Metalation *vs* Nucleophilic Addition in the Reactions of *N*-Phenethylimides with Organolithium Reagents. Ready Access to Isoquinoline Derivatives *via N*-Acyliminium Ions and Parham-Type Cyclizations

M. Isabel Collado, Izaskun Manteca, Nuria Sotomayor, María-Jesús Villa, and Esther Lete*

Departamento de Química Orgánica, Facultad de Ciencias, Universidad del País Vasco, Apdo. 644, 48080 Bilbao, Spain

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Sequential carbophilic addition of organolithium reagents and *N*-acyliminium ion cyclization of *N*-phenethylimides **1** affords the substituted isoquinolones **3** in high yields, with the possibility of varying the substituent at the C-1 position of the isoquinoline ring by changing the organolithium reagent. Ready access to the isoquinoline nucleus *via* Parham-type cyclization of imides **2** is also described. We have shown that iodinated imides **2** tolerate the metal−halogen exchange in the presence of the imide group, and the intramolecular cyclization of the so-obtained aromatic organometallic derivatives leads to the corresponding enamides **4**. Both approaches have allowed the efficient preparation of various types of the isoquinoline class of alkaloids, just by changing the substitution pattern on the readily available starting imides. Thus, we have developed convenient alternative routes for the synthesis of benzo[*a*]quinolizidones and their 2-oxa analogs, isoindoloisoquinolones, dibenzo[*a,h*]quinolizidones, and thiazolo- and oxazolo[4,3-*a*]isoquinolones.

Introduction

Within the scope of the aromatic directed metalation reaction, a protocol which is enjoying increasing utility in organic synthesis, the intramolecular capture of the aryllithium intermediate by internal electrophiles (*ortho*-lithiation−cyclization strategy) has proven to be an effective method for the construction of carbocyclic and heterocyclic systems.[1,2] However, certain electrophilic groups, such as ketones and imides, do not remain passive during the metalation process, and competitive nucleophilic attack by organolithium base may occur. Advantage can be taken of the very fast rate of metal−halogen exchange compared with nucleophilic addition to carbonyl groups to allow survival of acidic sites and other electrophilic groups under low-temperature RLi conditions.[3] In their work on Parham-type cyclizations,[3] Wolfe[4] reported that the *N*-acyl groups of *N*-acyl-2-bromobenzamides tolerated metal−bromine exchange when the imide nitrogen was either deprotonated by sodium hydride or carried an alkyl substituent. The resulting *ortho*-lithium intermediates underwent cyclization to yield 3-alkylidenephthalimidines. Narasimhan[5] has described a novel synthesis of 1-arylbenzocyclobutenols and benzocyclobutenes from deoxybenzoins using a similar metal−halogen exchange strategy.

Here we detail[6] the utility of the reactions of *N*-phenethylimides with organolithium compounds for the synthesis of different isoquinoline alkaloids using two basic strategies. First, it was expected that a tandem carbophilic addition−*N*-acyliminium ion cyclization sequence could be performed on *N*-phenethylimides **1**, leading to the substituted isoquinolones **3** through a preferential attack to the imidic carbonyl group (Scheme 1). The key step involves *N*-acyliminium ion-mediated carbon−carbon bond-forming reactions, which have found an impressive number of synthetic applications.[7] *N*-Acyliminium ions have demonstrated significant utility as intermediates in various types of cyclization reactions using different types of π nucleophiles.[8] In our strategy, the appropriate choice of the organolithium reagent at the first step would allow the introduction of functionality on the pendant side chain of **3**, giving rise to useful precursors for the construction of more complex isoquinoline alkaloids, such as the *Erythrina* type.[9] The second approach relied on assembling the isoquinoline nucleus *via* Parham-type cyclization of imides **2**, since halogenated imides **2** could tolerate the metal−halogen exchange in the presence of the imide group, and the intramolecular cyclization of the so-obtained aromatic organometallic derivatives would lead to the corresponding enamides **4** (Scheme 1). In view of the ready availability of a wide array of substituted imides, both approaches seemed well suited to provide access to a wide variety of isoquinoline alkaloids.

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Scheme 1

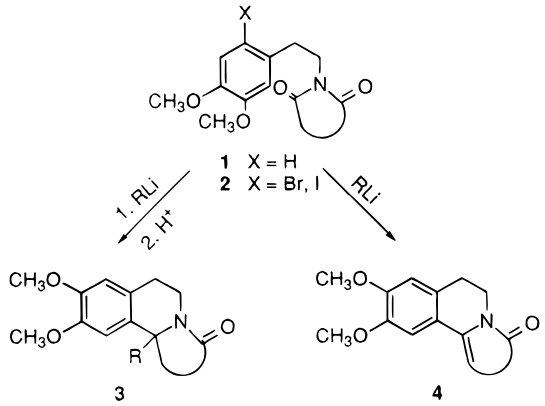
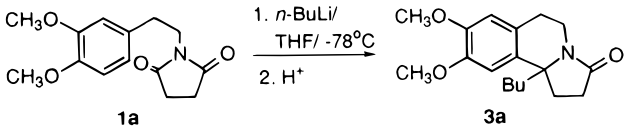


Table 1. One Pot Addition−Cyclization of 1a with *n*-BuLi

	conditions[a]		
entry	*n*-BuLi (equiv)	quenching agent	yield[b] (%) of product **3a**
1	1.1	12 M HCl	26
2	2.2	12 M HCl	40
3	2.2	TFA	92

[a] Reactions carried out in THF at −78 °C for 6 h. [b] Yields of isolated products.

Scheme 2



Results and Discussion

Carbophilic Addition−*N*-Acyliminium Ion Cyclization. A preliminary study of the reaction conditions for the tandem one-pot addition−cyclization reaction was carried out using succinimide **1a** as substrate, prepared by condensation of 3,4-dimethoxyphenethylamine with succinic anhydride. Representative results are summarized in Table 1 (Scheme 2).

When **1a** was treated with 1 equiv of *n*-BuLi at −78 °C for 6 h, quenching the reaction mixture with 12 M HCl once at room temperature, complete conversion was not accomplished, and the cyclization product **3a** was isolated in low yield (26%), together with starting material (entry 1). A better yield of **3a** (40%) was obtained using 2 equiv of *n*-BuLi under the same conditions (entry 2). However, treatment with 2 equiv of *n*-BuLi at −78 °C for 6 h, followed by TFA quench at room temperature, afforded **3a** in high yield. As expected, conversion **1a** to **3a** involves the initial formation of an alkoxide derivative, *via* addition of the organolithium reagent to the imidic carbonyl group, followed by protonation and subsequent dehydration to produce the corresponding *N*-acyliminium salt. The former salt readily cyclized to the 8,9-disubstituted pyrroloisoquinolone **3a** by electrophilic attack of the aromatic ring. In fact, the intermediate addition products could be isolated as tautomeric mixtures of hydroxy lactams **5** and oxo amides **6** when the reaction was quenched with water (Scheme 3). The structure of the acidic catalyst is of great influence on the outcome of the cyclization reaction, as it has been observed in other amidoalkylation reactions.[7] In this case, the fact that TFA affords the pyrroloisoquinolone **3a** in better yield than HCl could indicate that TFA favors the formation of the *N*-acyliminium ion, which is probably the rate-determining step.

Scheme 3

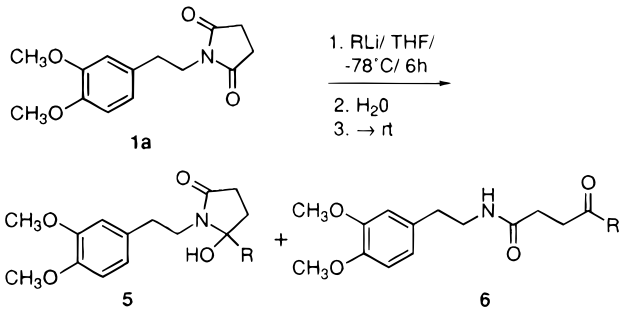


Table 2. Products from the RLi Carbophilic Addition Step of the Sequence with 3a

		products		
entry	RLi	R	yield[a] (%)	ratio **5**/**6**[b]
1	*n*-BuLi	**a**, *n*-Bu	61	4.2/1
2	MeLi	**b**, Me	87	c
3	*s*-BuLi	**c**, *s*-Bu	52	d
4	*t*-BuLi	**d**, *t*-Bu	53	d
5	Me_3SiCH_2Li	**b**, Me	60	4.8/1
6	PhLi	**e**, Ph	95	1/3
7	PhC≡CLi	**f**, PhC≡C	61	d
8	CH_2=$CHCH_2Li$	**g**, CH_2=$CHCH_2$	e	1.9/1

[a] Yields of the mixture of tautomers **5** and **6**. [b] Determined by ^{1}H NMR. [c] Only the hydroxy lactam **5** was isolated. [d] Only the oxo amide **6** was isolated. [e] Yields could not be accurately calculated due to contamination with the stannane derivative formed in the transmetalation.

In order to study the influence of steric and electronic effects in both the addition and cyclization reactions, succinimide **1a** was treated with a range of organolithium reagents. Allyllithium was prepared by transmetalation of allyltriphenyltin with PhLi, according to literature procedures.[10] Addition reactions were thus carried out with 2 equiv of the organolithium reagent at −78 °C over 6 h and quenched by addition of water at low temperature. After workup, equilibrium mixtures of the hydroxy lactams **5**, and the corresponding tautomeric oxo amides **6** were obtained, as summarized in Table 2 (Scheme 3).

The fact that no open-chain hydroxy amides resulting from RLi attack to the ketone carbonyl in **6** have been detected suggests that these oxo amides **6** are formed during aqueous workup, and not by ring opening of the intermediate lithium alkoxide. In cases **a** and **b** (R = Bu, Me, entries 1 and 5, Table 2), the tautomers **5** and **6** could be chromatographically separated and identified by NMR, while in the other cases decomposition occurred during the purification processes. However, since the subsequent cyclization of both compounds leads to the same pyrroloisoquinolone, no previous separation is required and NMR resonances can be used in the determination of the tautomers ratio from the mixture. The most significant signals were the NH triplet for the oxo amides **6** (i.e.: 5.67 ppm for **6a**) in the ^{1}H NMR spectrum and the ^{13}C NMR shift of the carbinolic or ketonic carbon (i.e.: 92.2 ppm for **5a** and 210.1 for **6a**, respectively).

Both yield and product distribution are affected by the steric and electronic nature of the carbon atom directly attached to the metal in the alkyllithium used as nucleophile (Table 2). The ratio of oxo amides **6** increases

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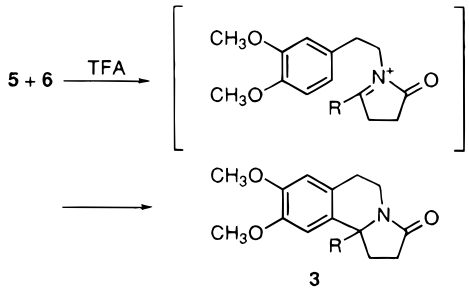
Scheme 4



3

with the substitution (entries 1−4). Thus, only the cyclic tautomer was isolated when the reaction was carried out with MeLi (entry 2), and it is the major tautomer in the reaction with *n*-BuLi. Just in one experiment, formation of the 4-oxopentanamide **6b** (R = CH_3) could be detected by ^{1}H NMR of the crude reaction mixture, in a 4.8/1 ratio favoring the hydroxy lactam **5b**. The ratio is inverted in the case of *s*-BuLi and *t*-BuLi (entries 3 and 4), where oxo amides **6c** and **6d** were the only products isolated. However, in the case of R = *s*-Bu, the presence of a minor amount of hydroxy lactam could be detected by ^{1}H NMR of the crude reaction mixture, whose ratio could not be determined due to overlapping of representative signals, and could not be isolated. A GC-MS analysis showed the presence of a peak of mass 303 ($M^+ - 18$) that could correspond to hydroxy lactam **5c** in a 19/1 **6c**/**5c** ratio. The use of Me_3SiCH_2Li (entry 5) afforded a mixture of **5b** and **6b** (R = Me) in a 4.8/1 ratio favoring the hydroxy lactam. This result can be rationalized assuming that a carbon to oxygen migration of the trimethylsilyl group[11−13] had occurred, followed by hydrolysis of the O−Si bond during workup. Both tautomers could be separated by column chromatography and identified.

As one can see from Table 2, hybridization change on the nucleophilic carbon atom of the organolithium reagent also exerts a strong effect, inverting the **5**/**6** ratio. In fact, the hydroxy lactams **5e** and **5f** (entries 6 and 7) are more unstable due to inductive effects on C-4, which favor the equilibrium toward the open chain isomer **6**.[14] Yield of the tautomeric mixture of **5/6g** could not be accurately calculated due to contamination with the stannane derivative formed in the transmetalation, even after chromatography, but conversion was complete and NMR spectra of the crude reaction mixtures only showed signals due to both tautomers and the organotin compound. However, hydroxy lactam **5g** decomposed during chromatography, and only the corresponding oxo amide **6g** could be isolated and identified.

Cyclization of the tautomeric mixture of **5** and **6** was accomplished with TFA in CH_2Cl_2 or $CHCl_3$ to afford the desired 10b-substituted tetrahydropyrroloisoquinolones **3** (Scheme 4). As shown on Table 3, high cyclization yields were generally obtained, though the rate was strongly influenced by the nature of the R group at C-10b. Higher temperatures and longer reaction times are required as the steric bulk increases (entry 2 *vs* 1 and 3) or as the R group diminishes the electrophility of the intermediate *N*-acyliminium ion by resonance effect

Table 3. Products from the Cyclization Step of 5 + 6

entry	substrate	conditions [time (h), *T*]	R	product	yield (%)
1	**5a** + **6a**	18, reflux[a]	*n*-Bu	3a	95
2	5b	4, rt[a]	Me	3b	98
3	6c	120, reflux[b]	*s*-Bu	3c	93
4	6d	-	*t*-Bu		c
5	**5e** + **6e**	36, reflux[a]	Ph	3e	98
6	6f	-	PhC≡C	3f	c
7	**5g**+ **6g**	6, reflux[a]	CH_2=$CHCH_2$	3g	97[d]

[a] CH_2Cl_2 was used as solvent. [b] $CHCl_3$ was used as solvent. [c] Starting material was recovered under various reaction conditions. [d] Based on GC-MS analysis.

(entry 5). The fact that no cyclization products were observed in the case of **6d** (R = *t*-Bu, entry 4) and in **6f** (R = PhC≡C, entry 6) could be explained by the above mentioned steric and electronic effects, respectively. In the other cases, yields were quantitative, and pure products were obtained from the crude reaction mixtures (GC analysis).

A rational extension of this methodology into other synthetically useful fields consists in the variation of the imide skeleton, thus providing a rapid, mild, and regiospecific entry to several heterocyclic systems, such as benzo[*a*]quinolizidones and their 2-oxa analogs, isoindoloisoquinolones, dibenzo[*a*,*h*]quinolizidones, and thiazolo- and oxazolo[4,3-*a*]isoquinolones. Thus, a series of imides **1i**−**p** were prepared as depicted in Scheme 5. Condensation of 3,4-dimethoxyphenethylamine **7** with cyclic anhydrides **8** under classical conditions afforded imides **1i**−**l**, while imides **1n** and **1p** were prepared by Mitsunobu reaction of 3,4-dimethoxyphenethyl alcohol **9** and imides **10**. Reaction of imides **1l** and **1n** with LDA/MeI yielded the corresponding dimethylated derivatives **1m** and **1o** (Scheme 5).

