 7.78−7.83 (m, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 20.9 (CH_3), 42.8 (CH_2), 81.2 (CH), 123.6 ($2CH_{aro}$), 127.8 (CH_{aro}), 128.7 ($2CH_{aro}$), 128.9 ($2CH_{aro}$), 130.0 (CH_{aro}), 131.4 (C_q), 132.6 (CH_{aro}), 136.9 (C_q), 144.1 (C_q), 167.3 (C═O), 176.7 (C═O). Anal. Calcd for $C_{17}H_{15}NO_3$ (281.11): C, 72.58; H, 5.37; N, 4.98. Found: C, 72.42; H, 5.28; N, 4.83.

2-Allyl-3-acetoxyisoindolin-1-one (3e). This product was isolated as a yellow oil: 84% yield; R_f 0.78 (cyclohexane/AcOEt 1:1); IR (KBr) ν 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.11 (s, 3H, CH_3), 3.92 (dd, 1H, J = 15.6 and 6.5 Hz, CH_2N), 4.36 (dd, 1H, J = 15.6 and 5.4 Hz, CH_2N), 5.20 (dd, 1H, J = 16.4 and 1.6 Hz, ═CH_2), 5.24 (dd, 1H, J = 7.7 and 1.6 Hz, ═CH_2), 5.72−5.92 (m, 1H, ═CH), 6.98 (s, 1H, CH), 7.49−7.57 (m, 3H, H_{aro}), 7.77−7.83 (m, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3), 43.2 (CH_2), 81.2 (CH), 118.1 (CH_2), 123.9 (CH_{aro}), 124.1 (CH_{aro}), 130.5 (CH_{aro}), 132.0 (C_q), 132.7 (CH_{aro}), 132.8 (CH_{aro}), 141.2 (C_q), 167.8 (C═O), 171.2 (C═O). Anal. Calcd for $C_{13}H_{13}NO_3$ (231.09): C, 67.52; H, 5.67; N, 6.06. Found: C, 67.40; H, 5.49; N, 5.94.

3-Acetoxy-2-(4-methoxybenzyl)-isoindolin-1-one (3f). This product was isolated as a yellow solid: 93% yield; R_f 0.58 (cyclohexane/AcOEt 1:1); mp 77 °C; IR (KBr) ν 1739, 1712, 1247 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 4.38 (d, 1H, J = 14.9 Hz, CH_2N), 4.89 (d, 1H, J = 14.9 Hz, CH_2N), 6.82 (d, 2H, J = 8.6 Hz, H_{aro}), 6.88 (s, 1H, CH), 7.22 (d, 2H, J = 8.6 Hz, H_{aro}), 7.43−7.55 (m, 3H, H_{aro}), 7.81−7.85 (m, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 21.0 (CH_3), 43.8 (CH_2), 55.4 (CH_3), 80.9 (CH), 114.2 ($2CH_{aro}$), 123.9 (CH_{aro}), 124.0 (CH_{aro}), 128.8 (C_q), 129.8 ($2CH_{aro}$), 130.5 (CH_{aro}), 132.0 (C_q), 132.6 (CH_{aro}), 141.1 (C_q), 159.3 (C_q), 168.0 (C═O), 171.2 (C═O). Anal. Calcd for $C_{18}H_{17}NO_4$ (311.12): C, 69.44; H, 5.50; N, 4.50. Found: C, 69.32; H, 5.38; N, 4.41.

7-Acetoxy-6,7-dihydro-6-(4-methoxybenzyl)-5*H*-pyrrolo[3,4-*b*]pyridin-5-one (3g). This product was isolated as a yellow solid: 100% yield; R_f 0.53 (cyclohexane/AcOEt 1:4); mp 81 °C; IR (KBr) ν 2981, 1744, 1717, 1612, 1473 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 4.49 (d, 1H, J = 14.9 Hz, CH_2N), 4.84 (d, 1H, J = 14.9 Hz, CH_2N), 6.83 (d, 2H, J = 8.6 Hz, H_{aro}), 6.99 (s, 1H, CH), 7.26 (d, 2H, J = 8.6 Hz, H_{aro}), 7.45 (dd, 1H, J = 7.8 and 4.7 Hz, H_{aro}), 8.12 (dd, 1H, J = 7.8 and 1.6 Hz, H_{aro}), 8.73 (dd, 1H, J = 4.7 and 1.6 Hz, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 20.9 (CH_3), 44.0 (CH_2), 55.5 (CH_3), 79.9 (CH), 114.3 ($2CH_{aro}$), 125.1 (CH_{aro}), 126.3 (C_q), 128.8 (C_q), 129.9 ($2CH_{aro}$), 132.1 (CH_{aro}), 155.5 (CH_{aro}), 159.2 (C_q), 161.1 (C_q), 166.3 (C═O), 170.6 (C═O). Anal. Calcd for $C_{17}H_{16}N_2O_4$ (312.11): C, 65.38; H, 5.16; N, 8.97. Found: C, 65.38; H, 5.16; N, 8.97.

