π-Aromatic and Sulfur Nucleophilic Partners in Cationic π-Cyclizations: Intramolecular Amidoalkylation and Thioamidoalkylation Cyclization via ω-Carbinol Lactams[1,2]

Nicolas Hucher, Bernard Decroix, and Adam Daïch*

Laboratoire de Chimie, URCOM, Faculté des Sciences & Techniques de l'Université du Havre, 25, rue Philippe Lebon, B.P: 540, F-76058 Le Havre Cedex, France

Adam.Daich@univ-lehavre.fr

Received March 13, 2001

$NaBH_4$ reduction of imides **1** and **6a**,**b**,**c** followed by a π-cyclization of the resultant *N*-acyliminium ions, generated in trifluoroacetic acid conditions, afforded two positional isomers, isoindolobenzothiazolinones **4** and **8**, respectively. These ring closures proceeded via an intramolecular α-amidoalkylation with the classical π-aromatic or the atypical sulfur atom as an internal nucleophile. A ready access to the related six-membered *N*,*S*-heterocyclic compounds such as isoindolobenzothiazinones **20a** and **21a** is also described. During this reaction, we have shown that ω-carbinol lactam precursor **14a** led to endocyclic and exocyclic *N*-acyliminium ions **18a** and **19a** in equilibrium via the cyclic aza-sulfonium ion **A**. The latter furnished the expected products **20a** and **21a** in good yields. Similarly, different ω-carbinol lactams **14b**−**e** substituted at *C*-angular position afforded the corresponding isoindolobenzothiazinones **20b**−**e** and **21b**−**e** bearing an angular alkyl, aralkyl, or aryl group. In the case of methyl **14b** and benzyl **14e** groups, an additional amount of the dehydration products **16b** and **31** was isolated. These results indicate that the isomerization-π-cyclization takes place via the cleavage of the thioether linkage in acidic medium.

Introduction

While the chemistry of the exocyclic *N*-acyliminium ion (Type A) is only known in succinimides series,[3−5b] the utilization of the endocyclic *N*-acyliminium ion (Type B) in intramolecular α-amidoalkylation cyclizations with various internal nucleophiles has been largely established. The π-aromatics, olefins, diolefins, alkynes, allyls, homoallyls, allylsilanes, active methylenes, and sulfur or silicon directive π-electron rich which constitute a class of nucleophiles (Type B) are well explored in organic synthesis.[4] They lead to numerous diverse natural alkaloids containing pyrrolizidine, indolizidine, or quinolizidine moieties.[5a−c] The use of a heteroatom as an external nucleophile has been also discussed. On the other hand, the sulfur atom as an internal nucleophile (Type C) was unprecedented before our previous work (Type C with R_1 = benzyl group)[6] (Chart 1).

Chart 1. Commonly Known (Types A and B) and the Newly (Type C) *N*-Acyliminiums Species

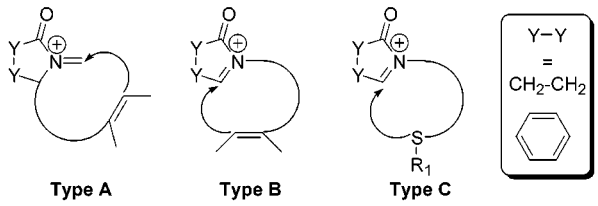
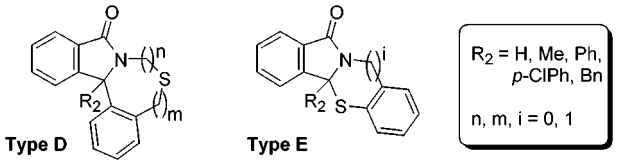


Chart 2. Targets Structures: Isoindolobenzo(or iso)thiazolinones and Isoindolobenzothiazinones



As a part of our continuing investigations of formation−cleavage of the thioether linkage for the preparation of isoindole derivatives containing heterocyclic systems, we wish to report herein the synthesis of some isoindolo[1,2 or 1,3]benzothiazoles (Chart 2, Type D: $n = m = 0$; Type E: $i = 0$) and isoindolo[1,3]benzothiazines (Chart 2, Type D: $n = 1$, $m = 0$; Type E: $i = 1$). These ring closure reactions proceed via a nucleophilic attack of the electron π-aromatic and/or the lone pair of the sulfur atom onto the endo- and/or the exocyclic *N*-acyliminium ions (Types A, B, and C) generated from the corresponding ω-carbinol lactams under strong acidic conditions.

Results and Discussion

In previous papers[7,8] we have described the acid-catalyzed conversion of aromatic isocyanates and cyclic

* To whom correspondence should be addressed. Phone: (+33) 02-32-74-44-03. Fax: (+33) 02-32-74-43-91. e-mail: Nicolas.Hucher@univ-lehavre.fr, Bernard.Decroix@univ-lehavre.fr.