The sequence of carbophilic addition−*N*-acyliminium ion cyclization was applied on these substrates under the usual conditions affording the heterocyclic systems in high overall yields. As in the previous cases described, when imides **1i**−**k** were subjected to reaction with *n*-BuLi (2 equiv), a smooth nucleophilic addition of the organolithium reagent was observed. A simple aqueous workup yielded the oxo amides **6i**−**j** or the cyclic tautomer, hydroxy lactam **5k**, in excellent yields. Subsequent treatment of these addition products with TFA in dichloromethane at room temperature resulted in the quantitative formation of the corresponding isoquinoline derivatives: benzo[*a*]quinolizidone **3i**, its 2-oxa analogue **3j**, and nuevamine-type isoindoloisoquinolone **3k** (Scheme 6). Comparable yields of isoquinoline derivatives **3i**−**k** were obtained by quenching the *n*-BuLi addition reactions with TFA, though in some cases, conversions were lower. NMR data, including ^{1}H−^{1}H homodecoupling and DEPT experiments, proved to be useful for structure determinations here. In the case of benzo[*a*]quinolizidone **3i**, owing to the complex NMR spectra, ^{1}H and ^{13}C resonances were assigned by analysis of 2D ^{1}H−^{1}H COSY and HMQC spectra. The latter spectrum was particularly helpful to distinguish between vicinal and geminal proton signals in the CH_2CH_2 and $CH_2CH_2CH_2$ parts of quinolizidone ring.

The homophthalimide **1l** underwent rapid deprotonation at the benzylic position using the *n*-BuLi addition conditions (D_2O quench). Therefore, **1l** was converted in its silyl enol derivative by deprotonation with *n*-BuLi (1.1 equiv) in THF at −78 °C, followed by addition of TMSCl, and then treated with *n*-BuLi in one pot. By this

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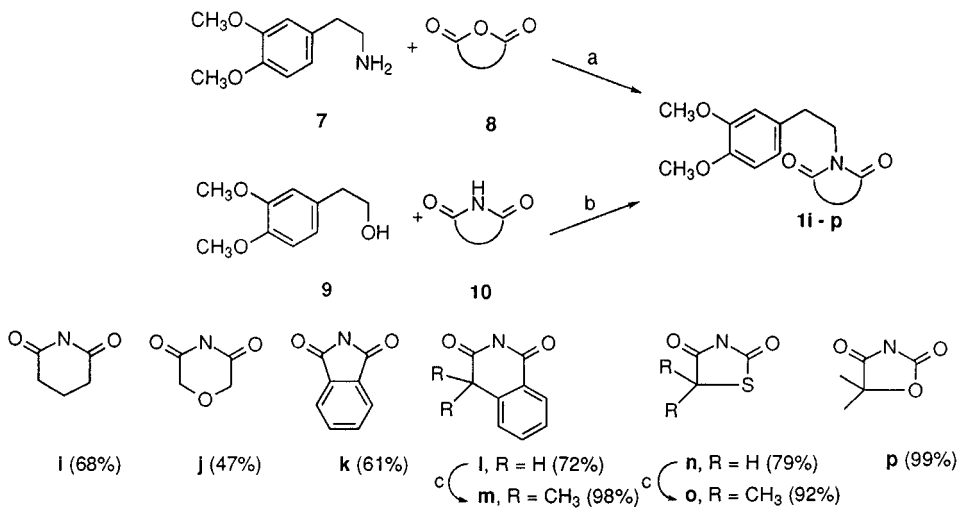
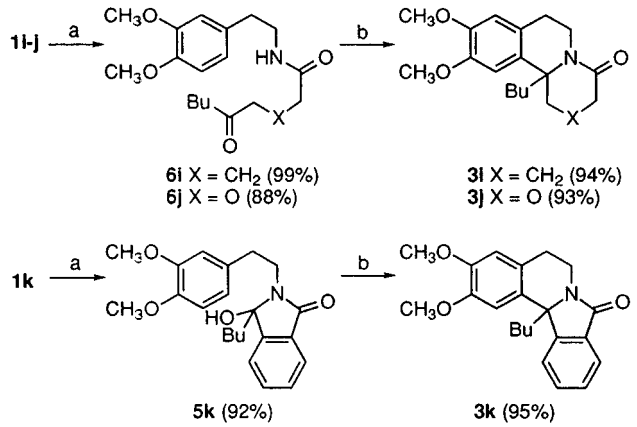
Scheme 5[a]



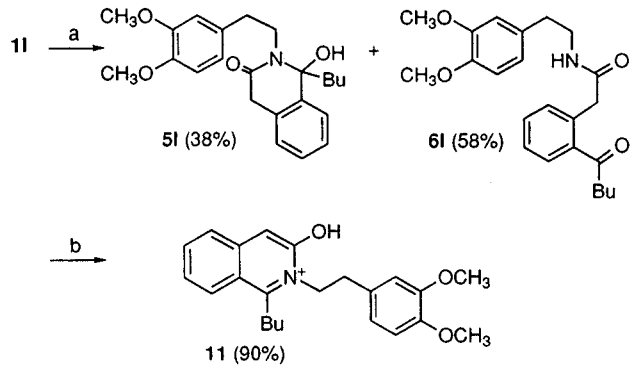
[a]Reagents: (a) AcOH, reflux, overnight; (b) PPh_3, DEAD, THF, 0°C→rt, overnight; (c) LDA, -78°C, 2h; then MeI / HMPA.

Scheme 6[a]



[a]Reagents: (a) *n*-BuLi (2 eq), -78°C, 6h; (b) TFA, CH_2Cl_2, rt, 16 h.

Scheme 7[a]

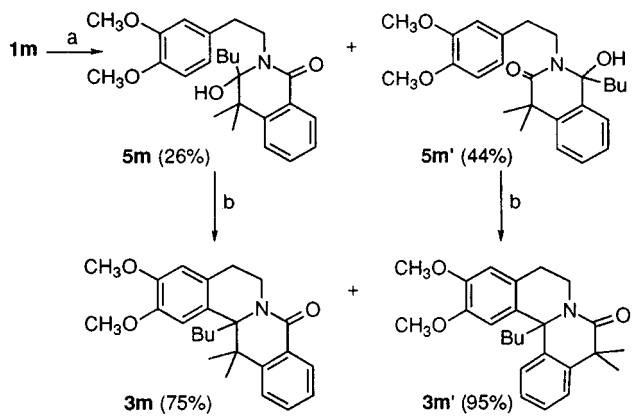


[a]Reagents: (a) *n*-BuLi (1.1 eq), -78°C, 1h, then TMSCl (1.0 eq), →rt, then *n*-BuLi (2 eq), -78°C, 6h ; (b) TFA, CH_2Cl_2, rt, 16 h.

procedure, both the benzylic position and the adjacent carbonyl group were protected against deprotonation and addition, respectively, and hydroxy lactam **5l** and oxo amide **6l** were obtained with complete regioselectivity in a 1/1.5 ratio and were chromatographically separated. However, when these *n*-BuLi addition products were submitted to cyclization with TFA, separately or directly from the crude reaction mixture, the 1-*n*-butyl-*N*-(3,4-dimethoxyphenethyl)-3-hydroxy isoquinolinium salt **11** was obtained as the major product (Scheme 7). In this case, the facile aromatization of the initially formed *N*-acyliminium salt prevented the cyclization.

This problem could be circumvented using the dimethylated homophthalimide **1m**. Two potential reaction pathways are possible. Addition to the carbonyl group in conjugation with the aromatic ring would result in the formation of a dibenzo[*a,h*]quinolizidinone, while attack to the carbonyl group at C-3 would lead to protoberberine system. Thus, when homophthalimide **1m** was subjected to the RLi addition−cyclization conditions, treatment with *n*-BuLi and TFA in the one-pot sequence afforded quantitatively a 1:1.7 mixture of the corresponding protoberberinone **3m** and dibenzo[*a,h*]-quinolizidinone **3m′**. In a separate experiment, hydroxy lactams **5m** and **5m′** were chromatographically separated, identified, and cyclized to the protoberberinone **3m**

Scheme 8[a]

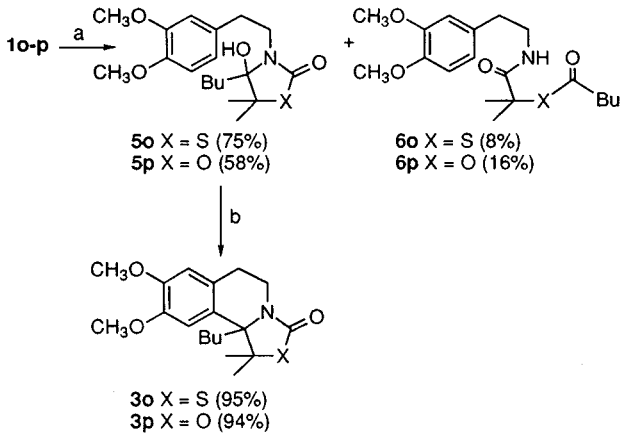


[a]Reagents: (a) *n*-BuLi (2 eq), -78°C, 6h ; (b) TFA, CH_2Cl_2, reflux, 6 days (for **3m**), rt, 48 h (for **3m'**).

(75% yield) and dibenzo[*a,h*]quinolizidinone **3m′** (95% yield), respectively (Scheme 8). The organolithium addition to this unsymmetrical imide was attended with modest regioselectivity, with preferential addition to the less hindered carbonyl group.

The relative regiochemistry of the products was determined by a combination of NOE measurements and

Scheme 9[a]



[a]Reagents: (a) *n*-BuLi (2.1 eq), -78°C, 6h ; (b) TFA, CH_2Cl_2, reflux, 24 h.

comparison of trends in the NMR data. When one examines ^{1}H NMR resonances, a downfield shift of one aromatic proton for protoberberine **3m** can be observed, relative to the other regioisomer (δ 8.14 for **3m** *vs* δ 7.64 for **3m′**). These values are consistent with the proposed structure, and the downfield shift observed may be attributed to the anisotropy of the carbonyl group. Besides, the conjugation of one of the carbonyl groups with the aromatic ring is also reflected in the difference of chemical shifts of the two carbonyl carbons in their ^{13}C NMR spectra (δ 163.6 for **3m** *vs* δ 175.7 for **3m′**). Although these data are in accordance with those reported for similar systems,[15] one should ideally have both isomers in order to compare values for unambiguous use of these spectroscopic data as diagnosis. Nevertheless, nuclear Overhauser effect difference spectroscopy can be used to confirm the regiochemistry and solve the problem. Thus, protoberberinone **3m** demonstrated an enhancement of the signal of the methyl protons at C-13 upon irradiation of the methylene protons of the *n*-butyl group (those directly bonded to the heterocyclic ring), and *vice versa*. On the other hand, dibenzoquinolizidinone **3m′** showed no NOE between the above-mentioned methyl and methylene protons. Similar criteria were used to distinguish the hydroxy lactams **5m** and **5m′** and to assign the structure of their analogue **5l**.

The extension of this methodology to other heteroatom-inserted imide derivatives was anticipated. It should be noted that heterocycle-fused isoquinolines, such as thiazolo- and oxazolo[4,3-*a*]isoquinolines, would be attractive for their potentially biological activities.[16] Addition of *n*-BuLi to heteroatom-inserted imides **1o** and **1p** occurred with high regioselectivity at the more electrophilic amide carbonyl group (Scheme 9), affording the hydroxy lactams **5o** and **5p** as the major products (75% and 58%, respectively). Addition to the carbamate or thiocarbamate carbonyl groups also occurred, and the oxo amides **6o** and **6p** could be isolated in minor amounts (8% and 16%, respectively). In this case, the open chain oxo amide is favored *versus* the cyclic hydroxy lactam, due to the inductive effect of the oxygen or sulfur atom, as previously discussed. In fact, cyclization attempts of oxo amides **6o** and **6p** failed, due to the lower reactivity of the ester or thio ester carbonyl groups toward nucleophilic attack of the amide nitrogen. On the contrary, treatment of the hydroxy lactams **5o** and **5p** with TFA provided in high yields the corresponding heterocycle-fused isoquinolines **3o** and **3p**, respectively.

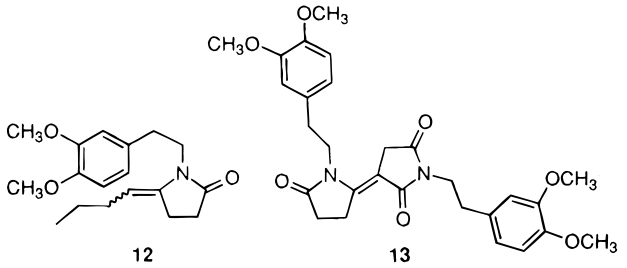


Figure 1.

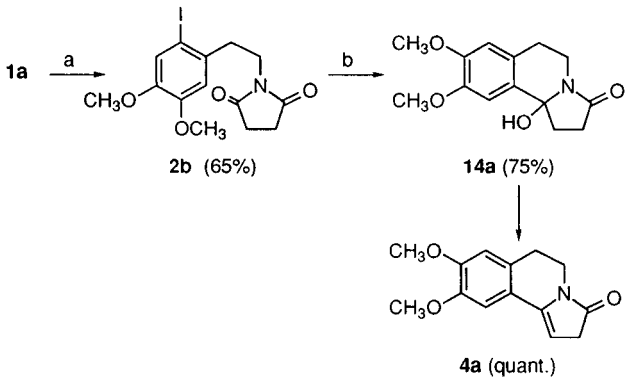
In addition to high field ^{1}H and ^{13}C NMR spectra, COSY, NOESY, and HMQC spectra were necessary to confirm the regiochemistry, due to the complexity of the spectra. These 2D NMR techniques have also allowed us to unequivocally assign the chemical shifts of all protons and carbons. The diagnostic carbonyl carbon and *n*-Bu−*C*−N quaternary carbon resonances, together with the presence or absence of NOE among the methyl protons at C-13 and the methylene protons of the *n*-butyl group (those directly bonded to the heterocyclic ring), are the most significant facts. Besides, the NOE observed between the methyl group at C-13 and the aromatic H-10 proton in the isoquinoline derivatives also supported the assignments.

Parham Cyclizations. Our next concern was the synthesis of isoquinolones **4** by Parham cyclization of the halogenated imides **2**. A preliminary study of the reaction conditions for the Parham cyclization reaction was carried out using brominated succinimide **2a** (Scheme 1, X = Br) as substrate, prepared by treatment of **1a** with bromine in acetic acid.[17] Although a variety of experimental conditions were tested, the desired pyrroloisoquinolines **4** could not be detected in the crude product mixture from **2a**. When **2a** was treated with *n*-BuLi (1 equiv) at −78 °C for 2.5 h and the reaction quenched by the addition of HCl, **3a** was isolated as the major product (34%). Metalation of **2a** took place partially because debromination was observed, but lithium−bromine exchange is not fast enough to compete effectively with *n*-BuLi addition to the imide carbonyl group. In fact, when **2a** was treated under the same conditions previously used for **1a**, the 10b-substituted pyrroloisoquinolone **3a** was isolated in a similar yield (52%). When the reaction was quenched by the addition of water it afforded the hydroxy lactam **5a** (45%), while using more diluted acid (6 M HCl) enamide **12** was obtained as the major product (26%) (Figure 1). This compound also cyclized to **3a** when stronger acidic medium (TFA or 12 M HCl) and/or prolonged stirring times were used.

The use of *t*-BuLi gave also addition to the carbonyl group, together with bromine−lithium exchange. Thus, when **2a** was treated with *t*-BuLi (2.1 equiv) at −78 °C, only the oxo amide **6d** was isolated (40%). In addition, when a larger excess of *t*-BuLi (4 equiv) was used and the reaction mixture stirred for 4 h at −78 °C before quenching, a dimeric byproduct (mass spectroscopy, elemental analysis) was also isolated (15−18%) (Figure

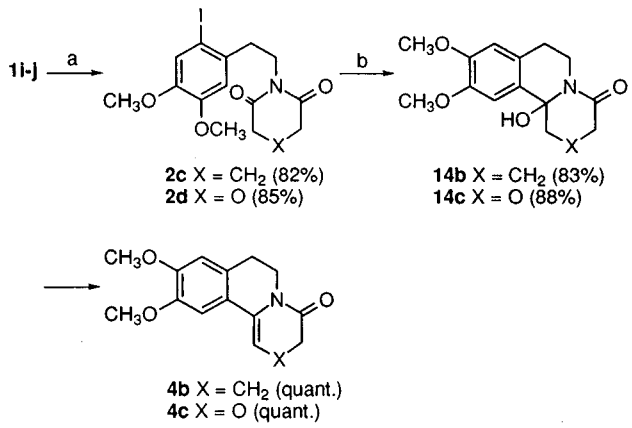
(15) Vicente, T.; Martínez de Marigorta, E.; Domínguez, E.; Carrillo, L.; Badía, M. D. *Heterocycles* **1993**, *36*, 2067.
(16) Kano, S.; Yuasa, Y.; Shibuya, S. *Synth. Commun.* **1985**, *15*, 883.
(17) Domínguez, E.; Lete, E.; Iriondo, C.; Villa, M. J. *Bull. Soc. Chim. Belg.* **1984**, *93*, 1099.