3-Acetoxy-2,3-dihydro-2-(4-methoxybenzyl)-1*H*-pyrrolo[3,4-*b*]quinolin-1-one (3h). This product was isolated as a brown solid: 92% yield; R_f 0.43 (cyclohexane/AcOEt 1:1); mp 144 °C; IR (KBr) ν 1749, 1716, 1635, 1614 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 4.57 (d, 1H, J = 14.9 Hz, CH_2N), 4.90 (d, 1H, J = 14.9 Hz, CH_2N), 6.83 (d, 2H, J = 8.6 Hz, H_{aro}), 7.10 (s, 1H, CH), 7.30 (d, 2H, J = 8.6 Hz, H_{aro}), 7.64 (dd, 1H, J = 7.8 and 7.0 Hz, H_{aro}), 7.83 (dd, 1H, J = 8.6 and 7.0 Hz, H_{aro}), 8.18 (d, 1H, J = 7.8 Hz, H_{aro}), 8.19 (d, 1H, J = 8.4 Hz, H_{aro}), 8.61 (s, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 21.0 (CH_3), 44.2 (CH_2), 55.5 (CH_3), 80.3 (CH), 114.3 ($2CH_{aro}$), 123.2 (C_q), 128.0 (CH_{aro}), 128.3 (C_q), 128.8 (C_q), 129.8 (CH_{aro}), 129.9 ($2CH_{aro}$), 130.0 (CH_{aro}), 132.0 (CH_{aro}), 133.2 (CH_{aro}), 150.3 (C_q), 159.2 (C_q), 159.4 (C_q), 166.3 (C═O), 170.7 (C═O). Anal. Calcd for $C_{21}H_{18}N_2O_4$ (362.13): C, 69.60; H, 5.01; N, 7.73. Found: C, 69.49; H, 4.87; N, 7.66.

5-Acetoxy-1-(2-bromobenzyl)-pyrrolidin-2-one (3i). This product was isolated as a colorless oil: 96% yield; R_f 0.52 (cyclohexane/AcOEt 1:1); IR (KBr) ν 3154, 1706, 1602 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 (s, 3H, CH_3), 2.01−2.15 (m, 1H, CH_2), 2.20−2.70 (m, 3H, CH_2), 4.41 (d, 1H, J = 15.7 Hz, CH_2N), 4.80 (d, 1H, J = 15.7 Hz, CH_2N), 6.06 (d, 1H, J = 5.5 Hz, CH), 7.08−7.18 (m, 1H, H_{aro}), 7.22−7.28 (m, 2H, H_{aro}), 7.53 (d, 1H, J = 7.8 Hz, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3), 26.3 (CH_2), 28.3 (CH_2), 44.9 (CH_2), 85.1 (CH), 123.9 (C_q), 127.9 (CH_{aro}), 129.5 (CH_{aro}), 130.2 (CH_{aro}), 133.2 (CH_{aro}), 135.4 (C_q), 170.6 (C═O), 175.9 (C═O). Anal. Calcd for $C_{13}H_{14}BrNO_3$ (311.02): C, 50.02; H, 4.52; N, 4.49. Found: C, 49.00; H, 4.39; N, 4.40.

3-Acetoxy-2-phenethylisoindolin-1-one (3j). This product was isolated as a colorless oil: 100% yield; R_f 0.60 (cyclohexane/AcOEt 1:1); IR (KBr) ν 3064, 3030, 2939, 1739, 1713, 1618, 1604, 1497, 1470, 1414, 1372 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.13 (s, 3H, CH_3), 2.85−3.18 (m, 2H, CH_2), 3.48 (ddd, 1H, J = 14.5, 9.0, and 6.2 Hz, CH_2N), 4.03 (ddd, 1H, J = 14.5, 8.6, and 6.3 Hz, CH_2N), 6.89 (s, 1H, CH), 7.21−7.29 (m, 5H, H_{aro}), 7.49−7.56 (m, 3H, H_{aro}), 7.79−7.84 (m, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3), 34.8 (CH_2), 42.1 (CH_2), 81.4 (CH), 123.7 (CH_{aro}), 124.0 (CH_{aro}), 126.7 (CH_{aro}), 128.8 ($2CH_{aro}$), 129.0 ($2CH_{aro}$), 130.4 (CH_{aro}), 132.1 (C_q), 132.5 (CH_{aro}), 138.6 (C_q), 141.0 (C_q), 168.0 (C═O), 171.3 (C═O). Anal. Calcd for $C_{18}H_{17}NO_3$ (295,12): C, 73.20; H, 5.80; N, 4.74. Found: C, 73.09; H, 5.69; N, 4.68.

3-Acetoxy-2-(phenoxymethyl)-isoindolin-1-one (3k). This product was isolated as a white solid: 83% yield; R_f 0.53 (cyclohexane/AcOEt 1:1); mp 127 °C; IR (KBr) ν 1725, 1599, 1497, 1470 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.14 (s, 3H, CH_3), 5.36 (d, 1H, J = 10.5 Hz, CH_2N), 5.77 (d, 1H, J = 10.5 Hz, CH_2N), 6.93−7.07 (m, 3H, H_{aro}), 7.18 (s, 1H, CH), 7.22−7.31 (m, 2H, H_{aro}), 7.49−7.54 (m, 3H, H_{aro}), 7.81−7.87 (m, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3),

68.3 (CH_2), 80.3 (CH), 115.7 (2CH_{aro}), 122.2 (CH_{aro}), 124.4 (CH_{aro}), 124.5 (CH_{aro}), 129.8 (2CH_{aro}), 130.7 (CH_{aro}), 131.1 (C_q), 133.4 (CH_{aro}), 141.4 (C_q), 156.4 (C_q), 167.8 (C═O), 171.1 (C═O). Anal. Calcd for $C_{17}H_{15}NO_4$ (297.1): C, 68.68; H, 5.09; N, 4.71. Found: C, 68.60; H, 5.00; N, 4.59.