(1) This work was presented in part at the XVIIIth European Colloquium on Heterocyclic Chemistry (ECHC 98), Rouen, France, October 4−7, 1998.

(2) This work was also presented at the American Chemical Society National Meeting, Poster 367, San Francisco, CA, March 26−30, 2000.

(3) (a) Castelhano, A. L.; Krantz, A. *J. Am. Chem. Soc.* **1984**, *106*, 1877. (b) Hart, D. J.; Yang, T. K. *J. Org. Chem.* **1985**, *50*, 235.

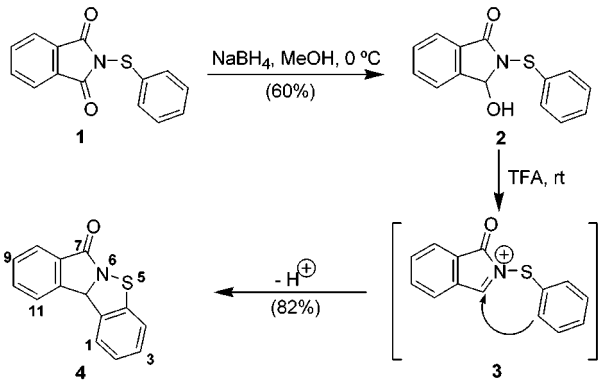
(4) (a) Speckamp, W. N. *Rec. Trav. Chim. Pays Bas* **1981**, *100*, 345. (b) Speckamp, W. N.; Hiemstra, H. *Tetrahedron* **1985**, *41*, 4367.

(5) (a) Hiemstra, H.; Speckamp, W. N. In *The Alkaloids*; Brossi, A., Ed.; Academic Press: New York, 1988; Vol. 32, chapter 4, pp 271−339. (b) Hiemstra, H.; Speckamp, W. N. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I.; Eds.; Pergamon Press: Oxford, 1991; Vol. 2, pp 1047−1082. (c) Speckamp, W. N.; Moolenaar, M. J. *Tetrahedron* **2000**, *56*, 3817.

(6) (a) Hucher, N.; Daïch, A.; Netchitaïlo, P.; Decroix, B. *Tetrahedron Lett.* **1999**, *40*, 3363. (b) For more experimental details, see experimental procedures in the Supporting Information, Part.

10.1021/jo0156316 CCC: $20.00
Published on Web 05/26/2001

Scheme 1. Bicyclic Thiolactam 4 via Intramolecular Amidoalkylation Process

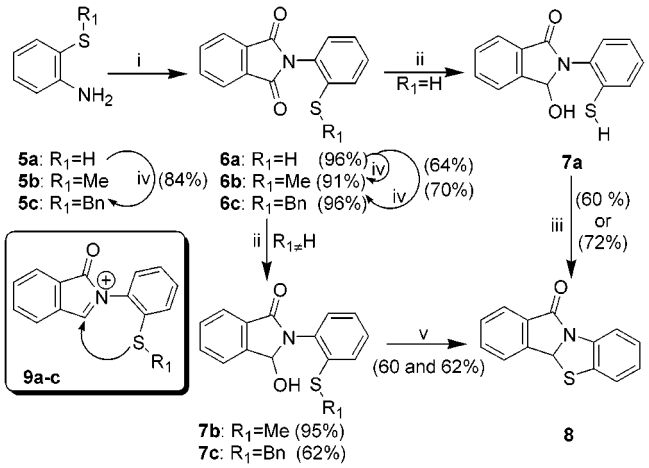


thiepinones into thiazolinones and isothiazolinones, respectively, instead of the possible aromatic thiazocinones. More recently,[6] we have reported the first synthesis of isoindolo(or pyrrolo)[1,3]benzothiazines from ω-carbinol lactam in acid conditions. Such cyclization−rearrangements occurred through an cyclic sulfonium intermediate, respectively, by interaction of sulfur lone electron pair with electron-deficient nitrogen,[7,8] carbon[9,10] or *N*-acyliminium ion[6] followed by cleavage of the thioether bond with[6,7,9,10] or without[8] the loss of the stable benzylic group. Just as Bates et al.[11] outlined the loss of an ethyl group during the intramolecular cyclization of 1-, 2-, and 3-acylpyrrole derivatives.

Isoindolo[2,1-*b*]benzoisothiazolin-7(11b*H*)-one (4) and Isoindolo[1,2-*b*]benzothiazolin-6-(10b*H*)-one (8). As depicted in Scheme 1, reduction[12] of the commercially available *N*-phenylthiophthalimide (**1**) with a large excess of sodium borohydride in dry methanol at 0 °C under carefully controlled conditions gave ω-carbinol lactam **2** (60%) which was converted into the title product **4** (82%). This reaction occurred via the intramolecular π-cyclization of the classical endocyclic *N*-acyliminium ion precursor **3** during the treatment of **2** with neat trifluoroacetic acid (TFA) at room temperature.