Scheme 10[a]



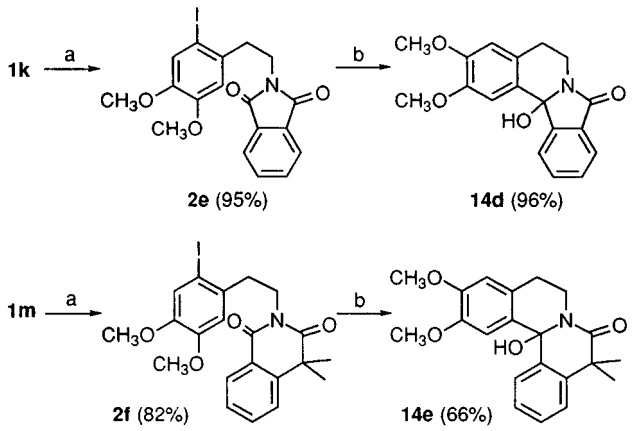
[a]Reagents: (a) ICl, AcOH, reflux, 2h ; (b) *n*-BuLi (2 eq), -78 °C, 2.5 h

Scheme 11[a]



[a]Reagents: (a) ICl, AcOH, reflux, 2h ; (b) *n*-BuLi (2 eq), -78 °C, 2.5 h

Scheme 12[a]



[a]Reagents: (a) ICl, AcOH, reflux, 2h ; (b) *n*-BuLi (2 eq), -78 °C, 2.5 h

1). The ^{1}H and ^{13}C NMR indicated the presence of four methoxyl groups, six aromatic protons, and seven methylene groups. Further spectroscopic analysis, which included ^{1}H−^{1}H decoupling experiments and 2D C-H correlation, led us to propose the structure of *N*-(3,4-dimethoxyphenethyl)-5-[*N*-(3,4-dimethoxyphenethyl)succinimid-3-ylidene]-2-pyrrolidinone (**13**) for this dimeric product. Its formation could be explained by aldol-type condensation of the succinimide. Analogous succinimide enolate formation have been reported.[18]

In view of these results the iodinated succinimide **2b**, prepared by treatment of **1a** with ICl, was tested as a substrate for the Parham cyclization. As expected, iodine−lithium exchange was faster than addition to the carbonyl group of the imide, and the initially formed anion was trapped intramolecularly by the imide carbonyl to afford an intermediate 10b-hydroxypyrroloisoquinolone, that dehydrated during workup to afford **4a** (75%) (Scheme 10).

These conditions were applied to the synthesis of more complex isoquinoline alkaloids. Thus, the iodinated imides **2c** and **2d** were prepared by treatment of **1i** and **1j** with ICl in glacial acetic acid. When **2c** and **2d** were treated under the previously tested conditions, the 11b-hydroxylated benzo[*a*]quinolizidone **14b** and its 2-oxa analogue **14c** were obtained in high yields. These products spontaneously dehydrated to the corresponding 1,11b-didehydrobenzo[*a*]quinolizidones **4b** and **4c** in chloroform solution (Scheme 11). Similarly, the hydroxy-substituted isoindoloisoquinolone **14d** and dibenzo[*a,h*]-quinolizidone **14e** were obtained from the iodinated imides **2e** and **2f** (Scheme 12). In the latter case, cyclization took place regioselectively at the less hindered carbonyl group. The structures were also established by NMR analysis through the observation of coupling constants, anisotropic shielding, C−H correlations, and NOEs, following the criteria previously explained (*vide supra*).

Conclusions

In summary, the application of the carbophilic addition−*N*-acyliminium ion cyclization sequence on imides **1a, i−p** constitutes an effective route to several types of isoquinoline alkaloids, with the ability to introduce a variety of substituents R at the C-1 position of the isoquinoline unit by changing the organolithium reagent used in the first step. It has also been shown that the tautomeric oxo amide−hydroxy lactam equilibrium and the *N*-acyliminium ion cyclization are strongly influenced by the stereoelectronic effects of the substituent R. Alternatively, bromine−lithium exchange in **2a** is not fast enough to compete effectively with organolithium addition to the imide carbonyl group. However, iodinated imides **2b−f** tolerate fast iodine−lithium exchange, giving rise to the isoquinoline nucleus *via* a Parham-type cyclization. Thus, convenient alternative routes for the synthesis of benzo[*a*]quinolizidones and their 2-oxa analogs, isoindoloisoquinolones, dibenzo[*a,h*]quinolizidones, and thiazolo- and oxazolo [4,3-*a*]isoquinolones[19] have been developed.

Experimental Section

General. Melting points were determined in unsealed capillary tubes and are uncorrected. IR spectra were obtained on KBr pellets (solids) or $CHCl_3$ solution (oils). NMR spectra

(18) Speckamp, W. N. *Heterocycles* **1984**, *21*, 211.

(19) For a few representative examples, see: (a) Benzo[*a*]quinolizidines: ref 14; Orito, L.; Matsuzaki, T.; Suginome, H. *Heterocycles* **1988**, *27*, 2403. (b) Isoindoloisoquinolines: Alonso, R.; Castedo, L.; Domínguez, D. *Tetrahedron Lett.* **1985**, *26*, 2925. Heaney, H.; Shuhaibar, K. F. *Tetrahedron Lett.* **1994**, *35*, 2751; ref 8a. (c) Dibenzo-[*a,h*]quinolizidines: Kametani, T.; Fukumoto, K. In *Heterocyclic Compounds. Isoquinolines. Part 1;* Grethe, G., Ed.; John Wiley & Sons: New York, 1981; vol. 38, p 183. (d) Heterocycle-fused isoquinolines: Hamersma, J. A. M.; Speckamp, W. N. *Tetrahedron* **1982**, *38*, 3255. Kohn, H.; Liao, Z.-K. *J. Org. Chem.* **1982**, *47*, 2787. Kano, S.; Yuasa, Y.; Yokomatsu, T.; Shibuya, S. *J. Org. Chem.* **1983**, *48*, 3835−3837. Kano, S., Yuasa, Y.; Shibuya, S. *Heterocycles* **1985**, *23*, 395.

were recorded at 20−25 °C, running at 250 MHz for ^{1}H and 62.8 MHz for ^{13}C in $CDCl_3$ solutions, unless otherwise stated. Assignment of individual ^{13}C resonances are supported by DEPT experiments. ^{1}H−{^{1}H} NOE experiments were carried out in the difference mode by irradiation of all the lines of a multiplet.[20] ^{1}H−{^{1}H} COSY, NOESY, and HMQC spectra were recorded at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C in $CDCl_3$ solutions. Mass spectra were recorded under electron impact at 70 eV. GC-MS analyses were performed using a HP-5 column (5% phenyl methyl polysiloxane, 30 m × 0.25 mm × 0.25 μm). TLC was carried out with 0.2 mm thick silica gel plates (Merck Kiesegel GF_{254}). Visualization was accomplished by UV light or by spraying with Dragendorff's reagent.[21] Flash column chromatography[22] on silica gel was performed with Merck Kiesegel 60 (230−400 mesh). HPLC was performed using a LiChrosorb Si60 (7 μm) column with a refraction index detector. All solvents used in reactions were anhydrous and purified according to standard procedures.[23] Organolithium reagents were titrated with diphenylacetic acid periodically prior to use. All air- or moisture-sensitive reactions were performed under argon; the glassware was dried (130 °C) and purged with argon.

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]succinimide (1a).** A solution of homoveratrylamine **7** (3 g, 16.5 mmol) and succinic anhydride (2.97 g, 29.7 mmol) in glacial acetic acid (35 mL) was heated at reflux overnight. The mixture was cooled, and the acetic acid was evaporated under reduced pressure. Pure imide **1a** was obtained by recrystallization from MeOH (3.46 g, 79%): mp 124−125 °C; IR (KBr) 1700, 1770 cm^{-1}; ^{1}H NMR ($CDCl_3$) 2.5 (s, 4H), 2.68 (t, J = 7.7 Hz, 2H), 3.57 (t, J = 7.7 Hz, 2H), 3.71 (s, 3H), 3.73 (s, 3H), 6.58−6.67 (m, 3H); ^{13}C NMR ($CDCl_3$) 27.5, 32.5, 39.3, 55.3, 110.7, 110.8, 120.3, 129.7, 147.4, 148.3, 176.5; MS (EI) m/z (rel intensity) 263 (M$^+$, 23), 164 (100), 151 (52), 107 (9), 91 (8), 77 (9), 65 (6), 55 (13). Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87, H, 6.51, N, 5.32. Found: C, 63.96, H, 6.47, N, 5.37.

10b-Butyl-8,9-dimethoxy-1,5,6,10b-tetrahydropyrrolo-[2,1-*a*]isoquinolin-3(2*H*)-one (3a). One-Pot Procedure. To a solution of the succinimide **1a** (263 mg, 1 mmol) in dry THF (20 mL), was added *n*-BuLi (1.45 mL of a 1.5 M solution in hexane, 2.2 mmol) at −78 °C. The resulting mixture was stirred at this temperature for 6 h, allowed to warm to 20 °C, and then quenched by addition of TFA (0.5 mL). Et_2O (5 mL) and H_2O (10 mL) were added, the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, 20% CH_2Cl_2/AcOEt) afforded the pyrroloisoquinolone **3a** (288 mg, 92%): IR ($CHCl_3$) 1680, 1515 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.89 (t, J = 7.0 Hz, 3H), 1.26−1.35 (m, 4H), 1.88 (t, J = 7.8 Hz, 2H), 2.35−2.45 (m, 1H), 2.61−2.70 (m, 1H), 2.76−3.04 (m, 4H), 3.34 (ddd, J = 13.2, 10.2, 5.5 Hz, 1H), 3.87 (s, 3H), 3.89 (s, 3H), 4.27 (ddd, J = 13.2, 6.2, 2.3 Hz, 1H), 6.57 (s, 1H), 6.65 (s, 1H); ^{13}C NMR ($CDCl_3$) 13.5, 22.6, 26.0, 27.2, 30.6, 31.6, 36.6, 41.4, 56.0, 56.2, 68.0, 108.3, 112.0, 124.5, 133.5, 147.6, 147.6, 173.1; MS (EI) m/z (rel intensity) 303 (M$^+$, 1), 246 (100), 230 (2), 202 (8), 185 (4), 123 (8), 109 (4), 87 (3), 77 (4).

Addition of RLi to Succinimide 1a. Preparation of Hydroxy Lactams 5 and Oxo Amides 6. General Procedure. To a solution of the succinimide **1a** (263 mg, 1 mmol) in dry THF (20 mL) was added RLi (2.2 mmol) at −78 °C. The resulting mixture was stirred at this temperature for 6 h, quenched by the addition of H_2O (5 mL), and allowed to warm to 20 °C. Et_2O (5 mL) was added, the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford mixtures of hydroxy lactams **5** and oxo amides **6**.

Addition of *n*-BuLi. 4-Butyl-*N*-[2-(3,4-dimethoxyphenyl)ethyl]-4-hydroxy-γ-lactam (5a) and *N*-[2-(3,4-Dimethoxyphenyl)ethyl]-4-oxooctanamide (6a). According to General Procedure, imide **1a** (526 mg, 2 mmol) was treated with *n*-BuLi (4.90 mL of a 0.9 M solution in hexanes, 4.4 mmol) to afford hydroxy lactam **5a** and oxo amide **6a** (370 mg, 61% overall) in a **5a**/**6a** 4.2/1 ratio. Both tautomers were separated by column chromatography (silica gel, 5% CH_2Cl_2/MeOH). **Hydroxy lactam 5a**: IR ($CHCl_3$) 3380, 1740, 1520 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.86 (t, J = 7.8 Hz, 3H), 1.15−1.33 (m, 4H), 1.52 (t, J = 7.3 Hz, 2H), 1.68−1.93 (m, 2H), 2.10−2.95 (m, 4H), 3.10−3.35 (m, 3H), 3.78 (s, 3H), 3.80 (s, 3H), 6.60−6.80 (m, 3H); ^{13}C NMR ($CDCl_3$) 13.6, 22.6, 25.4, 29.1, 34.5, 37.4, 40.6, 41.0, 55.7, 92.2, 114.1, 114.6, 120.7, 137.0, 147.4, 148.7, 171.9; MS (EI) m/z (rel intensity) 303 (M$^+$ − 18, 2), 274 (1), 164 (100), 151 (9), 124 (3), 105 (2), 91 (3), 77(3). Anal. Calcd for $C_{18}H_{27}NO_4$: C, 67.26, H, 8.47, N, 4.36. Found: C, 67.20, H, 9.17, N, 4.22. **Oxo amide 6a**: IR ($CHCl_3$) 3380, 1720, 1660, 1520, 1265 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.89 (t, J = 7.3 Hz, 3H), 1.31−1.49 (m, 2H), 1.52−1.60 (m, 2H), 2.38 (t, J = 6.7 Hz, 2H), 2.41 (t, J = 7.3 Hz, 2H), 2.72 (t, J = 6.7 Hz, 2H), 2.75 (t, J = 7.0 Hz, 2H), 3.46 (dt, J = 7.0, 6.2 Hz, 2H), 3.86 (s, 3H), 3.88 (s, 3H), 5.67 (broad s, 1H), 6.60−6.80 (m, 3H); ^{13}C NMR ($CDCl_3$) 13.8, 22.3, 25.9, 29.9, 32.2, 35.2, 37.6, 42.5, 55.8, 111.3, 111.9, 120.6, 131.4, 147.6, 149.0, 171.9, 210.1; MS (EI) m/z (rel intensity) 321 (M$^+$, 2), 264 (1), 164 (100), 151 (13), 121 (3), 107 (4), 85 (6), 77(4), 57 (10).

Addition of MeLi. *N*-[2-(3,4-dimethoxyphenyl)ethyl]-4-hydroxy-4-methyl-γ-lactam (5b). According to General Procedure, imide **1a** (526 mg, 2 mmol) was treated with MeLi (2.75 mL of a 1.6 M solution in Et_2O, 4.4 mmol) to afford hydroxy lactam **5b** (460 mg, 87%) that was purified by column chromatography (silica gel, 5% CH_2Cl_2/MeOH): mp (CH_2Cl_2/MeOH) 81−83 °C; IR ($CHCl_3$) 3360, 1740, 1520; ^{1}H NMR ($CDCl_3$) 1.39 (s, 3H), 1.95−2.13 (m, 2H), 2.38−2.2 (m, 1H), 2.56−2.40 (m, 1H), 2.95−2.67 (m, 3H), 3.50−3.29 (m, 2H), 3.81 (s, 3H), 3.83 (s, 3H), 6.68−6.80 (m, 3H); ^{13}C NMR ($CDCl_3$) 26.1, 29.1, 34.5, 34.7, 40.7, 55.5, 89.7, 111.1, 111.9, 120.5, 131.6, 147.2, 148.6, 174.5; MS (EI) m/z (rel intensity) 261 (M$^+$ − 18, 8), 164 (100), 151 (30), 110 (10), 91 (11), 82 (29). Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50, H, 7.58, N, 5.01. Found: C, 64.23, H, 7.71, N, 4.96.

Addition of *s*-BuLi. *N*-[2-(3,4-Dimethoxyphenyl)ethyl]-5-methyl-4-oxoheptanamide (6c). According to General Procedure, imide **1a** (526 mg, 2 mmol) was treated with *s*-BuLi (5.50 mL of a 0.8 M solution in pentane, 4.4 mmol) to afford oxo amide **6c** that was purified by column chromatography (silica gel, 60% hexane/AcOEt) (315 mg, 52% overall): IR ($CHCl_3$) 1715, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.84 (t, J = 7.5 Hz, 3H), 1.04 (d, J = 6.9 Hz, 3H), 1.31−1.42 (m, 1H), 1.60−1.68 (m, 1H), 2.35 (t, J = 6.5 Hz, 2H), 2.45 (q, J = 6.9 Hz, 1H), 2.68−2.78 (m, 4H), 3.43 (m, 2H), 3.82 (s, 3H), 3.84 (s, 3H), 5.70 (broad s, 1H), 6.68−6.79 (m, 3H); ^{13}C NMR ($CDCl_3$) 11.5, 15.7, 25.8, 29.8, 35.2, 36.1, 40.7, 47.6, 55.7, 111.2, 111.8, 120.5, 131.4, 147.5, 148.9, 171.8, 213.7; MS (EI) m/z (rel intensity) 321 (M$^+$, 2), 264 (2), 165 (16), 164 (100), 151 (11), 149 (9), 141 (3), 121 (2), 85 (5), 57 (8).