3-Acetoxy-2-((3,5-dimethoxyphenoxy)methyl)-isoindolin-1-one (3l). This product was isolated as a white solid: 100% yield; R_f 0.53 (cyclohexane/AcOEt 1:1); mp 102 °C; IR (KBr) ν 2964, 2843, 1724, 1598, 1471 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.14 (s, 3H, CH_3), 3.73 (s, 6H, OCH_3), 5.32 (d, 1H, J = 11.0 Hz, CH_2N), 5.73 (d, 1H, J = 11.0 Hz, CH_2N), 6.09 (s broad, 1H, H_{aro}), 6.26 (s broad, 2H, H_{aro}), 7.16 (s, 1H, CH), 7.52−7.57 (m, 3H, H_{aro}), 7.84 (d, 1H, J = 6.3 Hz, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3), 55.6 (2OCH_3), 68.1 (CH_2), 80.3 (CH), 94.1 (2CH_{aro}), 94.7 (CH_{aro}), 124.4 (CH_{aro}), 124.5 (CH_{aro}), 130.7 (CH_{aro}), 131.1 (C_q), 134.4 (CH_{aro}), 141.4 (C_q), 158.2 (C_q), 161.7 (2C_q), 167.8 (C═O), 171.1 (C═O). Anal. Calcd for $C_{19}H_{19}NO_6$ (357.12): C, 63.86; H, 5.36; N, 3.92. Found: C, 63.69; H, 5.27; N, 3.77.

3-Acetoxy-2-((4-methoxyphenylthio)methyl)-isoindolin-1-one (3n). This product was isolated as a white solid: 66% yield; R_f 0.62 (cyclohexane/AcOEt 1:1); mp 108 °C; IR (KBr) ν 1721, 1594 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.09 (s, 3H, CH_3), 3.74 (s, 3H, OCH_3), 4.44 (d, 1H, J = 14.1 Hz, CH_2N), 5.30 (d, 1H, J = 14.1 Hz, CH_2N), 6.76 (d, 2H, J = 8.6 Hz, H_{aro}), 7.16 (s, 1H, CH), 7.35 (d, 2H, J = 8.6 Hz, H_{aro}), 7.44−7.56 (m, 3H, H_{aro}), 7.70−7.80 (m, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3), 46.4 (CH_2), 55.5 (OCH_3), 80.3 (CH), 114.9 (2CH_{aro}), 123.5 (C_q), 124.0 (CH_{aro}), 124.5 (CH_{aro}), 130.5 (CH_{aro}), 131.5 (C_q), 133.0 (CH_{aro}), 135.1 (2CH_{aro}), 141.1 (C_q), 160.1 (C_q), 167.2 (C═O), 171.1 (C═O). Anal. Calcd for $C_{18}H_{17}NO_4S$ (343.09): C, 62.96; H, 4.99; N, 4.08. Found: C, 62.8196; H, 4.80; N, 4.00.

3-Acetoxy-2-(*o*-methoxycarbonylphenylthiomethyl)-isoindolin-1-one (3o). This product was isolated as a yellow solid: 93% yield; R_f 0.64 (cyclohexane/AcOEt 1:1); mp 103 °C; IR (KBr) ν 1718, 1605, 1422 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.12 (s, 3H, CH_3), 3.86 (s, 3H, OCH_3), 4.61 (d, 1H, J = 14.1 Hz, CH_2N), 5.55 (d, 1H, J = 14.1 Hz, CH_2N), 7.13 (s, 1H, CH), 7.14−7.22 (m, 1H, H_{aro}), 7.38−7.64 (m, 5H, H_{aro}), 7.75−7.80 (m, 1H, H_{aro}), 7.88 (dd, 1H, J = 7.8 and 1.6 Hz, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3), 42.7 (CH_2), 52.4 (OCH_3), 80.6 (CH), 124.0 (CH_{aro}), 124.7 (CH_{aro}), 125.8 (CH_{aro}), 128.5 (CH_{aro}), 129.6 (C_q), 130.6 (CH_{aro}), 131.3 (C_q), 131.4 (CH_{aro}), 132.8 (CH_{aro}), 133.1 (CH_{aro}), 137.4 (C_q), 141.2 (C_q), 167.1 (C═O), 167.6 (C═O), 171.0 (C═O). Anal. Calcd for $C_{19}H_{17}NO_5S$ (371.08): C, 61.44; H, 4.61; N, 3.77. Found: C, 61.31; H, 4.54; N, 3.59.