Our approach to the isoindolo[1,2-*b*]benzothiazolin-6(11b*H*)-one (**8**),[13a] the positional isomer of **4**, focused on the construction of the C(10b)−S(11) bond and started with the amino derivatives **5** as shown in Scheme 2. Thus, the *o*-aminothiophenol (**5a**) was transformed into phthalimide derivative **6a** (96%) when warming under azeotropic conditions with catalytic amount of anhydrous triethylamine.[13b] Reduction of **6a** with sodium borohydride in methanol at 0−5 °C gave the desired *N*-acyliminium ion precursor **7a**. Because of the difficulty

Scheme 2.[a] Bicyclic Thiolactam 8 via the Newly Intramolecular Thioamidoalkylation Process



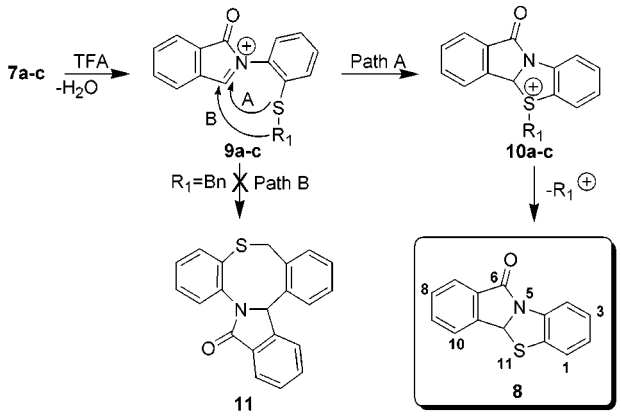
[a] Key: (i) Phthalic anhydride, toluene, NEt_3, reflux. (ii) $NaBH_4$, MeOH, 0−5 °C. (iii) 20% HCl or TFA, rt. (iv) MeONa or NaH, DMF, MeI or BnCl. (v) TFA, rt.

encountered during isolation of this ω-carbinol lactam, the unpurified crude reaction mixture was reacted with 20% hydrochloric acid solution[14] or TFA for 12 h at room temperature and yielded the cyclized product **8** in a 60% or 72% yield, respectively. The same product was isolated in comparable yield when an ethanolic hydrogen chloride solution (3/1 in v/v) was added at regular intervals during the reduction reaction of the imide **6a**. For a generalization of this unusual intramolecular α-heteroamidoalkylation cyclization, we decided to examine the effect of a good leaving group such as methyl and benzyl groups on the sulfur atom nucleophilicity. So, *S*-alkylation of **5a** into **5c** was accomplished with sodium methoxide (or sodium hydride) and benzyl chloride in dry DMF at room temperature in 84% yield[15a] (this product was also obtained in 72% yield by comparable procedure).[15b] Amines **5b**[9] and **5c** were then transformed into imides **6b** and **6c** in 91 and 96% yields,[16] respectively; selective reduction using the same procedure outlined above gave the expected ω-carbinol lactams **7b** (95%) and **7c** (62%) (**6b** and **6c** could also be prepared in 64 and 71% yields, respectively, by *S*-alkylation of **6a** using MeONa(or NaH) as a base and methyl iodide or benzyl chloride as an alkylating agent in DMF at room temperature. Exposure of **7b** or **7c** to TFA at room temperature for 12 h furnished the bicyclic thiolactam **8** in 60 and 62% yields, respectively. The cyclized product **8** is the result of the nucleophilic attack of the sulfur atom onto the endocyclic *N*-acyliminium ion in the intermediates **9a**−**c**, followed by the loss of the methyl or the benzylic cation of the cyclic sulfonium salts **10a**−**c** (Scheme 3, path A).

The stability of the leaving group R_1^+ (R_1 = H, Me, Bn) from cleavage of the thioether bond in acidic medium, as mentioned above,[6−11] combined with the good nucleo-