Addition of *t*-BuLi. *N*-[2-(3,4-Dimethoxyphenyl)ethyl]-5,5-dimethyl-4-oxohexanamide (6d). According to General Procedure, imide **1a** (526 mg, 2 mmol) was treated with *t*-BuLi (3.85 mL of a 1.3 M solution in pentane, 4.4 mmol). After workup, the residue was purified by flash column chromatography (silica gel, 20% CH_2Cl_2/AcOEt) to afford oxo amide **6d** (340 mg, 53%): mp (Et_2O) 134−136 °C, IR ($CHCl_3$) 1710, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.07 (s, 9H), 2.29 (t, J = 6.5 Hz, 2H), 2.66 (t, J = 6.5 Hz, 2H), 2.77 (t, J = 6.7 Hz, 2H), 3.38 (q, J = 6.7 Hz, 2H), 3.78 (s, 3H), 3.80 (s, 3H), 5.78 (broad s, 1H), 6.63−6.74 (m, 3H); ^{13}C NMR ($CDCl_3$) 26.3, 30.0, 32.0, 35.1, 40.7, 43.8, 55.7, 55.8, 111.2, 111.8, 120.5, 131.3, 147.4, 148.8, 172.0, 215.0; MS (EI) m/z (rel intensity) 321 (M$^+$, 2), 264 (4), 165 (21), 164 (100), 151 (11), 149 (10), 113 (7), 77 (3), 57 (8).

Addition of TMS-CH_2Li. *N*-[2-(3,4-Dimethoxyphenyl)ethyl]-4-hydroxy-4-methyl-γ-lactam (5b) and *N*-[2-(3,4-Dimethoxyphenyl)ethyl]-4-oxopentanamide (6b). According to General Procedure, imide **1a** (526 mg, 2 mmol) was treated with TMS-CH_2Li (5.5 mL of a 0.8 M solution in pentane, 4.4 mmol) to afford hydroxy lactam **5b** and oxo amide **6b** (335 mg, 60% overall) in a **5b**/**6b** 4.8/1 ratio, that were

(20) Kinss, M.; Sanders, J. K. M. *J. Magn. Reson.* **1984**, *56*, 518.
(21) Stahl, E. *Thin-Layer Chromatography;* 2nd ed.; Springer Verlag: Berlin, 1969.
(22) Still, W. C.; Kann, H.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(23) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals,* 3rd ed.; Pergamon Press: Berlin, 1988.

separated by flash column chromatography (silica gel, 5% CH_2Cl_2/MeOH). Data for **5b** were identical to those previously reported (*vide supra*). Data for **6b**: IR ($CHCl_3$) 3370, 1725, 1660, 1530 cm^{-1}; ^1H NMR ($CDCl_3$) 2.18 (s, 3H), 2.35 (t, J = 6.4 Hz, 2H), 2.72 (t, J = 7.0 Hz, 2H), 2.75 (t, J = 6.4 Hz, 2H), 3.40 (dt, J = 7.0, 5.8 Hz, 2H), 3.85 (s, 3H), 3.87 (s, 3H), 5.7 (broad s, 1H), 6.69−6.78 (m, 3H); ^{13}C NMR ($CDCl_3$) 29.6, 35.0, 38.3, 40.6, 55.6, 111.1, 111.8, 120.4, 131.3, 147.4, 148.7, 171.6, 209.8.

Addition of PhLi. *N*-[2-(3,4-Dimethoxyphenyl)ethyl]-4-phenyl-4-hydroxy-γ-lactam (5e) and 3-Benzoyl-*N*-[2-(3,4-dimethoxyphenyl)ethyl]propionamide (6e). According to General Procedure, imide **1a** (526 mg, 2 mmol) was treated with PhLi (2.2 mL of a 2 M solution in benzene/Et_2O, 4.4 mmol) to afford hydroxy lactam **5e** and oxo amide **6e** in a **5e**/**6e** 1/3 ratio (650 mg, 95% overall). Tautomers could not be separated due to decomposition on elution through silica gel: IR ($CHCl_3$) 3350, 3340, 1700, 1690, 1620, 1520 cm^{-1}; ^1H NMR ($CDCl_3$) 2.35−2.45 (m, 2H, **5e**), 2.56 (t, J = 6.5 Hz, 2H, **6e**) 2.48−2.95 (m, 4H, **5e**), 3.00−3.18 (m, 2H, **5e**), 3.27 (t, J = 6.5 Hz, 2H, **6e**), 3.44 (dt, J = 7.1, 6.2 Hz, 2H, **6e**), 3.70 (s, 3H, **5e**), 3.74 (s, 3H, **5e**), 3.78 (s, 3H, **6e**), 3.82 (s, 3H, **6e**), 5.08 (s, 1H, **5e**), 6.29 (distorted t, 1H, **6e**), 6.53−6.72 (m, 3H, both tautomers), 7.24−7.57 (m, 3H, both tautomers), 7.92 (dd, J = 7.7, 1.4 Hz, 2H, both tautomers); ^{13}C NMR ($CDCl_3$) 29.6 (**5e**), 30.1 (**6e**), 34.0 (**6e**), 34.4 (**5e**), 35.2 (**5e**), 37.7 (**6e**), 40.9 (**5e**), 42.0 (**6e**), 55.7 (both tautomers), 55.8 (both tautomers), 93.0 (**5e**), 111.2 (**5e**), 111.4 (**5e**), 112.0 (**6e**), 112.1 (**6e**), 120.7 (both tautomers), 127.1 (**6e**), 127.3, 128.0, 128.4, 128.6, 128.8 (both tautomers), 131.5 (both tautomers), 136.5 (**6e**), 141.12 (**5e**), 147.6 (**6e**), 148.9 (**6e**), 172.2 (**6e**), 175.4 (**5e**), 199.0 (**6e**); MS (EI) m/z (rel intensity) 341 (M^+, 2), 164 (100), 133 (5), 105 (17), 91 (5), 77 (19).

Addition of PhC≡CLi. *N*-[2-(3,4-Dimethoxyphenyl)-ethyl]-6-phenyl-4-oxohex-5-ynamide (6f). According to General Procedure, imide **1a** (526 mg, 2 mmol) was treated with PhC≡CLi (4.4 mL of a 1.0 M solution in THF, 4.4 mmol). After workup, the residue was purified by flash column chromatography (silica gel, 5% CH_2Cl_2/MeOH) to afford oxo amide **6f** (445 mg, 61%): IR ($CHCl_3$) 3340, 2200, 1700, 1670, 1520 cm^{-1}; ^1H NMR ($CDCl_3$) 2.49 (t, J = 6.4 Hz, 2H), 2.76 (t, J = 6.9 Hz, 2H), 3.07 (t, J = 6.4 Hz, 2H), 3.49 (dt, J = 6.9, 5.8 Hz, 2H), 3.85 (s, 3H), 3.88 (s, 3H), 5.67 (broad s, 1H), 6.69−6.83 (m, 3H), 7.33−7.61 (m, 5H); ^{13}C NMR ($CDCl_3$) 29.9, 35.2, 40.7, 40.8, 55.9, 87.5, 91.4, 111.4, 111.9, 119.7, 120.6, 128.6, 130.8, 131.3, 133.0, 147.7, 149.0, 171.1, 186.2; MS (EI) m/z (rel intensity) 365 (M^+, 6), 207 (2), 165 (13), 164 (100), 151 (24), 149 (15), 129 (8), 107 (6), 91 (10), 77 (10).

Addition of Allyllithium. *N*-[2-(3,4-Dimethoxyphenyl)-ethyl]-4-oxohept-6-enamide (6g). PhLi (15 mL of a 1.2 M solution in benzene/ether, 18 mmol) was added over a suspension of allyltriphenyltin (6.39 g, 16 mmol) in Et_2O (32 mL), under argon, and the reaction mixture was stirred for 30 min. The so obtained yellow allyllithium solution was titrated with diphenylacetic acid, resulting in a 0.1 M solution. Allyllithium (22 mL, 2.2 mmol of the freshly prepared 0.1 M solution) was then added over a solution of imide **1a** (263 mg, 1 mmol) at −78 °C, according to General Procedure. After workup, ^1H NMR of the crude reaction mixture showed the quantitative formation of hydroxy lactam **5g** and oxo amide **6g** in a 1.9/1 ratio. Purification by column chromatography (silica gel, 5% CH_2Cl_2/MeOH) gave only oxo amide **6g**, though contaminated with Ph_4Sn: IR ($CHCl_3$) 3350, 1660, 1640, 1515 cm^{-1}; ^1H NMR ($CDCl_3$) 1.87−2.05 (m, 2H) 2.12−2.22 (m, 2H), 2.49−2.68 (m, 2H), 2.7 (t, J = 6.9 Hz, 2H), 3.41 (dt, J = 6.9, 5.1 Hz, 2H), 3.84 (s, 3H), 3.85 (s, 3H), 4.95−5.10 (m, 2H), 5.45 (broad s, 1H), 5.63 (ddt, J = 11.0, 7.3, 5.3 Hz, 1H), 6.69−6.78 (m, 3H); ^{13}C NMR ($CDCl_3$) 31.1, 35.0, 37.0, 40.7, 48.4, 55.8, 55.9, 111.3, 111.8, 119.0, 120.6, 131.2, 133.6, 145.5, 147.7, 173.8, 209.7; MS (EI) m/z (rel intensity) 305 (M^+, <1), 161 (100), 133 (17), 105 (35), 77 (24).

Cyclization Reactions. Synthesis of Pyrroloisoquinolones. General Procedure. To a solution of the mixture of hydroxy lactams **5** and oxo amides **6** (1 mmol) in CH_2Cl_2 or $CHCl_3$ (10 mL) was added TFA (0.80 mL, 10.5 mmol), and the resulting solution was stirred at 20 °C or heated at reflux until complete evolution of the starting material was observed (^1H NMR monitoring). The reaction mixture was treated with saturated aqueous Na_2CO_3, the organic layer was decanted, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine (2 × 10 mL), dried (Na_2SO_4), and concentrated *in vacuo*.

10b-Butyl-8,9-dimethoxy-1,5,6,10b-tetrahydropyrrolo-[2,1-*a*]isoquinolin-3(2*H*)-one (3a). According to General Procedure, the mixture of hydroxy lactam **5a** and oxo amide **6a** (320 mg, 1 mmol) was treated with TFA in CH_2Cl_2 at reflux for 18 h. After workup, pure pyrroloisoquinolone **3a** was obtained (287 mg, 95%) as a reddish oil. Data for **3a** were identical to those previously reported (*vide supra*).

8,9-Dimethoxy-10b-methyl-1,5,6,10b-tetrahydropyrrolo-[2,1-*a*]isoquinolin-3(2*H*)-one (3b). According to General Procedure, hydroxy lactam **5b** (280 mg, 1 mmol) was treated with TFA in CH_2Cl_2 at 20 °C for 4 h. After workup, pure pyrroloisoquinolone **3b** was obtained (255 mg, 98%) as a reddish oil: IR ($CHCl_3$) 1685, 1520 cm^{-1}; ^1H NMR ($CDCl_3$) 1.62 (s, 3H), 2.25−2.35 (m, 1H), 2.52−2.63 (m, 1H), 2.75−3.09 (m, 4H), 3.29 (td, J = 12.2, 5.1 Hz, 1H), 3.88 (s, 3H), 3.89 (s, 3H), 4.27 (ddd, J = 12.2, 6.2, 1.8 Hz, 1H), 6.58 (s, 1H), 6.63 (s, 1H); ^{13}C NMR ($CDCl_3$) 27.0, 27.6, 30.0, 34.4, 36.0, 55.2, 55.9, 64.6, 107.9, 116.8, 125.5, 133.3, 147.7, 147.9, 175.7; MS (EI) m/z (rel intensity) 261 (M^+, 8), 246 (100), 230 (14), 202 (9), 185 (4), 172 (4), 123 (6), 117 (4), 91 (5), 77 (8).

10b-*sec*-Butyl-8,9-dimethoxy-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one (3c). According to General Procedure, oxo amide **6c** (320 mg, 1 mmol) was treated with TFA in $CHCl_3$ under reflux for 5 days. After workup, the residue was purified by column chromatography (silica gel, 20% AcOEt/hexane) to afford pure pyrroloisoquinolone **3c** (242 mg, 93%) as a reddish oil: IR ($CHCl_3$) 1685, 1520 cm^{-1}; ^1H NMR ($CDCl_3$) 0.81−0.90 (m, 3H), 0.97 (d, J = 6.7 Hz, 3H), 1.06−1.43 (m, 1H), 1.60−1.85 (m, 2H), 2.10−2.28 (m, 1H), 2.31−2.47 (m, 2H), 2.53−2.60 (m, 1H), 2.65−2.79 (m, 1H), 2.83−2.98 (m, 1H), 3.09−3.27 (m, 1H), 3.84 (s, 3H), 3.85 (s, 3H), 4.19−4.23 (m, 1H), 6.56 (s, 1H), 6.59 (s, 1H); ^{13}C NMR ($CDCl_3$) 13.3, 14.3, 23.5, 25.0, 26.8, 31.4, 35.3, 44.8, 55.8, 67.2, 109.2, 111.5, 125.5, 134.2, 147.2, 147.7, 175.7; MS (EI) m/z (rel intensity) 303 (M^+, <1), 247 (17), 246 (100), 230 (10), 202 (6), 185 (3), 172 (3), 146 (1), 132 (1), 117 (2), 91 (1).

8,9-Dimethoxy-10b-phenyl-1,5,6,10b-tetrahydropyrrolo-[2,1-*a*]isoquinolin-3(2*H*)-one (3e). According to General Procedure, the mixture of hydroxy lactam **5e** and oxo amide **6e** (341 mg, 1 mmol) was treated with TFA in CH_2Cl_2 at reflux for 36 h. After workup, pure pyrroloisoquinolone **3e** was obtained (314 mg, 98%) as a reddish oil: IR ($CHCl_3$) 1685, 1520 cm^{-1}; ^1H NMR ($CDCl_3$) 2.43−2.70 (m, 4H), 2.81−2.95 (m, 2H), 3.12−3.20 (m, 1H), 3.78−4.0 (m, 1H)*, 3.85 (s, 3H)*, 3.90 (s, 3H)*, 6.62 (s, 1H), 6.80 (s, 1H), 7.1−7.32 (m, 5H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 26.9, 30.7, 35.5, 36.2, 55.9, 56.2, 67.2, 109.2, 111.4, 126.1, 126.7, 127.3, 128.4, 132.6, 144.8, 147.5, 148.2, 176.4; MS (EI) m/z (rel intensity) 323 (M^+, 8), 246 (100), 230 (8), 202 (5), 185 (2), 117 (2), 91 (2), 77 (6). Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28, H, 6.55, N, 4.33. Found: C, 73.72, H, 6.79, N, 3.96.