(4*R*,5*S*)-4,5-Diacetoxy-1-phenethylpyrrolidin-2-one (3p). This product was isolated as a colorless oil: 95% yield; R_f 0.51 (cyclohexane/AcOEt 1:1); IR (KBr) ν 1748, 1714, 1455, 1422, 1376 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.02 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.62 (t, 2H, J = 8.6 Hz, CH_2), 2.70−2.98 (m, 2H, CH_2), 3.23 (ddd, 1H, J = 14.8, 8.6, and 6.3 Hz, CH_2), 3.80 (ddd, 1H, J = 14.8, 8.6, and 6.3 Hz, CH_2), 5.14 (td, 1H, J = 8.6 and 5.5 Hz, CH), 6.17 (d, 1H, J = 4.7 Hz, CH), 7.15−7.32 (m, 5H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 20.7 (CH_3), 21.0 (CH_3), 34.0 (CH_2), 34.2 (CH_2), 42.6 (CH_2), 66.3 (CH), 82.1 (CH), 126.9 (CH_{aro}), 128.8 (2CH_{aro}), 128.9 (2CH_{aro}), 138.1 (C_q), 170.1 (C═O), 170.6 (C═O), 171.8 (C═O). Anal. Calcd for $C_{16}H_{19}NO_5$ (305.13): C, 62.94; H, 6.27; N, 4.59. Found: C, 62.82; H, 6.14; N, 4.41.

5-Acetoxy-2,5-dihydro-3-methyl-1-phenethyl-1*H*-pyrrol-2-one (3q). This product was isolated as a yellow oil: 85% yield; R_f 0.65 (cyclohexane/AcOEt 1:1); IR (KBr) ν 1736, 1710, 1658, 1455, 1418, 1373, 1233 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.89 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.72−2.90 (m, 2H, CH_2), 3.33 (ddd, 1H, J = 14.8, 8.6, and 6.2 Hz, NCH_2), 3.79 (ddd, 1H, J = 14.8, 8.6, and 7.1 Hz, NCH_2), 6.24 (s, 1H, CH), 6.49 (s, 1H, ═CH), 7.16−7.31 (m, 5H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 11.1 (CH_3), 21.1 (CH_3), 34.8 (CH_2), 42.2 (CH_2), 81.7 (CH), 126.7 (CH_{aro}), 128.7 (2CH_{aro}), 129.0 (2CH_{aro}), 134.8 (CH_{aro}), 138.7 (2C_q), 170.8 (C═O), 170.9 (C═O). Anal. Calcd for $C_{15}H_{17}NO_3$ (259.12): C, 69.48; H, 6.61; N, 5.40. Found: C, 69.31; H, 6.49; N, 5.31.

General Procedure for the Intermolecular and Intramolecular Bi(OTf)$_3$ α-Amidoalkylation of the Acetates 3a−i and 3j−q. To a stirred solution of the *N*-acyliminium ion precursor **3** (1 equiv) and allyltrimethylsilane (1.2 equiv) (2-trimethylsiloxypropene (1.5 equiv) or 1-phenyl-1-trimethylsiloxyethylene (1.5 equiv)) in dry CH_3CN (5 mL per 1 mmol of the acetate **3a−q**) was added in one portion of $Bi(OTf)_3$ (0.01 equiv). In the intramolecular $Bi(OTf)_3$ α-amidoalkylation version, no external C-nucleophile was needed. When the reaction was over (monitored by TLC using CH_2Cl_2 as eluent), a saturated aqueous solution of $NaHCO_3$ was added. The aqueous layer was then extracted with CH_2Cl_2 (10 mL), and the organic layers were combined, dried over $MgSO_4$, and evaporated. The resulting product was purified by chromatography on a silica gel column or by recrystallization to give the expected products in appreciable yields.

3-Allyl-2-(furan-2-ylmethyl)-isoindolin-1-one (4a). This product was isolated as a colorless oil: 64% yield; R_f 0.61 (cyclohexane/AcOEt 1:1); IR (KBr) ν 2927, 1794, 1683, 1470, 1431, 1411 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.70−2.77 (m, 2H, CH_2), 4.24 (d, 1H, J = 15.6 Hz, CH_2N), 4.51 (dd, 1H, J = 5.5 and 3.9 Hz, CH), 4.95 (d, 1H, J = 9.4 Hz, CH_2═), 5.02 (d, 1H, J = 15.6 Hz, CH_2═), 5.21−5.43 (m, 1H, CH═), 5.26 (d, 1H, J = 15.6 Hz, CH_2N), 6.28 (d, 2H, J = 1.6 Hz, H_{fur}), 7.24−7.53 (m, 4H, H_{aro}), 7.82 (d, 1H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 35.4 (CH_2), 36.8 (CH_2), 58.7 (CH), 108.6 (CH_{aro}), 110.6 (CH_{aro}), 119.4 (CH_2), 122.5 (CH_{aro}), 123.9 (CH_{aro}), 128.3 (CH_{aro}), 131.4 (CH_{aro}), 131.6 (CH_{aro}), 132.3 (C_q), 142.5 (CH_{aro}), 145.0 (C_q), 150.7 (C_q), 168.3 (C═O). Anal. Calcd for $C_{16}H_{15}NO_2$ (253.11): C, 75.87; H, 5.97; N, 5.53. Found: C, 75.66; H, 5.80; N, 5.42.