(7) Jilale, A.; Decroix, B.; Morel, J. *Chem. Script.* **1987**, *27*, 423.
(8) Daïch, A.; Decroix, B. *J. Heterocycl. Chem.* **1991**, *28*, 1881.
(9) Stacy, G. W.; Villaescusa, F. W.; Wollner, T. E. *J. Org. Chem.* **1965**, *30*, 4074.
(10) Stacy, G. W.; Eck, D. L.; Wollner, T. E. *J. Org. Chem.* **1970**, *35*, 3495.
(11) (a) Bates, D. K.; Winters, R. T.; Picard, J. A. *J. Org. Chem.* **1992**, *57*, 3095. (b) Tafel, K. A.; Bates, D. K. *J. Org. Chem.* **1992**, *57*, 3676. (c) Bates, D. K.; Tafel, K. A. *J. Org. Chem.* **1994**, *59*, 8076. (d) Xia, M.; Chen. S.; Bates, D. K. *J. Org. Chem.* **1996**, *61*, 9289.
(12) The reduction was performed with addition or not at regular intervals of hydrochloric acid and was monitored by TLC (silica gel, dichloromethane/hexane: 9.5/0.5). To use similar conditions see: Pigeon, P.; Decroix, B. *J. Heterocycl. Chem.* **1996**, *33*, 129.
(13) (a) This product **8** was obtained by thermal dehydration of 2-(*o*-carboxyphenyl)benzothiazoline, and it should be added that the reported mp for **8** is 172−174 °C: Oliver, G. L.; Dann, J. R.; Gates, J. W., Jr. *J. Am. Chem. Soc.* **1958**, *80*, 702. (b) Alkhathlan, H. Z. *J. Chem. Res. (S)* **1992**, 260.
(14) The hydrochloric acid solution (20%) was prepared in methylene chloride as solvent. The use of the concentrated hydrochloric acid caused some complications during the separation procedure of the cyclized product **8**.
(15) (a) Jilale, A.; Decroix, B. *Chem. Script.* **1987**, *27*, 417. (b) Chen, L. C.; Wang, H. M.; Kang, I. J. *Heterocycles* **1999**, *51*, 1437.
(16) An alternative way for synthesis of **6c** was explored from **6a** by *S*-alkylation with 1.2 equiv of benzyl chloride and 1 equiv of sodium methoxide unvariably in DMF or DMSO as solvent at 45−50 °C. The reaction yield is about 70% in both cases; see ref 15 and Supporting Information, Part.

Scheme 3. Mechanism of the Intramolecular α-Thioamidoalkylation Cyclization Process

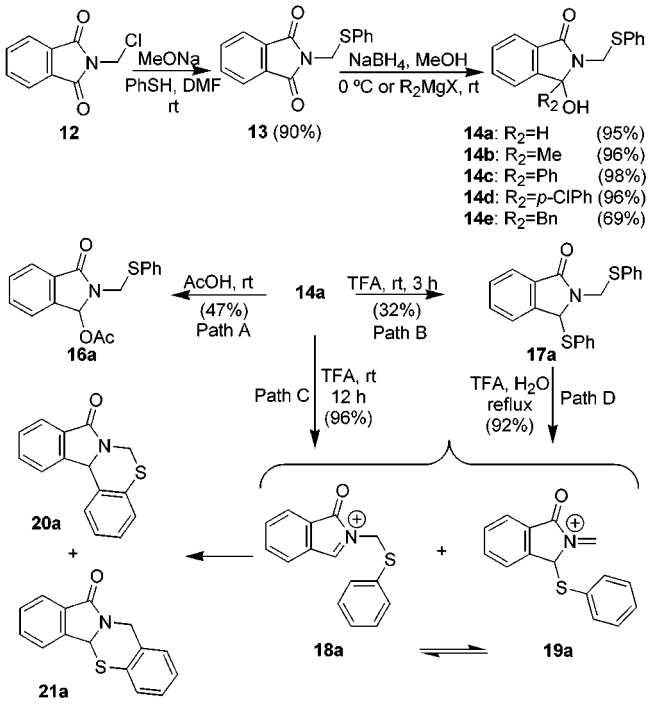


philicity of the sulfur atom constitutes a significant competing process for the cyclization reaction to the detriment of the π-aromatic α-amidoalkylation cyclization (Scheme 3, path B), leading to **11**. Modifications of the experimental conditions (presence of solvents, variation of the temperature or the volume of TFA, etc.) did not change the reaction. Compound **8** and some derivatives have been previously synthesized from substituted *o*-aminothiophenol and *o*-acylbenzoic acid by a cyclodehydration process.[13a,17] It was also mentioned that these products have antiinflammatory properties, analgesic activity, and immunosuppressive effects.[18]

6,12b-Dihydroisoindolo[2,1-*c*][1,3]benzothiazin-8-one (20a), 5,11b-Dihydroisoindolo[1,2-*b*][1,3]benzothiazin-7-one (21a), 12b-Alkyl(or aryl)-6,12b-dihydroisoindolo[2,1-*c*][1,3]benzothiazin-8-ones (20b−e), and 11b-Alkyl(or aryl)-5,11b-dihydroisoindolo[1,2-*b*][1,3]benzothiazin-7-ones (21b−e). On the basis of the preceding results, it was envisioned that this strategy could be applied to imides including a N−CH_2−S−Ar sequence which could give access to endo- and/or exocyclic *N*-acyliminium ion intermediate precursors of isoindolobenzo[1,3]thiazine systems as an attractive target. The model imide **13**[19a] (Scheme 4), was obtained by condensation of *N*-chloromethylphthalimide (**12**)[19b] with sodium thiophenate in DMF at room temperature for 5 h (90%).[15a] Reduction reaction of **13** into **14a** (R_2 = H) was carried out with 6 equiv of $NaBH_4$ in MeOH at 0 °C with portionwise addition of an ethanolic hydrochloric acid solution according to the previously reported procedure (95%).[20] On the other hand, the addition of Grignard reagents (R_2−MgX with R_2X = MeI, PhBr, *p*-ClPhBr, and BnCl) occurred with moderate to excellent yields (69−98%) to give ω-substituted-ω-carbinol lactams **14b**−**e**.