10b-Allyl-8,9-dimethoxy-1,5,6,10b-tetrahydropyrrolo-[2,1-*a*]isoquinolin-3(2*H*)-one (3g). According to General Procedure, the mixture of hydroxy lactam **5g** and oxo amide **6g** (1 mmol), taken from the crude reaction mixture of the addition reaction (*vide supra*) without further purification, was treated with TFA in CH_2Cl_2 at reflux for 6 h. After workup, the residue was purified by column chromatography (silica gel, 60% hexane/AcOEt) to afford pyrroloisoquinolone **3g**, though contaminated with residual stannane (290 mg), as a reddish oil. An injection of the crude reaction mixture on GC showed quantitative formation of the desired pyrroloisoquinoline (97%): IR ($CHCl_3$) 1685, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) 2.67 (t, J = 7.9 Hz, 2H), 2.76 (d, J = 6.9 Hz, 2H), 2.96 (t, J = 6.9 Hz, 2H), 3.1 (dd, J = 19.0, 7.9 Hz, 1H), 3.27 (dd, J = 19.0, 7.9 Hz, 1H), 3.83 (s, 3H)*, 3.83 (s, 3H)*, 3.84−3.88 (m, 2H)*, 5.10−5.25 (m, 2H), 5.35−5.48 (m, 1H), 6.76 (s, 1H), 6.83 (s, 1H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 29.8, 30.8, 32.3, 45.7, 46.4, 55.9, 55.9, 77.0 (overlapped with $CDCl_3$), 107.7, 112.3, 121.8, 129.8, 138.5, 147.7, 148.6, 180.2;

MS (EI) *m*/*z* (rel intensity) 287 (M^+, 19), 272 (7), 246 (100), 230 (10), 202 (7), 185 (3), 123 (3).

Preparation of Imides. General Procedure A. A solution of homoveratrylamine **7** (181 mg, 1 mmol) and the corresponding anhydride **8** (1.8 mmol) in glacial acetic acid (2 mL) was heated at reflux overnight. The mixture was cooled, and the acetic acid was evaporated under reduced pressure. Pure imides **1** were obtained by recrystallization from MeOH.

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]glutarimide (1i).** According to General Procedure A, amine **7** (3 g, 16.5 mmol) was treated with glutaric anhydride (3.38 g, 29.7 mmol), affording glutarimide **1i**, which was crystallized from MeOH (3.1 g, 68%): mp 111−113 °C; IR (KBr) 1690, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) 1.84 (quin, J = 6.5 Hz, 2H), 2.57 (t, J = 6.5 Hz, 4H), 2.68−2.74 (m, 2H), 3.80 (s, 3H), 3.83 (s, 3H), 3.90−3.96 (m, 2H), 6.73 (broad s, 3H); ^{13}C NMR ($CDCl_3$) 16.9, 32.5, 33.4, 40.5, 55.6, 110.9, 111.9, 120.7, 130.9, 147.3, 148.5, 172.1; MS (EI) *m*/*z* (rel intensity) 277 (M^+, 8), 164 (100), 151 (25), 121 (4), 107 (6), 91 (6), 77 (7), 55 (20), 42 (8). Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97, H, 6.91, N, 5.05. Found: C, 64.88, H, 6.85, N, 5.12.

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]diglycolimide (1j).** According to General Procedure A, amine **7** (544 mg, 3 mmol) was treated with diglycolic anhydride (626 g, 5.4 mmol), affording imide **1j**, that was crystallized from MeOH (397 mg, 47%): mp 137−138 °C; IR (KBr) 1700, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) 2.76−2.83 (m, 2H), 3.85 (s, 3H), 3.88 (s, 3H), 3.95−4.01 (m, 2H), 4.32 (s, 4H), 6.74−6.82 (m, 3H); ^{13}C NMR ($CDCl_3$) 33.0, 39.4, 55.4, 67.2, 110.9, 111.7, 120.5, 130.1, 147.3, 148.5, 168.6; MS (EI) *m*/*z* (rel intensity) 279 (M^+, 16), 164 (100), 151 (62), 121 (5), 107 (11), 91 (10), 77 (10), 65 (8), 42 (27). Anal. Calcd for $C_{14}H_{17}NO_5$: C, 60.21, H, 6.14, N, 5.02. Found: C, 60.18, H, 6.07, N, 5.06.

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]phthalimide (1k).** According to General Procedure A, amine **7** (1 g, 5.5 mmol) was treated with phthalic anhydride (1.5 g, 10 mmol), affording imide **1k**, that was crystallized from MeOH (1.05 g, 61%): mp 168−170 °C; IR (KBr) 1715, 1770 cm^{-1}; ^1H NMR ($CDCl_3$) 2.89 (t, J = 7.6 Hz, 2H), 3.76 (s, 3H), 3.79 (s, 3H), 3.86 (t, J = 7.6 Hz, 2H), 6.70−6.73 (m, 3H), 7.63−7.68 (m, 2H), 7.73−7.78 (m, 2H); ^{13}C NMR ($CDCl_3$) 33.9, 39.2, 55.7, 111.2, 111.8, 120.7, 123.0, 130.3, 131.9, 133.7, 147.6, 148.7, 168.7; MS (EI) *m*/*z* (rel intensity) 311 (M^+, 23), 164 (100), 151 (99), 133 (4), 107 (12), 91 (8), 77 (22), 65 (7), 51 (8).

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]homophthalimide (1l).** According to General Procedure A, amine **7** (860 mg, 4.7 mmol) was treated with homophthalic anhydride (1 g, 6.2 mmol), affording imide **1l**, that was crystallized from MeOH (1.11 g, 72%): mp 142−143 °C; IR (KBr) 1665, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) 2.84−2.90 (m, 2H), 3.85 (s, 3H), 3.86 (s, 3H), 4.02 (s, 2H), 4.17−4.23 (m, 2H), 6.78−6.86 (m, 3H), 7.26−7.29 (m, 1H), 7.42−7.48 (m, 1H), 7.56−7.62 (m, 1H), 8.21−8.23 (m, 1H); ^{13}C NMR ($CDCl_3$) 33.6, 36.3, 41.5, 55.8, 111.1, 112.0, 120.8, 125.3, 127.0, 127.6, 129.0, 131.0, 134.0, 133.5, 147.5, 148.7, 164.6, 169.7; MS (EI) *m*/*z* (rel intensity) 325 (M^+, 6), 164 (100), 149 (18), 107 (6), 91 (11), 77 (7), 65 (5), 51 (3). Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14, H, 5.89, N, 4.30. Found: C, 69.87, H, 5.77, N, 4.39.

Preparation of Imides. Typical Procedure B. *N*-[2-(3,4-Dimethoxyphenyl)ethyl]-4,4-dimethylhomophthalimide (1m). A solution of homophthalimide **1l** (162 mg, 0.5 mmol) in THF (5 mL) was added dropwise over a solution of LDA [1 mmol, prepared from diisopropylamine (0.14 mL, 1 mmol) and *n*-BuLi (1.3 mL of a 1.3 M solution, 1 mmol)] in THF (5 mL) at −78 °C. After 2 h, HMPA (0.18 mL, 1 mmol) and methyl iodide (0.12 mL, 2 mmol) were added, and the resulting solution was stirred 2 h at −78 °C. The reaction mixture was allowed to warm up to 20 °C, saturated NH_4Cl (5 mL) was added, and the aqueous layer was extracted with Et_2O (5 mL) and CH_2Cl_2 (3 × 5 mL). The combined organic extracts were washed with brine (2 × 5 mL) and dried (Na_2SO_4), and the solvent was evaporated *in vacuo*. The residue was purified by column chromatography (silica gel, 60% hexane/AcOEt) to afford **1m** as a colorless oil (173 mg, 98%): IR (KBr) 1660, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) 1.54 (s, 6H), 2.82−2.88 (m, 2H), 3.80 (s, 3H), 3.81 (s, 3H), 4.16−4.22 (m, 2H), 6.72−6.81 (m, 3H), 7.39−7.43 (m, 2H), 7.59 (t, J = 8.0 Hz, 1H), 8.19 (d, J = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) 29.1, 33.4, 41.5, 43.3, 55.6, 55.7, 111.1, 112.0, 120.9, 123.6, 125.0, 127.1, 128.7, 130.9, 133.8, 144.9, 147.4, 148.6, 163.9, 176.7; MS (EI) *m*/*z* (rel intensity) 353 (M^+, 7), 164 (100), 149 (14), 91 (5), 77 (5). Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37, H, 6.56, N, 3.96. Found: C, 71.56, H, 6.85, N, 3.79.

Preparation of Imides. Typical Procedure C. 3-[2-(3,4-Dimethoxyphenyl)ethyl]thiazolidine-2,4-dione (1n). To a solution of thiazolidine-2,4-dione (937 mg, 8 mmol), 2-(3,4-dimethoxyphenyl)ethanol (**9**) (1.34 g, 8 mmol), and triphenylphosphine (2.1 g, 8 mmol) in THF (16 mL) at 0 °C was added dropwise DEAD (1.2 mL, 8 mmol), and the mixture was stirred at 20 °C overnight. The solvent was removed *in vacuo*, and the residue was partioned between CH_2Cl_2 (15 mL) and 5% aqueous KOH (5 mL). The organic layer was then washed sequentially with 2 M HCl (1 × 2 mL), saturated Na_2CO_3 (2 mL), and brine (2 × 2 mL). The organic extracts were dried (Na_2SO_4), and the solvent was evaporated. The residue was crystallized from MeOH, to afford imide **1n** (1.77 g, 79%): mp 124−126 °C; IR (KBr) 1685, 1745 cm^{-1}; ^1H NMR ($CDCl_3$) 2.82−2.88 (m, 2H), 3.83−3.87 (m, 2H)*, 3.85 (s, 2H)*, 3.88 (s, 3H), 3.89 (s, 3H), 6.72−6.82 (m, 3H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 32.9, 33.6, 43.1, 55.8, 111.3, 111.9, 120.9, 129.7, 147.8, 148.9, 171.3, 171.7; MS (EI) *m*/*z* (rel intensity) 281 (M^+, 1), 217 (3), 205 (11), 177 (100), 167 (6), 131 (19), 105 (71), 77 (10), 59 (2). Anal. Calcd for $C_{13}H_{15}NO_4S$: C, 55.50, H, 5.37, N, 4.98. Found: C, 55.74, H, 5.20, N, 4.90.

3-[2-(3,4-Dimethoxyphenyl)ethyl]-5,5-dimethylthiazolidine-2,4-dione (1o). According to the Typical Procedure B described for the synthesis of **1m**, **1n** (843 mg, 3 mmol) was treated with LDA [6 mmol, prepared from diisopropylamine (0.85 mL, 6 mmol) and *n*-BuLi (7.8 mL of a 1.3 M solution, 6 mmol)], HMPA (1.1 mL, 6 mmol), and methyl iodide (0.75 mL, 12 mmol). After column chromatography (silica gel, 60% hexane/AcOEt), **1o** was obtained as a white solid (834 mg, 92%): mp (Et_2O) 83−85 °C; IR (KBr) 1740, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) 1.48 (s, 6H), 2.77−2.83 (m, 2H), 3.73−3.76 (m, 2H)*, 3.75 (s, 3H)*, 3.78 (s, 3H), 6.62−6.71 (m, 3H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 27.5, 32.5, 42.3, 53.5, 55.5, 55.6, 111.0, 111.9, 120.8, 129.4, 147.6, 148.6, 169.9, 177.8; MS (EI) *m*/*z* (rel intensity) 309 (M^+, 27), 164 (100), 151 (42), 107 (7), 91 (6), 77 (5). Anal. Calcd for $C_{15}H_{19}NO_4S$: C, 58.23, H, 6.19, N, 4.53. Found: C, 58.37, H, 6.29, N, 4.51.

3-[2-(3,4-Dimethoxyphenyl)ethyl]-5,5-dimethyloxazolidine-2,4-dione (1p). According to the Typical Procedure C described for the synthesis of **1n**, 5,5-dimethyloxazolidine-2,4-dione (774 mg, 6 mmol) was treated with 2-(3,4-dimethoxyphenyl)ethanol (**9**) (1 g, 6 mmol), triphenylphosphine (1.6 g, 6 mmol), and DEAD (0.9 mL, 6 mmol). After workup, the residue was column chromatographed (silica gel, 60% hexane/AcOEt) to afford imide **1p** (1.74 g, 99%): mp (CH_3OH) 90−91 °C; IR (KBr) 1730, 1810 cm^{-1}; ^1H NMR ($CDCl_3$) 1.34 (s, 6H), 2.87 (t, J = 7.3 Hz, 2H), 3.69 (t, J = 7.3 Hz, 2H), 3.76 (s, 3H), 3.78 (s, 3H), 6.63−6.67 (m, 3H); ^{13}C NMR ($CDCl_3$) 23.1, 32.3, 40.3, 55.6, 83.2, 111.0, 111.7, 120.8, 129.0, 147.7, 148.7, 154.2, 175.6; MS (EI) *m*/*z* (rel intensity) 293 (M^+, 22), 164 (100), 151 (55), 121 (3), 107 (6), 91 (5),77 (5).

Addition of *n*-BuLi to Imides 1i−p. Preparation of Hydroxy Lactams 5 and Oxo Amides 6. General Procedure. To a solution of the imide **1** (1 mmol) in dry THF (20 mL) was added *n*-BuLi (2 mmol) at −78 °C. The resulting mixture was stirred at this temperature for 6 h, quenched by the addition of H_2O (5 mL), and allowed to warm to 20 °C. Et_2O (5 mL) was added, the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford mixtures of hydroxy lactams **5** and oxo amides **6**.

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]-5-oxononanamide (6i).** According to General Procedure, glutarimide **1i** (1.11 g, 4 mmol) was treated with *n*-BuLi (5.3 mL of a 1.5 M solution in hexanes, 8 mmol) to afford oxo amide **6i** (1.32 g, 99%). An analytical sample was obtained by crystallization from Et_2O / pentane: mp 72−74 °C; IR ($CHCl_3$) 3300, 1710, 1640, 1520

cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.88 (t, J = 7.3 Hz, 3H), 1.28 (sext, J = 7.3 Hz, 2H), 1.50 (quin, J = 7.3 Hz, 2H), 1.90 (quin, J = 7.1 Hz, 2H), 2.13 (t, J = 7.1 Hz, 2H), 2.37 (t, J = 7.3 Hz, 2H), 2.44 (t, J = 7.1 Hz, 2H), 2.75 (t, J = 7.0 Hz, 2H), 3.44−3.52 (m, 2H), 3.85 (s, 3H), 3.86 (s, 3H), 5.54 (distorted t, 1H), 6.70−6.82 (m, 3H); ^{13}C NMR ($CDCl_3$) 13.7, 19.6, 22.1, 25.7, 35.1, 35.3, 40.5, 41.3, 42.3, 55.7, 55.7, 111.2, 111.8 120.5, 131.2, 147.5, 148.9, 172.2, 210.8; MS (EI) m/z (rel intensity) 335 (M^+, 1), 164 (100), 151 (10), 85 (3), 57 (5). Anal. Calcd for $C_{19}H_{29}NO_4$: C, 68.03, H, 8.71, N, 4.18. Found: C, 67.98, H, 9.04, N, 4.08.

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]-2-(2-oxohexoxy)acetamide (6j).** According to General Procedure, diglycolimide **1j** (279 mg, 1 mmol) was treated with *n*-BuLi (1.3 mL of a 1.5 M solution in hexanes, 2 mmol) to afford oxo amide **6j** (296 mg, 88%). An analytical sample was obtained by crystallization from MeOH: mp 105−106 °C; IR ($CHCl_3$) 3340, 1730, 1670, 1525 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.88 (t, J = 7.2 Hz, 3H), 1.28 (sext, J = 7.2 Hz, 2H), 1.54 (quin, J = 7.2 Hz, 2H), 2.30 (t, J = 7.2 Hz, 2H), 2.78 (t, J = 7.2 Hz, 2H), 3.48−3.57 (m, 2H), 3.83 (s, 3H), 3.85 (s, 3H), 3.97 (s, 2H), 4.11 (s, 2H), 6.71−6.80 (m, 3H), 7.01 (broad s, 1H); ^{13}C NMR ($CDCl_3$) 13.7, 22.2, 25.3, 35.1, 38.3, 40.1, 55.8, 71.2, 76.0, 111.2, 111.8, 120.5, 131.1, 147.6, 148.9, 168.8, 207.0; MS (EI) m/z (rel intensity) 337 (M^+, 1), 207 (4), 164 (100), 151 (30), 107 (5), 85 (7), 57 (17).