3(*S*)- and 3(*R*)-2-(1(*S*)-Phenylethyl)isoindolin-1-one (4cA and 4cB). This mixture was isolated as a brown oil in an inseparable 75:25 ratio: 97% yield; R_f 0.72 (cyclohexane/AcOEt 1:1); IR (KBr) ν 1677, 1470, 1451, 1398 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.78 (d, 1H, J = 7.0 Hz, CH_3), 1.82 (d, 2H, J = 7.0 Hz, CH_3), 2.15−2.29 (m, 0.7H, CH_2 maj. + min.), 2.44−2.67 (m, 1.3H, CH_2 maj. + min.), 4.26 (dd, 0.4H, J = 6.3 and 2.4 Hz, CH−CH_2), 4.62−4.93 (m, 2H, ═CH_2), 4.66−4.71 (m, 0.6H, CH−CH_2), 5.05−5.25 (m, 0.7H, CH═), 5.22−5.39 (m, 0.3H, CH═), 5.50 (q, 0.7H, J = 7.0 Hz, NCH−CH_3), 5.62 (q, 0.3H, J = 7.0 Hz, NCH−CH_3), 7.18−7.50 (m, 8H, H_{aro}), 7.81−7.86 (m, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 17.7 (CH_3 maj.), 18.5 (CH_3 min.), 36.6 (CH_2 maj.), 37.0 (CH_2 min.), 50.7 (CH maj.), 51.3 (CH min.), 58.9 (CH maj.), 59.2 (CH min.), 119.1 (CH_2 maj.), 119.3 (CH_2 min.), 122.5 (CH_{aro} min.), 122.6 (CH_{aro} maj.), 123.8 (CH_{aro} min.), 123.8 (CH_{aro} maj.), 127.6 (2CH_{aro} maj.), 127.6 (2CH_{aro} min.), 127.8 (CH_{aro} min.), 127.9 (CH_{aro} maj.), 128.2 (CH_{aro} min.), 128.3 (CH_{aro} maj.), 128.6 (2CH_{aro} maj.), 128.8 (2CH_{aro} min.), 131.4 (CH_{aro} maj.), 131.5 (CH_{aro} min.), 131.6 (CH_{aro}), 132.5 (C_q min.), 132.8 (C_q maj.), 140.4 (C_q min.), 142.0 (C_q maj.), 145.3 (C_q), 169.1 (C═O min.), 169.2 (C═O maj.). Anal. Calcd for $C_{19}H_{19}NO$ (277.15): C, 82.28; H, 6.90; N, 5.05. Found: C, 82.05; H, 6.77; N, 4.87.

3-Allyl-2-benzylisoindolin-1-one (4d). This product was isolated as a colorless oil: 99% yield; R_f 0.71 (cyclohexane/AcOEt 1:1); IR (KBr) ν 3687, 1681, 1520, 1414 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.58−2.65 (m, 2H, CH_2), 4.11 (d, 1H, J = 15.6 Hz, CH_2N), 4.37 (t, 1H, J = 4.7 Hz, CH), 4.90−5.02 (m, 2H, ═CH_2), 5.22−5.31 (m, 1H, ═CH), 5.38 (d, 1H, J = 15.6 Hz, CH_2N), 7.20−7.50 (m, 8H, H_{aro}), 7.83 (d, 1H, J = 6.3 Hz, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 35.4 (CH_2), 44.0 (CH_2), 58.1 (CH), 119.5 (CH_2), 122.6 (CH_{aro}), 124.0 (CH_{aro}), 127.8 (CH_{aro}), 128.3 (2CH_{aro}), 128.4 (CH_{aro}), 129.0 (2CH_{aro}), 131.4 (CH_{aro}), 131.6 (CH_{aro}), 132.5 (C_q), 137.3 (C_q), 145.0 (C_q), 168.7 (C═O). Anal. Calcd for $C_{18}H_{17}NO$ (263.13): C, 82.10; H, 6.51; N, 5.32. Found: C, 82.01; H, 6.34; N, 5.21.

3-Allyl-2-(4-methoxybenzyl)-isoindolin-1-one (4f). This product was isolated as a yellow oil: 87% yield; R_f 0.56 (cyclohexane/AcOEt 1:1); IR (KBr) ν 3681, 1679, 1513, 1470, 1412 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.63−2.73 (m, 2H, CH_2), 3.78 (s, 3H, OCH_3),

4.10 (d, 1H, J = 14.9 Hz, CH_2N), 4.41 (t, 1H, J = 4.7 Hz, CH), 4.95−5.01 (m, 2H, $=CH_2$), 5.27−5.45 (m, 1H, J = 7.7 Hz, =CH), 5.36 (d, 1H, J = 14.9 Hz, CH_2N), 6.84 (d, 2H, J = 8.6 Hz, H_{aro}), 7.22 (d, 2H, J = 8.6 Hz, H_{aro}), 7.35−7.52 (m, 3H, H_{aro}), 7.88 (d, 1H, J = 6.3 Hz, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 35.2 (CH_2), 43.3 (CH_2), 55.4 (CH_3), 57.9 (CH), 114.2 ($2CH_{aro}$), 119.3 (CH_2), 122.5 (CH_{aro}), 123.8 (CH_{aro}), 128.2 (CH_{aro}), 129.2 (C_q), 129.6 ($2CH_{aro}$), 131.4 (CH_{aro}), 131.5 (CH_{aro}), 132.5 (C_q), 145.0 (C_q), 159.1 (C_q), 168.5 (C=O). Anal. Calcd for $C_{19}H_{19}NO_2$ (293.14): C, 77.79; H, 6.53; N, 4.77. Found: C, 77.62; H, 6.41; N, 4.59.