To our knowledge, the *N*-arylthiomethylhydroxylactam function is not explored extensively in the literature. Regarding the reactivity of this group in acidic medium,

Scheme 4. Access to Isoindolo[1,3]benzothiazinones 20a and 21a via Isomerization of the *N*-Acyliminium Ions Intermediates 18a and 19a



we have previously reported the synthesis of thienothiazinoisoindolones.[21] In a similar manner, the hydroxy lactam **14a** was allowed to react under various cyclization conditions (Scheme 4). **14a** with neat acetic acid for 3 h at room temperature (Scheme 4, path A) led to the acetate derivative **16a** in a yield of 47%, and the prolonged reaction time (12 h) left **16a** unchanged. Stirring **14a** with neat TFA, HCl, or H_2SO_4 at room temperature for 3 h (Scheme 4, path B) gave **17a** in acceptable yields of 32, 30, and 27%, respectively (in these conditions, **17a** may be obtained at maximum efficiency in 50% yield). Interestingly, in the case of TFA with a reaction time of 12 h (Scheme 4, path C), the reaction afforded a mixture of the cyclized products **20a** and **21a** in an excellent yield of 96%.

Mechanistically, these cyclization reactions involve an intramolecular cationic π-cyclization of aromatic tethered to endocyclic *N*-acyliminium ion as in **18a** and **19a.** Thus a 5.5/4.5 mixture of cyclic lactams **20a** and **21a** was obtained. Evidence of the rearrangement of the initially formed endocyclic *N*-acyliminium ion **18a** to the exocyclic one **19a** was obtained while examining the behavior of the adduct **17a.** Thus, treatment of this ω-phenylthio lactam with TFA (Scheme 4, path D) in the presence of 2 to 5 equiv of water at reflux quickly produced a mixture of **20a** and **21a** in the same ratio (92%). From these results we concluded that generation of the endocyclic *N*-acyliminium ion **18a** could be obtained classically from **14a** or from **17a** (Scheme 4, path B) by the loss of thiophenol.[22] In our knowledge, this process constitutes the first example in the generation of *N*-acyliminium ions in the phthalimide series (Scheme 4).[23] As for the exocyclic *N*-acyliminium ion **19a**, its formation could be explained by isomerization of **18a** via the cyclic aza-

(17) Hoehn, H.; Schulze, E. United States Patent 3,591,599; *Chem. Abstr.* **1971**, *75*, 76777c.

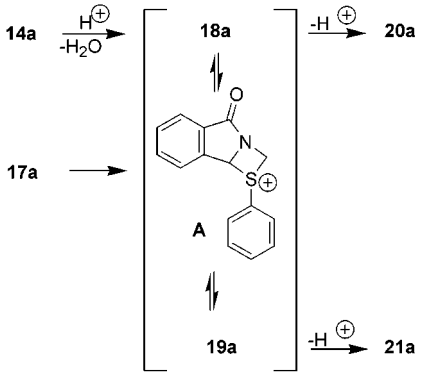
(18) See ref 13a for synthesis. (b) see the US patent in ref 17. (c) Martens, A.; Zilch, H.; König, B.; Schäfer, W.; Poll, T.; Kampe, W.; Seidel, H.; Leser, U.; Leinert, H. *J. Med. Chem.* **1993**, *36*, 2526 and references therein.

(19) (a) Böhme, H.; Müller, A. *Arch. Pharm. (Weinheim, Ger.)* **1964**, *296*, 54. (b) Cherbuliez, E.; Sulzer, G. *Helv. Chem. Acta* **1925**, *8*, 567.

(20) (a) Arai, Y.; Matsui, M.; Koizumi, T.; Shiro, M. *J. Org. Chem.* **1991**, *56*, 1983. (b) Arai, Y.; Kontani, T.; Koizumi, T. *J. Chem. Soc., Perkin Trans. 1* **1994**, 15. When the reduction time exceed more than 1 h, the hydroxylactam **14a** was accompanied with small amounts (12−17%) of the opened amide-alcohol **15a** which resulted from an additional reduction of α-hydroxylacatm **14a**.

(21) Netchitaïlo, P.; Othman, M.; Decroix, B. *J. Heterocycl. Chem.* **1997**, *34*, 321.

Scheme 5. Mechanism of the Intramolecular Amido- and α-Thioamidoalkylation Cyclization

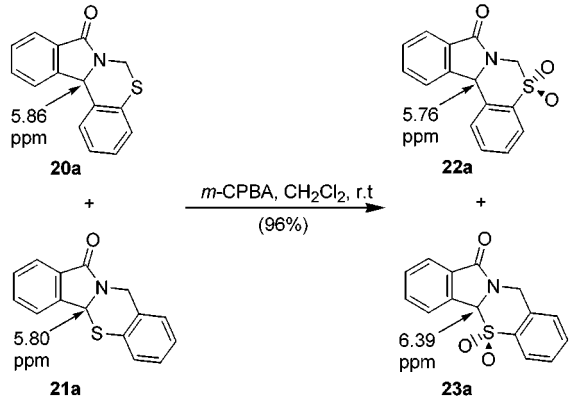


sulfonium ion **A** or by departure of thiophenol under acidic medium in the intermediate **17a** (Scheme 4, path A) as shown in Scheme 5.