3-*n*-Butyl-*N*-[2-(3,4-dimethoxyphenyl)ethyl]-3-hydroxy-1,3-dihydroisoindol-1(2*H*)-one (5k). According to General Procedure, phthalimide **1k** (311 mg, 1 mmol) was treated with *n*-BuLi (1.3 mL of a 1.5 M solution in hexanes, 2 mmol) to afford hydroxy lactam **5k** (339 mg, 92%). An analytical sample was obtained by crystallization from MeOH: mp 105−106 °C; IR (KBr) 3440, 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.47−0.67 (m, 1H), 0.72 (t, J =7.3 Hz, 3H)*, 0.74−0.96 (m, 1H)*, 1.07−1.23 (m, 2H), 1.91−2.13 (m, 2H), 2.72−2.86 (m, 1H), 2.90−3.02 (m, 1H), 3.14−3.26 (m, 1H), 3.59−3.71 (m, 1H), 3.77 (s, 3H)#, 3.79 (s, 3H)#, 3.76−3.79 (m, 1H)#, 6.70−6.72 (m, 3H), 7.28−7.34 (m, 1H), 7.39−7.45 (m, 2H), 7.48−7.52 (m, 1H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.7, 22.3, 25.3, 34.3, 35.8, 40.5, 55.7, 91.2, 111.2, 112.0, 120.6, 121.5, 122.8, 129.1, 131.1, 131.7, 132.0, 146.8, 147.4, 148.7, 167.4. Anal. Calcd for $C_{22}H_{27}NO_4$: C, 71.52, H, 7.37, N, 3.79. Found: C, 71.11, H, 7.37, N, 3.79.

1-*n*-Butyl-*N*-[(3,4-dimethoxyphenyl)ethyl]-1-hydroxy-3(2*H*)-isoquinolone (5l) and *N*-[2-(3,4-Dimethoxyphenyl)-ethyl]-2-(2-pentanoylphenyl)acetamide (6l). To a solution of homophthalimide **1l** (162 mg, 0.5 mmol) in THF (10 mL) at −78 °C was added *n*-BuLi (0.47 mL of a 1.18 M solution in hexanes, 0.55 mmol), and the resulting solution was stirred for 75 min. Then, TMSCl (0.14 mL, 0.55 mmol) was added, and the reaction mixture was allowed to warm up to 20 °C. After 70 min, the resulting solution was cooled to −78 °C, *n*-BuLi (0.85 mL of a 1.18 M solution in hexanes, 1 mmol) was added, and the reaction mixture was stirred for 6 h. The reaction was quenched by the addition of H_2O (5 mL) and allowed to warm to rt. Et_2O (10 mL) was added, the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a mixture of hydroxy lactam **5l** and oxo amide **6l**, that were separated by HPLC (20% AcOEt/hexane, 6 mL/min). **Hydroxy lactam 5l** (73 mg, 38%): IR ($CHCl_3$) 3200, 1670 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.76 (t, J = 7.2 Hz, 3H), 0.94−1.05 (m, 2H), 1.11−1.16 (m, 2H), 1.77−1.86 (m, 2H), 1.90 (s, 1H), 2.70−3.00 (m, 2H), 3.55 (s, 3H)*, 3.52−3.63 (m, 1H)*, 3.68 (s, 2H), 3.82 (s, 3H), 3.97−4.07 (m, 1H), 6.54 (d, J = 1.5 Hz, 1H), 6.68−6.76 (m, 2H), 7.26−7.31 (m, 1H), 7.34−7.38 (m, 3H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.8, 22.4, 25.6, 34.7, 36.8, 41.2, 43.5, 55.4, 55.9, 88.4, 111.3, 112.0, 120.9, 125.0, 126.9, 127.1, 128.6, 129.8, 132.6, 138.1, 147.4, 148.7, 168.2; MS (EI) m/z (rel intensity) 383 (M^+, 1), 214 (2), 202 (6), 173 (14), 164 (100), 152 (16), 119 (8), 91 (10), 77 (6). **Oxo amide (6l)** (111 mg, 58%): IR ($CHCl_3$) 3320, 1680, 1590, 1520 cm^{-1}, ^{1}H NMR ($CDCl_3$) 0.93 (t, J = 7.4 Hz, 3H), 1.36 (sext, J = 7.4 Hz, 2H), 1.64 (quin, J = 7.4 Hz, 2H), 2.68 (t, J = 7.1 Hz, 2H), 2.91 (t, J = 7.4 Hz, 2H), 3.37−3.45 (m, 2H), 3.59 (s, 2H), 3.79 (s, 3H), 3.82 (s, 3H), 6.54-6.69 (m, 3H), 6.98 (distorted t, 1H), 7.29−7.35 (m, 1H), 7.43−7.45 (m, 2H), 7.66 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.8, 22.3, 26.5, 35.0, 40.7, 41.0, 41.7, 55.7, 55.8, 111.1, 111.8, 120.5, 126.9, 128.8, 131.4, 131.9, 132.1, 135.3, 137.5, 147.3, 148.7, 171.0, 205.6; MS (EI) m/z (rel intensity) 383 (M^+, 1), 202 (3), 175 (5), 164 (100), 151 (9), 119 (6), 91 (7), 77 (3). Anal. Calcd for $C_{23}H_{29}NO_4$: C, 72.04, H, 7.62, N, 3.65. Found: C, 71.84, H, 7.73, N, 3.63.

3-*n*-Butyl-*N*-[2-(3,4-dimethoxyphenyl)ethyl]-3-hydroxy-4,4-dimethyl-3,4-dihydroisoquinolin-1(2*H*)-one (5m) and 1-Butyl-*N*-[2-(3,4-dimethoxyphenyl)ethyl]-1-hydroxy-4,4-dimethyl-1,4-dihydroisoquinolin-3(2*H*)-one (5m′). According to General Procedure, homophthalimide **1m** (65 mg, 0.18 mmol) was treated with *n*-BuLi (0.24 mL of a 1.5 M solution in hexanes, 0.36 mmol) to afford a mixture of isoquinolones **5m** and **5m′**, which were separated by HPLC (50% AcOEt/hexane, 6 mL/min). **Isoquinolone 5m** (20 mg, 26%): IR (neat) 3340, 1625 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.74 (t, J = 7.0 Hz, 3H), 0.85−1.21 (m, 3H)*, 1.07 (s, 3H)*, 1.43 (s, 3H), 1.56−1.63 (m, 3H), 2.14 (s, 1H), 2.88−2.97 (m, 1H), 3.00−3.10 (m, 1H), 3.55−3.66 (m, 1H), 3.86 (s, 3H), 3.87 (s, 3H), 4.10−4.22 (m, 1H), 6.83−6.85 (m, 3H), 7.30−7.36 (m, 2H), 7.43−7.49 (m, 1H), 8.07 (dd, J = 7.6, 1.2 Hz, 1H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.8, 20.8, 23.0, 26.1, 26.3, 35.2, 36.7, 43.2, 44.1, 55.9, 55.9, 91.1, 111.3, 112.5, 121.0, 123.3, 126.8, 127.7, 128.0, 132.4, 145.3, 147.6, 149.0, 164.2; MS (EI) m/z (rel intensity) 394 (M^+ − 17, 1), 378 (2), 242 (9), 229 (23), 214 (48), 200 (19), 164 (100), 129 (3), 115 (3), 103 (4), 91 (5), 77 (4), 56 (3). Anal. Calcd for $C_{25}H_{33}NO_4$: C, 72.96, H, 8.08, N, 3.40. Found: C, 72.93, H, 7.82, N, 3.01. **Isoquinolone 5m′** (33 mg, 44%): IR (neat) 3340, 1725 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.71−0.77 (m, 4H), 0.85−0.98 (m, 1H), 1.08−1.19 (m, 2H), 1.54 (s, 3H), 1.61 (s, 3H), 1.89 (td, J = 12.9, 4.6 Hz, 1H), 1.99−2.11 (m, 1H), 2.29 (s, 1H), 2.88−2.98 (m, 2H), 3.52−3.64 (m, 1H), 3.77 (s, 3H), 3.83 (s, 3H)*, 3.83−3.97 (m, 1H)*, 6.75−6.77 (m, 3H), 7.23−7.38 (m, 3H), 7.46 (d, J = 7.5 Hz, 1H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.7, 22.2, 26.4, 30.0, 30.8, 34.5, 40.7, 41.6, 43.8, 55.7, 55.8, 88.1, 111.2, 112.3, 121.0, 125.6, 125.9, 126.8, 128.8, 132.6, 134.8, 140.2, 147.4, 148.8, 174.3; MS (EI) m/z (rel intensity) 393 (M^+ − 18, 2), 378 (3), 242 (6), 229 (7), 214 (30), 200 (14), 184 (4), 164 (100), 149 (7), 128 (4), 103 (2), 91 (3), 77 (2). Anal. Calcd for $C_{25}H_{33}NO_4$: C, 72.96, H, 8.08, N, 3.40. Found: C, 72.81, H, 7.81, N, 3.11

4-*n*-Butyl-3-[2-(3,4-dimethoxyphenyl)ethyl]-4-hydroxy-5,5-dimethylthiazolidin-2-one (5o) and *S*-[1-[*N*-[2-(3,4-Dimethoxyphenyl)ethyl]carbamoyl]-1-methylethyl] Pentanethioate (6o). According to General Procedure, imide **1o** (322 mg, 1.04 mmol) was treated with *n*-BuLi (1.39 mL of a 1.5 M solution in hexanes, 2.08 mmol) to afford a mixture of hydroxy lactam **5o** and thio ester **6o**, which were separated by flash column chromatography (silica gel, 50% AcOEt/hexane). **Hydroxy lactam 5o** (275 mg, 75%): white solid, mp (Et_2O/pentane) 96−98 °C; IR (KBr) 3240, 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.88−0.95 (m, 3H), 1.21−1.90 (m, 6H)*, 1.36 (s, 3H)*, 1.45 (s, 3H)*, 2.37 (s, 1H), 2.69−3.00 (m, 2H), 3.33−3.45 (m, 1H), 3.58−3.69 (m, 1H), 3.86 (s, 3H), 3.87 (s, 3H), 6.69−6.79 (m, 3H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.8, 23.4, 24.8, 25.7, 26.2, 34.7, 34.9, 44.0, 55.8, 55.9, 56.3, 94.6, 111.3, 112.2, 120.8, 131.5, 147.7, 148.9, 169.8; MS (EI) m/z (rel intensity) 349 (M^+ − 18, 1), 185 (2), 164 (100), 151 (9), 138 (6), 107 (3), 91 (3), 79 (3), 55 (3). **Thioester 6o** (29 mg, 8%): IR ($CHCl_3$) 3420, 1670 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.88 (t, J = 7.2 Hz, 3H), 1.23−1.37 (m, 2H), 1.44−1.62 (m, 2H)*, 1.53 (s, 6H)*, 2.42 (t, J = 7.5 Hz, 2H), 2.73 (t, J = 7.1 Hz, 2H), 3.42−3.50 (m, 2H), 3.84 (s, 3H), 3.86 (s, 3H), 6.66−6.85 (m, 4H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.6, 22.0, 25.9, 27.4, 34.9, 41.2, 44.0, 52.2, 55.8, 55.8, 111.2, 112.0, 120.6, 131.4, 147.5, 148.9, 173.2, 199.4; MS (EI) m/z (rel intensity) 367 (M^+, 1), 249 (1), 164 (100), 151 (15), 85 (12), 77 (4), 57 (12). Anal. Calcd for $C_{19}H_{29}NO_4S$: C, 62.10, H, 7.95, N, 3.81. Found: C, 61.78, H, 8.05, N, 3.54.

4-*n*-Butyl-3-[2-(3,4-dimethoxyphenyl)ethyl]-4-hydroxy-5,5-dimethyloxazolidin-2-one (5p) and 1-[*N*-[2-(3,4-Dimethoxyphenyl)ethyl]carbamoyl]-1-methylethyl Pentanoate (6p). According to General Procedure, imide **1p** (117 mg, 0.4 mmol) was treated with *n*-BuLi (0.53 mL of a 1.5 M

solution in hexanes, 0.8 mmol) to afford a mixture of hydroxy lactam **5p** and ester **6p**, that were separated by fractional recrystallisation from hexane/AcOEt. **Hydroxy lactam 5p** (82 mg, 58%): IR (KBr) 3320, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) 0.87 (t, J = 6.9 Hz, 3H), 1.23−1.28 (m, 4H)*, 1.28 (s, 3H)*, 1.41 (s, 3H), 1.47−1.58 (m, 2H), 2.86 (t, J = 7.3 Hz, 2H), 3.26−3.38 (m, 1H), 3.41−3.55 (m, 1H), 3.84 (broad s, 7H), 6.71−6.80 (m, 3H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.8, 22.1, 23.2, 24.3, 25.5, 34.0, 35.0, 42.0, 55.8, 55.9, 85.5, 91.7, 111.2, 112.3, 121.0, 131.7, 147.7, 148.9, 157.7; MS (EI) m/z (rel intensity) 351 (M^+, 3), 208 (27), 164 (65), 151 (100), 135 (4), 107 (12), 91 (8), 77 (6), 59 (85). **Ester 6p** (21 mg, 16%): IR (KBr) 3300, 1740, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) 0.88 (t, J = 7.2 Hz, 3H), 1.23−1.37 (m, 3H), 1.46−1.55 (m, 1H)*, 1.58 (s, 6H)*, 2.21 (t, J = 7.5 Hz, 2H), 2.76 (t, J = 6.8 Hz, 2H), 3.46−3.54 (m, 2H), 3.84 (s, 3H), 3.86 (s, 3H), 6.06 (distorted t, 1H), 6.71−6.81 (m, 3H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.6, 22.1, 24.3, 26.9, 34.6, 35.1, 40.5, 55.8, 81.2, 111.2, 111.9, 120.6, 131.2, 147.7, 149.0, 171.9, 173.0; MS (EI) m/z (rel intensity) 351 (M^+, 4), 164 (100), 151 (11), 121 (2), 107 (3), 85 (12), 57 (12).

11b-*n*-Butyl-9,10-dimethoxybenzo[*a*]quinolizidin-4-one (3i). According to the general procedure described for the cyclization reactions, oxo amide **6i** (60 mg, 0.18 mmol) was treated with TFA (0.14 mL, 1.9 mmol) at 20 °C for 16 h to afford benzo[*a*]quinolizidinone **3j** (54 mg, 94%). An analytical sample was obtained by crystallization from MeOH: IR ($CHCl_3$) 1650 cm^{-1}; ^1H NMR ($CDCl_3$) 0.85 (t, J = 6.9 Hz, 3H), 1.19−1.38 (m, 4H), 1.59−1.68 (m, 1H), 1.82−2.03 (m, 4H), 2.24−2.33 (m, 1H), 2.39−2.47 (m, 2H), 2.52−2.62 (m, 1H), 2.84−3.05 (m, 2H), 3.84 (s, 3H), 3.85 (s, 3H), 4.83−4.90 (m, 1H), 6.57 (s, 1H), 6.64 (s, 1H); ^{13}C NMR ($CDCl_3$) 13.9, 17.0, 23.1, 27.0, 28.4, 32.1, 34.8, 36.2, 41.9, 55.7, 56.2, 61.4, 108.4, 111.7, 126.8, 134.0, 147.2, 147.6, 170.1; MS (EI) m/z (rel intensity) 317 (M^+, <1), 263 (25), 164 (100), 151 (52), 121 (4), 107 (7), 91 (6), 77 (7), 65 (6), 55 (11). Anal. Calcd for $C_{19}H_{27}NO_3$: C, 71.89, H, 8.57, N, 4.41. Found: C, 71.99, H, 8.86, N, 4.12.

11b-*n*-Butyl-9,10-dimethoxy-2-oxabenzo[*a*]quinolizidin-4-one (3j). According to the general procedure described for the cyclization reactions, oxo amide **6j** (200 mg, 0.59 mmol) was treated with TFA (0.47 mL, 6.2 mmol) at 20 °C for 16 h to afford oxabenzo[*a*]quinolizidinone **3j** (175 mg, 93%): IR ($CHCl_3$) 1650 cm^{-1}; ^1H NMR ($CDCl_3$) 0.88 (t, J = 7.1 Hz, 3H), 1.21−1.37 (m, 3H), 1.60−1.64 (m, 1H), 2.01−2.15 (m, 2H), 2.31−2.69 (m, 1H), 2.82−2.91 (m, 1H), 2.92−2.95 (m, 1H), 3.53 (d, J = 11.6 Hz, 1H), 3.85 (s, 3H), 3.86 (s, 3H), 4.14 (d, J = 16.7 Hz, 1H), 4.22 (d, J = 11.6 Hz, 1H), 4.33 (d, J = 16.7 Hz), 4.82−4.92 (m, 1H), 6.51 (s, 1H), 6.63 (s, 1H); ^{13}C NMR ($CDCl_3$) 13.9, 23.3, 27.1, 28.6, 35.5, 40.4, 55.8, 56.2, 59.9, 67.4, 74.2, 108.0, 111.9, 126.8, 128.5, 147.7, 148.1, 166.5; MS (EI) m/z (rel intensity) 319 (M^+, 1), 262 (100), 234 (10), 206 (6), 117 (4), 102 (4), 91 (2), 71 (1).