7-Allyl-6,7-dihydro-6-(4-methoxybenzyl)-pyrrolo[3,4-*b*]pyridin-5-one (4g). To a stirred cold solution of 7-acetoxy-6,7-dihydro-6-(4-methoxybenzyl)-5*H*-pyrrolo[3,4-*b*]pyridin-5-one (**3g**) (312 mg, 1 mmol) and allyltrimethylsilane (1.37 g, 1.2 equiv) in 10 mL of anhydrous CH_2Cl_2 was added aluminum trichloride (99.99%, 4.0 g, 30 mmol) over a period of 10 min at −5 to 0 °C, and the mixture was allowed to reach room temperature. After 3 h of reaction at room temperature, the organic layer was carefully neutralized with NaOH 2 N solution, separated, dried over $MgSO_4$, and evaporated to give after chromatograpic purification the title product **4g** as a yellow oil in 60% yield: R_f 0.42 (cyclohexane/AcOEt 1:4); IR ν 2984, 2953, 1685, 1611, 1514, 1474 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.72−2.97 (m, 2H, CH_2), 3.76 (s, 3H, OMe), 4.11 (d, 1H, J = 14.9 Hz, CH_2N), 4.45 (dd, 1H, J = 4.7 and 3.9 Hz, CH), 4.91 (d, 1H, J = 10.2 Hz, $=CH_2$), 4.98 (d, 1H, J = 18.0 Hz, $=CH_2$), 5.15−5.27 (m, 1H, =CH), 5.36 (d, 1H, J = 14.9 Hz, CH_2N), 6.83 (d, 2H, J = 8.6 Hz, H_{aro}), 7.21 (d, 2H, J = 8.6 Hz, H_{aro}), 7.36 (dd, 1H, J = 7.8 and 4.7 Hz, H_{aro}), 8.10 (d, 1H, J = 7.8 Hz, H_{aro}), 8.68 (d, 1H, J = 4.7 Hz, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 33.8 (CH_2), 43.5 (CH_2), 55.5 (CH_3), 59.6 (CH), 114.4 ($2CH_{aro}$), 119.7 (CH_2), 123.5 (CH_{aro}), 126.5 (C_q), 128.8 (C_q), 129.7 ($2CH_{aro}$), 130.8 (CH_{aro}), 132.0 (CH_{aro}), 152.5 (CH_{aro}), 159.4 (C_q), 164.9 (C_q), 166.8 (C=O). Anal. Calcd for $C_{18}H_{18}N_2O_2$ (294.14): C, 73.45; H, 6.16; N, 9.52. Found: C, 73.31; H, 6.08; N, 9.40.

3-Allyl-2,3-dihydro-2-(4-methoxybenzyl)-pyrrolo[3,4-*b*]quinolin-1-one (4h). This product was isolated as a yellow solid: 92% yield; R_f 0.56 (cyclohexane/AcOEt 1:1); mp 97 °C; IR (KBr) ν 2981, 1684, 1634, 1513, 1467 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.81−3.08 (m, 2H, CH_2), 3.76 (s, 3H, OCH_3), 4.18 (d, 1H, J = 14.9 Hz, CH_2N), 4.58 (dd, 1H, J = 4.7 and 3.9 Hz, CH), 4.88 (d, 1H, J = 10.2 Hz, $=CH_2$), 4.99 (d, 1H, J = 17.2 Hz, $=CH_2$), 5.19−5.36 (m, 1H, =CH), 4.43 (d, 1H, J = 14.9 Hz, CH_2N), 6.84 (d, 2H, J = 8.6 Hz, H_{aro}), 7.25 (d, 2H, J = 8.6 Hz, H_{aro}), 7.60 (dd, 1H, J = 7.8 and 7.0 Hz, H_{aro}), 7.83 (dd, 1H, J = 8.6 and 7.0 Hz, H_{aro}), 7.98 (d, 1H, J = 7.8 Hz, H_{aro}), 8.12 (d, 1H, J = 8.6 Hz, H_{aro}), 8.61 (s, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 34.4 (CH_2), 43.7 (CH_2), 55.5 (CH_3), 59.8 (CH), 114.4 ($2CH_{aro}$), 119.7 (CH_2), 124.2 (C_q), 127.1 (CH_{aro}), 127.8 (C_q), 128.7 (C_q), 129.4 (CH_{aro}), 129.7 (CH_{aro}), 129.8 ($2CH_{aro}$), 131.1 (CH_{aro}), 131.4 (CH_{aro}), 132.6 (CH_{aro}), 150.1 (C_q), 159.4 (C_q), 163.4 (C_q), 166.7 (C=O). Anal. Calcd for $C_{22}H_{20}N_2O_2$ (344.15): C, 76.72; H, 5.85; N, 8.13. Found: C, 76.58; H, 5.69; N, 8.04.