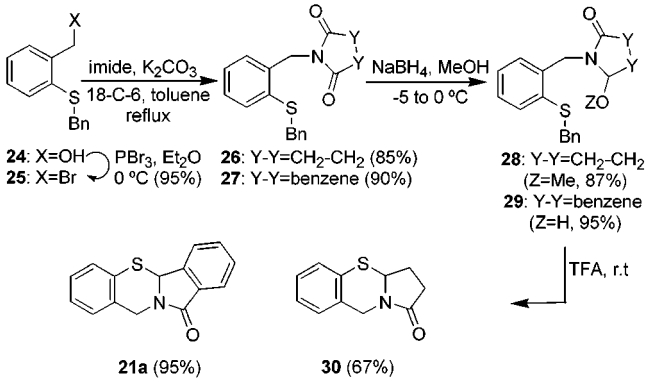
The rate of cyclization of both **14a** and **17a** decreased in the presence of methylene chloride as solvent at room temperature (3 days to 1 week were necessary for complete cyclization) or at lower temperature in the presence or absence of solvent (at −20 °C the cyclization reaction occurred after 1 week but in the presence of CH_2Cl_2 as solvent at the same temperature, more than 1 week was necessary), but when the reaction temperature was increased, the reaction proceeded swiftly. In all these cases, the cylization reaction furnished the same mixture of **20a** and **21a** with insignificant change of the 5.5/4.5 ratio. In conclusion, the preferred method for preparation of **20a** and **21a** of superior quality is to add **14a** or **17a** to neat TFA, respectively, at room temperature or under reflux under magnetic stirring.

Compounds **20a** and **21a** have comparable R_f values in numerous solvents, thus rendering their complete separation uncertain and difficult (nevertheless pure **20a** was separated by fractional recrystallization), and the structures of these products were established by spectroscopic analyses. The infrared spectrum indicated the absence of a O−H stretch; the ^{1}H NMR spectrum showed two methylene groups (H-6 and H-5) which appear as an AB system with coupling constants of J = 12.4 Hz (**20a**) and 17.5 Hz (**21a**) characteristic of geminate protons and two others protons (H-12b and H-11b) on a tertiary carbon which were shifted downfield compared to the same protons in ω-carbinol- and ω-phenylthio lactams precursors **14a** ($\Delta\delta$ = +0.02 to +0.08 ppm) and **17a** ($\Delta\delta$ = +0.05 to +0.11 ppm), respectively. Likewise, the ^{13}C NMR spectra of **20a** and **21a** revealed the presence of an additional quaternary carbon. These data,

Scheme 6. Chemical Separation of Isoindolo[1,3]benzothiazines 20a and 21a by *m*-CPBA Oxidation



Scheme 7. Structure Confirmation of Isoindolo[1,3]benzothiazinone 21a via an Intramolecular Thioamidoalkylation Strategy



the microanalyses, and the coupling GC-MS which showed a molecular ion at m/z = 253, clearly established the structure for **20a** and **21a** as 6,12b-dihydroisoindolo-[2,1-*c*][1,3]benzothiazin-8-one and 5,11b-dihydroisoindolo-[1,2-*d*][1,3]benzothiazin-7-one, respectively.

Interestingly, the oxidation of the mixture **20a** and **21a** by *m*-CPBA in dry methylene chloride afforded a mixture of sulfones **22a** and **23a** (96%) which were separated by crystallization in methylene chloride (Scheme 6). As for **23a**, the ^{1}H NMR spectrum revealed an important deshielding of about +0.59 ppm of proton H-11b adjacent to sulfur atom compared to the corresponding one in **21a** while the same proton in sulfone **22a** is hardly affected by this oxidation (Scheme 6).