12b-*n*-Butyl-2,3-dimethoxy-5,6-dihydroisoindoloisoquinolin-8(12b*H*)-one (3k). According to the general procedure described for the cyclization reactions, hydroxy lactam **5k** (160 mg, 0.43 mmol) was treated with TFA (0.35 mL, 4.5 mmol) at 20 °C for 16 h to afford isoindoloisoquinolone **3k**, as a white solid that was crystallized from MeOH (143 mg, 95%): mp 130−133 °C; IR ($CHCl_3$) 1690 cm^{-1}; ^1H NMR ($CDCl_3$) 0.76 (t, J = 7.2 Hz, 3H), 0.90−0.97 (m, 2H), 1.14−1.23 (m, 2H), 2.10−2.42 (m, 2H), 2.72 (dd, J = 16.0, 4.3 Hz, 1H), 3.05 (m, 1H), 3.28 (td, J = 12.8, 4.5 Hz, 1H), 3.82 (s, 3H), 3.93 (s, 3H), 4.62 (dd, J = 13.2, 6.6 Hz, 1H), 6.58 (s, 1H), 7.15 (s, 1H), 7.46 (t, J = 7.5 Hz, 1H), 7.60 (t, J = 7.5 Hz, 1H), 7.78 (d, J = 7.7 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.8, 22.4, 25.3, 29.1, 34.9, 40.3, 55.8, 56.3, 109.4, 112.0, 122.1, 123.8, 125.7, 128.2, 131.4, 131.7, 132.3 , 147.6, 148.1, 148.7, 167.9; MS (EI) m/z (rel intensity) 351 (M^+, 4), 200 (15), 164 (100), 149 (8), 115 (3), 91 (3), 77 (3). Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.19, H, 7.17, N, 3.98. Found: C, 75.11, H, 7.12, N, 4.20.

1-*n*-Butyl-*N*-[2-(3,4-dimethoxyphenyl)ethyl]-3-hydroxyisoquinolinium Trifluoracetate (11). According to the general procedure described for the cyclization reactions, the mixture of hydroxy lactam **5l** and oxo amide **6l** (150 mg, 0.39 mmol) was treated with TFA (0.31 mL, 4.1 mmol) at 20 °C for 16 h to afford isoquinolinium salt **11** (128 mg, 90%): ^1H NMR ($CDCl_3$) 0.97 (t, J = 7.2 Hz, 3H), 1.48 (hept, J = 7.1 Hz, 2H), 1.56−1.66 (m, 2H), 2.88−2.95 (m, 2H), 3.06 (t, J = 7.5 Hz, 2H), 3.72 (s, 3H), 3.85 (s, 3H), 4.53 (distorted t, 2H), 6.65−6.69 (m, 2H), 6.73−6.86 (m, 2H), 6.87−6.93 (m, 1H), 7.22−7.29 (m, 2H), 7.51 (d, J = 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.6, 22.9, 29.0, 31.6, 34.5, 47.6, 55.6. 55.9, 107.6, 111.3. 111.9, 115.5, 120.7, 122.0, 125.6, 130.7, 131.0, 142.4, 147.9, 149.0, 152.9, 160.5; MS (EI) m/z (rel intensity) 365 ($M^+ - 1$), 164 (73), 149 (26), 105 (56), 91 (21), 85 (44), 71 (59), 57 (100).

14-*n*-Butyl-13,13-dimethyl-2,3-dimethoxy-13,14-dihidroprotoberberin-8(2*H*)-one (3m). According to the general procedure described for the cyclization reactions, hydroxy lactam **5m** (20 mg, 0.047 mmol) was treated with TFA (0.05 mL, 0.49 mmol) at reflux for 6 days to afford protoberberinone **3m**, as an oil that was purified by HPLC (50% hexane/AcOEt, 6 mL/min) (14 mg, 75%): IR ($CHCl_3$) 1640 cm^{-1}; ^1H NMR ($CDCl_3$) 0.71 (t, J = 6.9 Hz, 3H), 0.89 (s, 3H), 1.01−1.15 (m, 2H), 1.20−1.29 (m, 2H), 1.48 (s, 3H), 1.74 (td, J = 12.6, 3.9 Hz, 1H), 1.99 (t, J = 12.6 Hz, 1H), 2.68 (m, 1H), 2.78−2.95 (m, 2H), 3.89 (s, 3H), 3.91 (s, 3H), 5.23-5.31 (m, 1H), 6.69 (s, 1H), 6.82 (s, 1H), 7.33−7.39 (m, 2H), 7.48 (t, J = 7.2 Hz, 1H), 8.14 (d, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.8, 21.8, 23.0, 27.0, 30.4, 35.8, 40.2, 44.6, 55.8, 56.3, 68.9, 111.2, 112.4, 123.9, 126.4, 126.6, 128.3, 128.7, 132.2, 132.7, 146.3, 146.5, 147.8, 163.6; MS (EI) m/z (rel intensity) 393 (M^+, 19), 336 (100), 321 (8), 306 (14), 248 (12), 146 (82), 131 (97), 117 (29), 103 (11), 91 (7), 78 (8).

13b-*n*-Butyl-9,9-dimethyl-2,3-dimethoxydibenzo[*a*,*h*]-quinolizidin-8-one (3m′). According to the general procedure described for the cyclization reactions, hydroxy lactam **5m′** (52 mg, 0.13 mmol) was treated with TFA (0.10 mL, 1.36 mmol) at 20 °C for 48 h to afford dibenzoquinolizidinone **3m′** (47 mg, 95%): ^1H NMR ($CDCl_3$) 0.83 (t, J =7.1 Hz, 3H), 0.9−1.32 (m, 4H)*, 1.01 (s, 3H)*, 1.68 (s, 3H), 2.35 (t, J = 8.0 Hz, 2H), 2.81 (dd, J = 16.6, 5.5 Hz, 1H), 3.12−3.26 (m, 1H), 3.39−3.51 (m, 1H), 3.63 (s, 3H), 3.81 (s, 3H), 4.99−5.08 (m, 1H), 6.57 (s, 1H), 6.58 (s, 1H), 7.36−7.46 (m, 3H), 7.62−7.66 (m, 1H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.9, 22.4, 26.1, 26.3, 26.4, 31.1, 36.2, 41.3, 55.8, 55.8, 64.5, 108.8, 112.3, 125.4, 125.7, 126.4, 127.0, 128.1, 132.4, 134.9, 142.6, 146.5, 147.8, 175.7; MS (EI) m/z (rel intensity) 393 (M^+, <1), 336 (100), 321 (12), 306 (4), 293 (4), 278 (8), 249 (3), 191 (1), 178 (1), 168 (2), 146 (16), 102 (1), 77 (1).

10b-*n*-Butyl-1,1-dimethyl-8,9-dimethoxy-1,5,6,10b-tetrahydrothiazolo[4,3-*a*]isoquinolin-3(2*H*)-one (3o). According to the general procedure described for the cyclization reactions, hydroxy lactam **5o** (100 mg, 0.27 mmol) was treated with TFA (0.20 mL, 2.86 mmol) at reflux for 24 h to afford thiazoloisoquinolone **3o** (87 mg, 95%): IR (KBr) 1670 cm^{-1}; ^1H NMR ($CDCl_3$) 0.82 (t, J = 7.1 Hz, 3H), 0.97−1.16 (m, 1H)*, 1.01 (s, 3H)*, 1.18−1.38 (m, 3H), 1.60 (s, 3H), 1.92−2.03 (m, 1H) 2.53−2.60 (dd, J = 12.8, 4.8 Hz, 1H), 2.64−2.70 (m, 1H), 2.84 (td, J = 15.3, 5.2 Hz, 1H), 3.06 (td, J = 12.4, 3.4 Hz, 1H), 3.87 (s, 3H), 3.90 (s, 3.90), 4.49 (dd, J = 12.7, 4.8 Hz, 1H), 6.63 (s, 1H), 6.68 (s, 1H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.9, 22.1, 23.3, 27.3, 28.7, 30.0, 36.5, 40.4, 55.7, 56.1, 59.1, 71.0, 108.2, 111.8, 126.9, 128.5, 147.8, 148.0, 169.5; MS (EI) m/z (rel intensity) 349 (M^+, <1), 149 (4), 136 (9), 121 (8), 109 (7), 95 (13), 69 (100), 55 (13). Anal. Calcd for $C_{19}H_{27}NO_3S$: C, 65.30, H, 7.79, N, 4.01. Found: C, 65.40, H, 7.85, N, 3.92.

10b-*n*-Butyl-1,1-dimethyl-8,9-dimethoxy-1,5,6,10b-tetrahydrooxazolo[4,3*a*]isoquinolin-3(2*H*)-one (3p). According to the general procedure described for the cyclization reactions, hydroxy lactam **5p** (88 mg, 0.25 mmol) was treated with TFA (0.19 mL, 2.62 mmol) at reflux for 24 h to afford oxazoloisoquinolone **3p**, as an oil (83 mg, 94%): IR (KBr) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) 0.86 (t, J = 7.1 Hz, 3H), 0.93 (s, 3H)*, 0.92−1.11 (m, 1H)*, 1.13−1.39 (m, 3H), 1.68 (s, 3H), 1.82−1.95 (m, 1H), 2.03−2.15 (m, 1H), 2.79 (dd, J = 15.6, 3.8 Hz, 1H), 2.94 (td, J = 15.6, 6.0 Hz, 1H), 3.26 (td, J = 13.1, 3.8 Hz, 1H), 3.87 (s, 3H), 3.90 (s, 3H), 4.12 (dd, J = 13.1, 6.0 Hz, 1H), 6.53 (s, 1H), 6.72 (s, 1H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 13.8, 21.8, 23.2, 25.3, 26.6, 29.6, 37.9, 38.0, 55.8, 56.2, 65.8, 86.4, 107.6, 111.9, 126.9, 127.1,

148.1, 156.1; MS (EI) *m/z* (rel intensity) 333 (M^+, <1), 276 (100), 232 (50), 216 (6), 205 (10), 201 (7), 186 (5), 172 (2), 159 (2), 146 (2), 131 (2), 116 (3), 109 (3), 100 (4), 91 (2),77 (2).

***N*-[2-(2-Bromo-4,5-dimethoxyphenyl)ethyl]succinimide (2a).** A solution of bromine (40 mmol, 6.4 g) in glacial acetic acid (26 mL) was added dropwise to a solution of succinimide **1a** (40 mmol, 10.5 g) in glacial acetic acid (200 mL), and the resulting mixture was stirred at 20 °C for 5 h. The acetic acid was eliminated under vacuum, and H_2O was added. The resulting precipitate was filtered and crystallized from MeOH to obtain pure succinimide **2a** as a white solid (13 g, 94%): mp 154−155 °C, IR (KBr) 1760, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) 2.63 (s, 4H), 2.93 (t, J = 7.0 Hz, 2H), 3.76 (t, J = 7.0 Hz, 2H), 3.80 (s, 3H), 3.81 (s, 3H), 6.68 (s, 1H), 6.94 (s, 1H); ^{13}C NMR ($CDCl_3$) 28.1, 33.4, 38.5, 56.0, 113.2, 114.3, 115.5, 129.2, 148.4, 176.9. Anal. Calcd for $C_{14}H_{16}BrNO_4$: C, 49.14, H, 4.71, N, 4.09. Found: C, 49.23, H, 4.85, N, 3.91.

N-[2-(3,4-Dimethoxyphenyl)ethyl]-5-butylidenepyrrolidin-2-one (12). To a solution of the succinimide **2a** (342 mg, 1 mmol) in dry THF (20 mL) was added *n*-BuLi (1.55 mL of a 1.42 M solution in hexanes, 2.2 mmol) at −78 °C. The resulting mixture was stirred at this temperature for 6 h, allowed to warm to rt, and then quenched by the addition of 6 M HCl (0.5 mL). Et_2O (5 mL) was added, the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a mixture of products. Flash column chromatography (silica gel, 25% AcOEt/hexane) afforded enamide **12** (82 mg, 27%): ^1H NMR ($CDCl_3$) 0.92 (t, J = 7.9 Hz, 3H), 1.39 (sext, J = 7.9 Hz, 2H), 1.98 (q, J = 7.9 Hz, 2H), 2.40−2.47 (m, 2H), 2.56−2.63 (m, 2H), 2.73−2.79 (m, 2H), 3.61−3.67 (m, 2H), 3.84 (s, 3H), 3.86 (s, 3H), 4.68 (t, J = 7.9 Hz, 1H), 6.73−6.81 (m, 3H); ^{13}C NMR ($CDCl_3$) 13.6, 21.3, 23.3, 28.7, 28.8, 32.2, 41.2, 55.8, 100.5, 111.2, 111.9, 120.6, 131.1, 138.9, 147.6, 148.8, 175.2. Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.26, H, 8.31, N, 4.62. Found: C, 71.44, H, 8.40, N, 4.56.

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]-5-[*N*-[2-(3,4-dimethoxyphenyl)ethyl]succinimid-3-ylidene]pyrrolidin-2-one (13).** To a solution of the succinimide **2a** (342 mg, 1 mmol) in dry THF (20 mL) was added *t*-BuLi (2.35 mL of a 1.7 M solution in hexanes, 4 mmol) at −78 °C. The resulting mixture was stirred at this temperature for 4 h, allowed to warm to 20 °C, and then quenched by addition of 6 M HCl (0.5 mL). Et_2O (5 mL) and H_2O (10 mL) were added, the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, 30% AcOEt/hexane) afforded the pyrrolidinone **13** (91 mg, 18%): IR ($CHCl_3$) 1740, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) 2.52−2.59 (m, 2H), 2.74−2.83 (m, 2H), 2.85−2.89 (m, 2H), 3.31−3.38 (m, 2H), 3.48 (broad s, 2H), 3.74−3.81 (m, 2H), 3.86−3.91(m, 2H)*, 3.85 (s, 3H)*, 3.86 (s, 3H)*, 3.88 (s, 6H)*, 6.70−6.83 (m, 6H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 25.7, 27.6, 33.2, 33.5, 34.98, 39.8, 42.8, 55.9, 56.0, 56.1, 95.1, 111.3, 111.5, 111.9, 112.0, 120.7, 120.8, 129.3, 130.5, 147.8, 148.2, 148.9, 149.2, 152.5, 170.8, 173.3, 177.6; MS (EI) *m/z* (rel intensity) 508 (M^+, 14), 344 (14), 165 (21), 164 (100), 151 (21), 149 (8), 95 (5), 81 (6), 69 (8), 68 (6), 58 (6), 57 (10), 55 (16), 53 (7). Anal. Calcd for $C_{28}H_{32}N_2O_7$: C, 66.13, H, 6.34, N, 5.51. Found: C, 66.02, H, 6.18, N, 5.42.

Iodination Reactions. General Procedure. A solution of ICl (325 mg, 2 mmol) in glacial acetic acid (2.5 mL) was added dropwise to a solution of the imide **1** (1 mmol) in glacial acetic acid (5 mL), and the resulting mixture was stirred at 20 °C for 2 h. The acetic acid was evaporated under vacuum, CH_2Cl_2 (5 mL) was added, and the resulting solution was treated with sodium thiosulfate (2 mL of a 10% aqueous solution). The aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL), dried (Na_2SO_4), filtered, and evaporated. The residue was crystallized from MeOH to afford pure imides **2**.