5-Allyl-1-(2-bromobenzyl)-pyrrolidin-2-one (4i). This product was isolated as a colorless oil: 73% yield; R_f 0.33 (cyclohexane/AcOEt 1:1); IR (KBr) ν 2929, 1676, 1441 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.70−1.87 (m, 1H, CH_2), 1.99−2.24 (m, 2H, CH_2), 2.29−2.58 (m, 3H, CH_2), 3.53 (septuplet, 1H, J = 3.9 Hz, CH), 4.27 (d, 1H, J = 15.6 Hz, CH_2N), 4.90 (d, 1H, J = 15.6 Hz, CH_2N), 5.08 (d, 1H, J = 13.1 Hz, $=CH_2$), 5.08 (d, 1H, J = 14.7 Hz, $=CH_2$), 5.53−5.74 (m, 1H, =CH), 7.06−7.18 (m, 1H, H_{aro}), 7.22−7.28 (m, 2H, H_{aro}), 7.53 (d, 1H, J = 7.8 Hz, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 23.5 (CH_2), 30.1 (CH_2), 37.6 (CH_2), 44.3 (CH_2), 57.0 (CH), 119.0 (CH_2), 123.5 (C_q), 127.9 (CH_{aro}), 129.2 (CH_{aro}), 129.7 (CH_{aro}), 132.8 (CH_{aro}), 133.1 (CH_{aro}), 136.0 (C_q), 175.6 (C=O). Anal. Calcd for $C_{14}H_{16}BrNO$ (293.04): C, 57.16; H, 5.48; N, 4.76. Found: C, 57.02; H, 5.35; N, 4.59.

3-(4-Methoxyphenylthio)-2-((4-methoxyphenylthio)methyl)-isoindolin-1-one (4n). This product was isolated as a colorless oil: 35% yield; R_f 0.60 (cyclohexane/AcOEt 1:1); IR (KBr) ν 1703, 1593, 1494 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.65 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 4.74 (d, 1H, J = 7.3 Hz, CH_2N), 5.54 (d, 1H, J = 7.3 Hz, CH_2N), 5.81 (s, 1H, CH), 6.52 (d, 2H, J = 8.6 Hz, H_{aro}), 6.75 (d, 2H, J = 8.6 Hz, H_{aro}), 6.86 (d, 2H, J = 8.6 Hz, H_{aro}), 7.26−7.38 (m, 1H, H_{aro}), 7.32 (d, 2H, J = 8.6 Hz, H_{aro}), 7.46−7.64 (m, 3H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 45.6 (CH_2), 55.3 (OCH_3), 55.5 (OCH_3), 65.5 (CH), 114.4 ($2CH_{aro}$), 114.9 ($2CH_{aro}$), 118.0 (C_q), 123.6 (C_q), 123.6 (CH_{aro}), 124.0 (CH_{aro}), 128.8 (CH_{aro}), 131.2 (C_q), 132.1 (CH_{aro}), 134.6 ($2CH_{aro}$), 137.4 ($2CH_{aro}$), 143.1 (C_q), 159.9 (C_q), 160.7 (C_q), 167.0 (C=O). Anal. Calcd for $C_{23}H_{21}NO_3S_2$ (423.1): C, 65.22; H, 5.00; N, 3.31; O, 11.33. Found: C, 65.22; H, 5.00; N, 3.31; O, 11.33.

3-(2-Methoxycarbonylphenylthio)-2-((2-methoxycarbonylphenylthio)methyl)-isoindolin-1-one (4o). This product was isolated as a colorless oil: 43% yield; R_f 0.53 (cyclohexane/AcOEt 1:1); IR (KBr) ν 1710, 1523, 1471, 1435 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.88 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.76 (d, 1H, J = 14.1 Hz, CH_2N), 5.84 (d, 1H, J = 14.1 Hz, CH_2N), 6.23 (s, 1H, CH), 7.14−7.28 (m, 4H, H_{aro}), 7.34−7.56 (m, 4H, H_{aro}), 7.64−7.72 (m, 3H, H_{aro}), 7.88 (dd, 1H, J = 7.8 and 1.6 Hz, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 42.5 (CH_2), 52.4 (OCH_3), 52.6 (OCH_3), 65.1 (CH), 123.8 (CH_{aro}), 124.1 (CH_{aro}), 125.5 (CH_{aro}), 127.8 (CH_{aro}), 128.3 (CH_{aro}), 129.1 (C_q), 129.2 (CH_{aro}), 130.7 (CH_{aro}), 131.1 (C_q), 131.4 (CH_{aro}), 131.8 (CH_{aro}), 132.5 (C_q), 132.6 (CH_{aro}), 132.8 (CH_{aro}), 133.0 (CH_{aro}), 134.1 (C_q), 137.7 (C_q), 142.8 (C_q), 167.1 (C=O), 167.2 (C=O), 167.3 (C=O). Anal. Calcd for $C_{25}H_{21}NO_5S_2$ (479.09): C, 62.61; H, 4.41; N, 2.92. Found: C, 62.50; H, 4.32; N, 2.79.