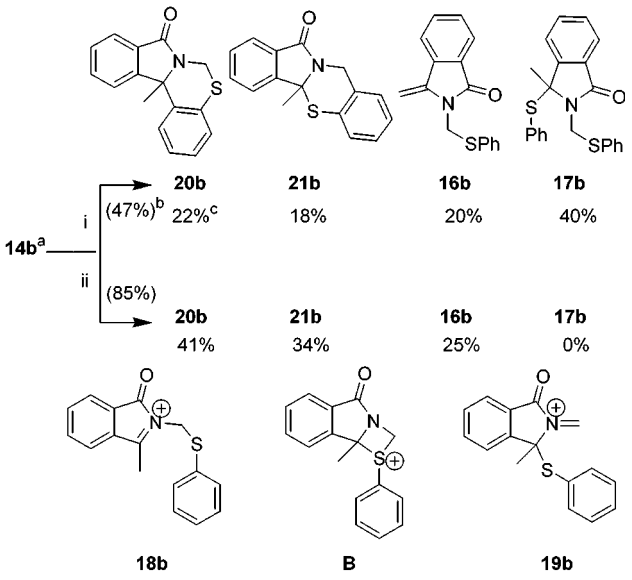
This result confirmed the proposed structures for **20a** and **21a** and structural similarities with other isoindolo-[1,3]benzothiazines recently described by us.[6] Indeed, according to the sequential method illustrated in Scheme 7, the ω-carbinol lactam **29** was easily obtained from bromide **25**.[24] Subjected to an acidic treatment, **29** yielded the cyclized lactam **21a** through the intramolecular sulfuration of the intermediate *N*-acyliminium ion and debenzylation. This process was extended successfully to the succinimide series. Thus, the pyrrolo[1,3]benzothiazine **30** was prepared in good yield via the ω-carbinol lactam **28**.

(22) Similar compounds using thiophenol in *N*-alkyl- or *N*-aryl-4-hydroxypyrrolidin-2-one series had been prepared and used successfully as cyclization radical precursors of pyrrolizidine and indolizidine alkaloids. For example see: (a) Burnett, D. A.; Choi, J. K.; Hart, D. J.; Tsai, Y. M. *J. Am. Chem. Soc.* **1984**, *106*, 8201. (b) Clauss, R.; Hunter, R. *J. Chem. Soc., Perkin Trans.1* **1997**, 71.

(23) Few reports concerning the generation of *N*-acyliminium ions, from corresponding ω-alkylthio- and ω-arylthio lactams, has been mentioned in the literature. For example see: Padwa, A.; Waterson, A. G. *J. Org. Chem.* **2000**, *65*, 235. Padwa, A.; Waterson, A. G. *Tetrahedron* **2000**, *56*, 10159 and references therein. Just now, only the hydroxy,[5a,b] alkoxy,[5a,b] chloro,[5b] (see also: (a) Zaugg, H. E.; Martin, W. B. *Org. React.* **1965**, *14*, 52. (b) Uray, G.; Ziegler, E. Z. *Naturforsch.* **1975**, *30B*, 245. (c) Böhme, U.; Hartke, K. *Chem. Ber.* **1963**, *96*, 600) mesyl lactams (see: Chamberlin, A. R.; Nguyen, H. D.; Chung, J. Y. L. *J. Org. Chem.* **1984**, *49*, 1682), carbamates were used intensively. For reviews concerning *N*-acyliminium ions chemistry see refs 5a−c.

(24) The chloride derivative, isomer to the bromide **25**, was prepared according to the procedure reported in the literature (78%)[9] but its use in the *N*-alkylation process, apparently, affected the reaction yield whatever the experimental conditions.

Scheme 8.[a] α-Methyl-α-hydroxylactam 14b toward Amidoalkylation Cyclization Conditions



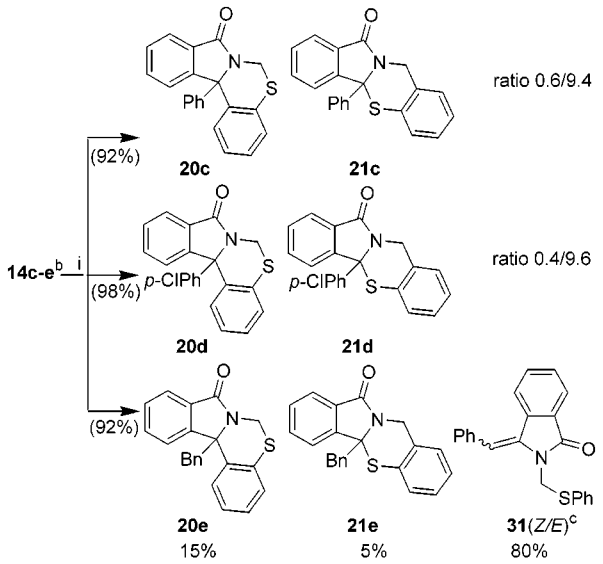
[a] Key: (i) TFA, rt, 3 h or TFA, rt, 12 h, CH_2Cl_2. (ii) TFA, rt, 12 h. [b] Yields of reaction were given in brackets. [c] Ratio of compounds was given in percent and was determined by GC-MS and ^{1}H NMR analyses.

We next examined the effect of a *C*-angular substituted product **14b** in the rearrangement−cyclization step. Thus, as depicted in Scheme 8 *ω*-carbinol-*ω*-methyl lactam **14b** upon treatment with TFA for 3 h or TFA−dichloromethane for 12 h at room temperature (conditions i) gave a mixture of the cyclized products **20b** (22%), **21b** (18%), the *ω*-methylidene lactam **16b** (20%), and the *ω*-phenylthio lactam **17b** (40%) in a low yield of 47% due to the presence of an important tar. With neat TFA at room temperature for 12 h (conditions ii), **14b** gave only three products **16b** (25%), **20b** (41%), and **21b** (34%) in good yield (85%). Invariably, the cyclized products **20b** and **21b** were obtained in a ratio of 5.5/4.5 identical to that reported above for **20a** and **21a** (Scheme 8).