***N*-[2-(2-Iodo-4,5-dimethoxyphenyl)ethyl]succinimide (2b).** According to the general procedure for iodination, succinimide **1a** (2.63 g, 10 mmol) was treated with ICl (3.25 g, 20 mmol). After workup, the residue was crystallized from MeOH to afford pure imide **2b** (2.53 g, 65%): mp 152−153 °C; IR (KBr) 1700, 1770 cm^{-1}; ^1H NMR ($CDCl_3$) 2.65 (s, 4H), 2.93 (t, J = 7.1 Hz, 2H), 3.72 (t, J = 7.1 Hz, 2H), 3.81 (s, 3H), 3.83 (s, 3H), 6.72 (s, 1H), 7.16 (s, 1H); ^{13}C NMR ($CDCl_3$) 28.1, 37.8, 38.7, 55.9, 56.0, 87.9, 112.4, 121.6, 133.1, 148.3, 149.3, 176.8; MS (EI) *m/z* (rel intensity) 389 (M^+, 28), 290 (100), 277 (46), 262 (26), 150 (12), 120 (12), 107 (7), 92 (7), 77 (14), 55 (10).

***N*-2-(4,5-Dimethoxy-2-iodophenyl)ethylglutarimide (2c).** According to the general procedure for iodination, glutarimide **1i** (1 g, 3.6 mmol) was treated with ICl (700 mg, 4.3 mmol). After workup, the residue was crystallized from MeOH to afford pure imide **2c** (1.19 g, 82%): mp 148−149 °C; IR (KBr) 1725, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) 1.91 (quin, J = 6.5 Hz, 2H), 2.62 (t, J = 6.5 Hz, 4H), 2.89 (t, J = 7.5 Hz, 2H), 3.83 (s, 3H), 3.85 (s, 3H), 3.99 (t, J = 7.5 Hz, 2H), 6.75 (s, 1H), 7.18 (s, 1H); ^{13}C NMR ($CDCl_3$) 17.1, 32.8, 38.2, 39.4, 55.9, 56.0, 88.0, 112.6, 121.5, 134.0, 148.1, 149.2, 172.3; MS (EI) *m/z* (rel intensity) 403 (M^+, 14), 290 (100), 277 (20), 150 (7), 120 (11), 107 (5), 77 (10), 55 (34). Anal. Calcd for $C_{15}H_{18}INO_4$: C, 44.68, H, 4.50, N, 3.47. Found: C, 44.85, H, 4.47, N, 3.47.

N-[2-(4,5-Dimethoxy-2-iodophenyl)ethyl]diglycolimide (2d). According to the general procedure for iodination, diglycolimide **1j** (558 mg, 2 mmol) was treated with ICl (390 mg, 2.4 mmol). After workup, the residue was crystallized from MeOH to afford pure imide **2d** (688 mg, 85%): mp 135−136 °C; IR (KBr) 1735, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) 2.95 (t, J = 7.3 Hz, 2H), 3.84 (s, 3H), 3.85 (s, 3H), 4.02 (t, J = 7.3 Hz, 2H), 4.32 (s, 4H), 6.73 (s, 1H), 7.20 (s, 1H); ^{13}C NMR ($CDCl_3$) 38.1, 38.5, 56.0, 56.1, 67.7, 88.1, 112.6, 121.7, 133.3, 148.3, 149.37, 168.9; MS (EI) *m/z* (rel intensity) 405 (M^+, 28), 290 (100), 277 (50), 150 (14), 120 (11), 107 (7), 77 (15). Anal. Calcd for $C_{14}H_{16}INO_5$: C, 41.50, H, 3.98, N, 3.46. Found: C, 41.55, H, 3.94, N, 3.45.

N-[2-(4,5-Dimethoxy-2-iodophenyl)ethyl]phthalimide (2e). According to the general procedure for iodination, phthalimide **1k** (311 mg, 1 mmol) was treated with ICl (195 mg, 1.2 mmol). After workup, the residue was crystallized from MeOH to afford pure imide **2e** (417 mg, 95%): mp 164−166 °C; IR (KBr) 1715, 1770 cm^{-1}; ^1H NMR ($CDCl_3$) 3.03 (t, J = 7.3 Hz, 2H), 3.67 (s, 3H), 3.79 (s, 3H), 3.89 (t, J = 7.3 Hz, 2H), 6.66 (s, 1H), 7.16 (s, 1H), 7.65−7.68 (m, 2H), 7.77−7.80 (m, 2H); ^{13}C NMR ($CDCl_3$) 37.7, 38.6, 55.7, 55.9, 88.0, 112.4, 121.6, 123.1, 131.9, 133.1, 133.8, 148.1, 149.2, 168.0; MS (EI) *m/z* (rel intensity) 437 (M^+, 38), 310 (55), 290 (91), 277 (100), 160 (34), 150 (22), 133 (16), 120 (13), 105 (24), 92 (13), 77 (56), 64 (12), 51 (18). Anal. Calcd for $C_{18}H_{16}INO_4$: C, 49.45, H, 3.69, N, 3.20. Found: C, 49.89, H, 3.47, N, 3.25.

N-[2-(4,5-Dimethoxy-2-iodophenyl)ethyl]-5,5-dimethylhomophthalimide (2f). According to the general procedure for iodination, homophthalimide **1m** (360 mg, 1 mmol) was treated with ICl (195 mg, 1.2 mmol). After workup, the residue was crystallized from MeOH to afford pure imide **2e** (392 mg, 82%): IR (KBr) 1667, 1712 cm^{-1}; ^1H NMR ($CDCl_3$) 1.57 (s, 6H), 3.02 (t, J = 7.5 Hz, 2H), 3.75 (s, 3H), 3.83 (s, 3H), 4.23 (t, J = 7.5 Hz, 2H), 6.76 (s, 1H), 7.20 (s, 1H), 7.43−7.46 (m, 2H), 7.60−7.66 (m, 1H), 8.22−8.25 (m, 1H); ^{13}C NMR ($CDCl_3$) 29.2, 38.2, 40.2, 43.4, 55.8, 56.0, 88.1, 112.6, 121.6, 123.8, 125.1, 127.3, 128.9, 133.8, 133.9, 145.01, 148.1, 149.2, 164.1, 176.1; MS (EI) m/z (rel intensity) 479 (M^+, 5), 352 (5), 290 (100), 275 (8), 164 (7), 145 (7), 120 (6), 117 (7), 91 (5), 77 (6), 51 (2). Anal. Calcd for $C_{21}H_{22}INO_4$: C, 52.62, H, 4.63, N, 2.92. Found: C, 52.65, H, 4.57, N, 2.98.

Parham Cyclizations. General Procedure. To a solution of the iodinated imide **2b**−**f** (1mmol) in dry THF (20 mL), *n*-BuLi (2 mmol) was added at −78 °C. The resulting mixture was stirred at this temperature for 4 h, quenched by the addition of H_2O (5 mL), and allowed to warm to 20 °C. Et_2O (15 mL) was added, the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford hydroxy lactams **14**, which dehydrated to give enamides **4.**

10b-Hydroxy-8,9-dimethoxy-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one (14a). According to the general procedure for Parham cyclizations, iodinated succin-

imide **2b** (389 mg, 1 mmol) was treated with *n*-BuLi (1.3 mL of a 1.5 M solution in hexanes, 2 mmol). After workup, the residue was identified without further purification as hydroxy lactam **14a** (200 mg, 75%): ^{1}H NMR ($CDCl_3$) 1.96−2.24 (m, 2H), 2.44−2.85 (m, 4H), 3.02−3.14 (m, 1H), 3.72 (s, 3H), 3.76 (s, 3H), 4.05−4.10 (m, 1H), 4.72−5.18 (broad s, 1H), 6.45 (s, 1H), 6.78 (s, 1H). Due to spontaneous dehydration, this product could not be fully characterized.

8,9-Dimethoxy-5,6-dihydropyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one (4a). Spontaneous dehydration of **14a** (200 mg) in $CHCl_3$ solution (1 mL) at 20 °C gave pyrroloisoquinolone **4a** (180 mg, quantitative): IR (neat) 1700, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$) 2.87 (t, J = 6.2 Hz, 2H), 3.21 (d, J = 2.8 Hz, 2H), 3.70 (t, J = 6.2 Hz, 2H), 3.87 (s, 3H), 3.88 (s, 3H), 5.42 (t, J = 2.8 Hz, 1H), 6.66 (s, 1H), 7.00 (s, 1H); ^{13}C NMR ($CDCl_3$) 28.3, 36.8, 38.0, 55.9, 56.0, 94.5, 106.5, 110.8, 119.4, 126.7, 139.4, 148.2, 149.8, 176.5.

11b-Hydroxy-9,10-dimethoxybenzo[*a*]quinolizidin-4-one (14b). According to the general procedure for Parham cyclizations, iodinated glutarimide **2c** (403 mg, 1 mmol) was treated with *n*-BuLi (1.3 mL of a 1.5 M solution in hexanes, 2 mmol). After workup, the residue was identified without further purification as hydroxy lactam **14b** (230 mg, 83%): ^{1}H NMR ($CDCl_3$) 1.64−1.74 (m, 2H), 2.11−2.40 (m, 2H), 2.30−2.45 (m, 2H), 2.45−2.55 (m, 1H), 2.72 (td, J = 14.3, 4.6 Hz, 1H), 2.97 (td, J = 12.5, 3.3 Hz, 1H), 3.79 (s, 3H), 3.80 (s, 3H), 4.59 (broad s, 1H), 4.65−4.71 (m, 1H), 6.52 (s, 1H), 6.90 (s, 1H); ^{13}C NMR ($CDCl_3$) 15.8, 28.7, 31.9, 35.2, 37.2, 55.8, 56.0, 82.7, 108.9, 110.7, 127.2, 131.4, 147.8, 148.7, 170.0; MS (EI) *m*/*z* (rel intensity) 259 (M^+ − 18, 95), 244 (100), 230 (42), 216 (28), 200 (17), 185 (6), 172 (6), 130 (7), 115 (10), 77 (10), 63 (6), 51 (6). Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97, H, 6.90, N, 5.05. Found: C, 65.22, H, 6.76, N, 4.95.

9,10-Dimethoxy-2,3,6,7-tetrahydrobenzo[*a*]quinolizin-4(4*H*)-one (4b). Spontaneous dehydration of **14b** (230 mg) in $CHCl_3$ solution (1 mL) at 20 °C gave pyrroloisoquinolone **4a** (210 mg, quantitative), whose data are identical to those reported in literature:[24] ^{1}H NMR ($CDCl_3$) 2.34−2.42 (m, 2H), 2.48−2.51 (m, 2H), 2.73 (t, J = 5.7 Hz, 2H), 3.81−3.86 (m, 2H)*, 3.84 (s, 3H)*, 3.86 (s, 3H)*, 5.65 (t, J = 4.8 Hz, 1H), 6.58 (s, 1H), 6.99 (s, 1H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 19.4, 28.6, 31.1, 38.3, 55.8, 55.9, 100.5, 106.8, 110.5, 122.3, 127.1, 135.5, 147.9, 146.1, 169.9.

11b-Hydroxy-9,10-dimethoxy-2-oxabenzo[*a*]quinolizidin-4-one (14c). According to the general procedure for Parham cyclizations, iodinated diglycolimide **2d** (405 mg, 1 mmol) was treated with *n*-BuLi (1.3 mL of a 1.5 M solution in hexanes, 2 mmol). After workup, the residue was identified without further purification as hydroxy lactam **14c** (245 mg, 88%): ^{1}H NMR ($CDCl_3$) 2.58−2.65 (m, 1H), 2.80 (td, J = 16.1, 4.5 Hz, 1H), 3.04 (td, J = 12.3, 3.3 Hz, 1H), 3.51 (d, J = 11.0 Hz, 1H), 3.7 (broad s, 1H), 3.81 (s, 6H), 4.10 (d, J = 16.2 Hz, 1H), 4.26 (d, J = 11.0 Hz, 1H), 4.31 (d, J = 16.2 Hz, 1H), 4.68 (dd, J = 12.3, 4.5 Hz, 1H), 6.60 (s, 1H), 6.76 (s, 1H); ^{13}C NMR ($CDCl_3$) 28.5, 34.3, 55.8, 55.9, 67.9, 73.9, 80.2, 108.8, 111.2, 125.2, 127.9, 147.9, 149.3, 165.9; MS (EI) *m*/*z* (rel intensity) 279 (21, M^+), 207 (79), 192 (4), 178 (50), 164 (100), 151 (57), 135 (14), 121 (6), 107 (11), 91 (9), 77 (11), 65 (5), 51 (4).

9,10-Dimethoxy-2-oxa-2,3,6,7-tetrahydrobenzo[*a*]quinolizin-4(4*H*)-one (4c). Spontaneous dehydration of **14c** (245 mg) in $CHCl_3$ solution (1 mL) at 20 °C gave pyrroloisoquinolone **4a** (225 mg, quantitative): IR (neat) 1685, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$) 2.81 (t, J = 5.9 Hz, 2H), 3.86 (s, 6H)*, 3.83−3.86 (m, 2H)*, 4.46 (s, 2H), 6.62 (s, 1H), 6.71 (s, 1H), 6.78 (s, 1H) (* designates partially overlapped signals); ^{13}C NMR ($CDCl_3$) 28.2, 37.7, 55.9, 56.0, 67.2, 105.0, 111.1, 119.4, 125.6, 126.1, 148.4, 148.7, 162.6.

12b-Hydroxy-2,3-dimethoxy-5,6-dihydroisoindoloisoquinolin-8(12b*H*)-one (14d). According to the general procedure for Parham cyclizations, iodinated phthalimide **2e** (437 mg, 1 mmol) was treated with *n*-BuLi (1.3 mL of a 1.5 M solution in hexanes, 2 mmol). After workup, the resulting oil was crystallized from MeOH to afford hydroxy lactam **14d** (300 mg, 96%): mp 157−159 °C dec; IR (KBr) 3340, 1670, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$) 2.64−2.72 (m, 1H), 2.86−3.00 (m, 1H), 3.41 (td, J = 12.5, 4.3 Hz, 1H), 3.74 (broad s, 1H), 3.83 (s, 3H), 3.95 (s, 3H), 4.18−4.25 (m, 1H), 6.57 (s, 1H), 7.42 (s, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.64 (td, J = 7.6, 1.2 Hz, 1H), 7.70 (d, J = 7.4 Hz, 1H), 7.99 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) 29.0, 34.7, 55.8, 56.1, 86.2, 110.3, 111.3, 122.9, 123.4, 127.4, 127.7, 129.2, 130.3, 132.4, 147.8, 148.1, 149.1, 167.3; MS (EI) *m*/*z* (rel intensity) 311 (M^+, 14), 294 (100), 278 (12), 264 (8), 250 (14), 220 (6), 151 (4), 130 (4), 105 (35), 91 (10), 77 (15), 71 (7), 57 (11). Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44, H, 5.50, N, 4.50. Found: C, 69.00, H, 5.43, N.4.60.

13b-Hydroxy-9,9-dimethyl-2,3-dimethoxydibenzo[*a*,*h*]quinolizidin-8-one (14e). According to the general procedure for Parham cyclizations, iodinated homophthalimide **2f** (479 mg, 1 mmol) was treated with *n*-BuLi (1.3 mL of a 1.5 M solution in hexanes, 2 mmol). After workup, the resulting oil was crystallized from Et_2O to afford hydroxy lactam **14e** (230 mg, 66%): ^{1}H NMR ($CDCl_3$) 1.01 (s, 3H), 1.62 (s, 3H), 2.80 (ddd, J = 16.5, 5.4, 2.1 Hz, 1H), 3.09 (ddd, J = 16.5, 6.8, 4.0 Hz, 1H), 3.28 (broad s, 1H), 3.67 (s, 3H), 3.83 (s, 3H), 3.84−3.98 (m, 1H), 4.64 (ddd, J = 12.9, 6.8, 2.1 Hz, 1H), 6.63 (s, 1H), 6.74 (s, 1H), 7.43−7.44 (m, 3H), 7.91−7.95 (m, 1H); ^{13}C NMR ($CDCl_3$) 25.1, 27.0, 29.9, 36.8, 42.0, 55.8, 83.4, 110.0, 111.8, 125.2, 126.0, 127.1, 127.5, 129.3, 130.1, 134.8, 140.6, 146.6, 148.9, 174.7.

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Supporting Information Available: Copies of ^{1}H NMR spectra for new compounds described (57 pages). This material is contained in libraries on microfiche, immediately follows this article in microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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