5,6-Dihydro-2-methylpyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one (4q). This product was isolated as a white solid: 76% yield; R_f 0.35 (cyclohexane/AcOEt 3:2); mp 107−109 °C; IR (KBr) ν 3009, 2994, 1703, 1612 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.34 (d, 3H, J = 7.8 Hz, CH_3), 2.94 (t, 2H, J = 6.3 Hz, CH_2), 3.24 (qd, 1H, J = 7.8 and 3.1 Hz, CH), 3.72 (t, 2H, J = 6.3 Hz, NCH_2), 5.64 (d, 1H, J = 3.1 Hz, =CH), 7.17−7.29 (m, 3H, H_{aro}), 7.52−7.56 (m, 1H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 15.4 (CH_3), 29.1 (CH_2), 37.0 (CH_2), 43.6 (CH), 104.0 (CH_{aro}), 124.4 (CH_{aro}), 127.2 (CH_{aro}), 128.7 (CH_{aro}), 129.0 (CH_{aro}), 134.1 ($2C_q$), 138.3 (C_q), 180.0 (C=O). Anal. Calcd for $C_{13}H_{13}NO$ (199.1): C, 78.36; H, 6.58; N, 7.03. Found: C, 78.21; H, 6.43; N, 6.89.

2-(Furan-2-ylmethyl)-3-(2-oxopropyl)-isoindolin-1-one (5a). This product was isolated as a brown solid: 71% yield; R_f 0.28 (cyclohexane/AcOEt 1:1); mp 100 °C; IR (KBr) ν 1718, 1687, 1471 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.11 (s, 3H, CH_3), 2.71 (dd, 1H, J = 17.2 and 7.0 Hz, CH_2), 3.04 (dd, 1H, J = 17.2 and 4.7 Hz, CH_2), 4.51 (d, 1H, J = 15.6 Hz, CH_2N), 4.94 (d, 1H, J = 15.6 Hz, CH_2N), 5.03 (dd, J = 7.0 and 4.7 Hz, 1H, CH), 6.25−6.31 (m, 2H, H_{fur}), 7.31 (s, 1H, H_{aro}), 7.37−7.47 (m, 3H, H_{aro}), 7.82 (d, 1H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 30.8 (CH_3), 37.7 (CH_2), 46.6 (CH_2), 55.8 (CH), 108.7 (CH_{aro}), 110.8 (CH_{aro}), 122.7 (CH_{aro}), 124.1 (CH_{aro}), 128.6 (CH_{aro}), 131.8 (C_q), 132.1 (CH_{aro}), 142.5 (CH_{aro}), 145.8 (C_q), 150.6 (C_q), 168.3 (C=O), 205.8 (C=O). Anal. Calcd for $C_{16}H_{15}NO_3$ (269.11): C, 71.36; H, 5.61; N, 5.20. Found: C, 71.22; H, 5.47; N, 5.06.

2-(Furan-2-ylmethyl)-3-(2-oxophenethyl)-isoindolin-1-one (6a). This product was isolated as a white solid: 84% yield; R_f 0.42 (cyclohexane/AcOEt 1:1); mp 104 °C; IR (KBr) ν 3684, 3620, 3019, 2400, 1686, 1523, 1427 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.01 (dd, 1H, J = 18.0 and 7.0 Hz, CH_2), 3.39 (dd, 1H, J = 18.0 and 5.0 Hz, CH_2), 4.33 (d, 1H, J = 15.6 Hz, CH_2N), 4.80 (d, 1H, J = 15.6 Hz, CH_2N), 5.07 (dd, 1H, J = 7.0 and 5.0 Hz, CH), 5.98−6.05 (m, 2H, H_{fur}), 7.01 (s, 1H, H_{fur}), 7.16−7.28 (m, 5H, H_{aro}), 7.33−7.41 (m, 1H, H_{aro}), 7.62−7.71 (m, 3H, H_{aro}); ^{13}C NMR ($CDCl_3$) δ 37.7 (CH_2), 42.2 (CH_2), 56.3 (CH), 108.8 (CH_{aro}), 110.7 (CH_{aro}), 123.1 (CH_{aro}), 124.0 (CH_{aro}), 128.3 ($2CH_{aro}$), 128.6 (CH_{aro}), 129.0 ($2CH_{aro}$), 131.8 (C_q), 132.0 (CH_{aro}), 133.8 (CH_{aro}), 136.6 (C_q), 142.5 (CH_{aro}), 146.1 (C_q), 150.5 (C_q), 168.4 (C=O), 197.3 (C=O). Anal. Calcd for $C_{21}H_{17}NO_3$ (331.12): C, 76.12; H, 5.17; N, 4.23. Found: C, 76.00; H, 5.05; N, 4.14.

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Supporting Information Available: Spectroscopic data of all compounds including ^{1}H NMR, ^{13}C NMR (DEPT program), and IR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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