From these results it seemed that both dilution and shorter reaction time favored the formation of the *ω*-phenylthio lactam **17b** (conditions i, 40%; conditions ii, 0%) which was separated from the mixture and easily purified by chromatography on silica gel (SiO_2 with CH_2Cl_2 as eluent). We next investigated other groups such as phenyl, *p*-chlorophenyl, and benzyl. Thus, as depicted in Scheme 9, according to conditions ii cited above, **14c** (R_2 = Ph), **14d** (R_2 = *p*-ClPh) or **14e** (R_2 = Bn)[25] produced the mixture of the two cyclized products **20c**,**d**,**e** and **21c**,**d**,**e** in comparable yields of 92%, 98%, and 92% respectively.

In the case of benzyl derivative, the reaction was straightforward and furnished **31** as a major product (80%) accompanied with cyclized products **20e** and **21e** in proportions of 15% and 5%, respectively. The dehydrated benzylidenephthalimidine product **31** as a 1/1 (*Z*/*E*) mixture were easily separated by chromatography on a silica gel column. The *Z* form of product **31** could be also obtained as a single product in 86% yield by

Scheme 9.[a] Intramolecular Amidoalkylation Cyclization of α-Substituted α-Hydroxylactams 14c−e



[a] Key: (i) TFA, rt, 12 h (conditions ii described in Scheme 8). [b] The ratio of compounds **20** and **21** was given in percent and was determined by GC-MS and ^{1}H NMR analyses. [c] Compound **31** as a *Z* form was also obtained easily in 86% yield by treatment of *ω*-carbinol lactam **14e** with catalytic amount of PTSA in dry CH_2Cl_2 at room temperature for 12 h.

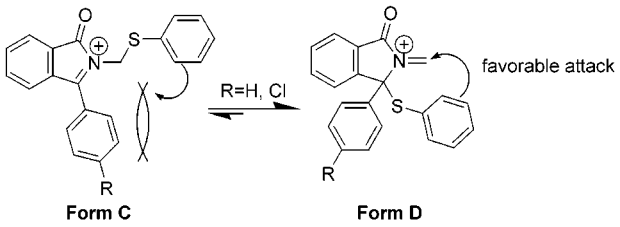
treatment of the *ω*-benzyl-*ω*-carbinol lactam **14e** with PTSA in dry methylene chloride at room temperature for 12 h. It seems that the ratio *Z*/*E* depends from the reaction temperature and that **31** (*Z*) is the stable thermodynamic isomer. Finally, the inversion ratio between product **20** and **21** seems to be sensitive to the class and range of the R_2 group while the dehydration product is favored by the high conjugation existing in the aromatic enamidone to the detriment of the cyclized products.

Indeed, the formation of methylidene(or benzylidene)-phthalimidine **16b** or **31**, easily separated by chromatography on silica gel and dichloromethane as eluent, could be explained by the dehydration reaction in acidic medium. Thus, this reaction is analogous to that already observed in phthalimidin-2-yl acetic acid derivatives series and methyl *o*-(phthalimidin-2-yl-methyl)benzene carboxylate series, respectively, when the mixture of 10% hydrochloric acid−acetic chloride[26] and PTSA in azeotropic conditions[27] were used as dehydrating agents. Furthermore, in the cases of phenyl or *p*-chlorophenyl groups, a high selectivity of the *π*-cyclization reaction was observed. This effect could be due probably to the fact that the steric hindrance of the phenyl group was favorable, as illustrated in Chart 3, for approach in form **D** (in equilibrium with form **C**) of the incoming *π*-aromatic system during the *π*-cationic cyclization step. Consequently, the ratio of the cyclized products were respectively 0.6/9.4 (for **20c**/**21c**) 0.4/9.6 (for **20d**/**21d**) in contrast to these observed for R_2 = H, Me and benzyl groups.

(25) Subjection of **14e** to TFA led to the expected formation of a six-membered rings **20e** and **21e** rather than a four-membered spirolactam derivative.

(26) Scartoni, V.; Fiaschi, R.; Catalano, S.; Morelli, I.; Marsili, A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1547.
(27) Daïch, A.; Marchalin, S.; Pigeon, P.; Decroix, B. *Tetrahedron Lett.* **1998**, *39*, 9187.

Chart 3. Correlation of Cyclization Ratio and *N*-Acyliminium Ion Geometry in the Case of 14c,d



Conclusion

Novel five-ring *N*,*S*-heterocyclic compounds **4** and **8**, are produced under acidic conditions via capture of an endocyclic *N*-acyliminium ions **3** and **9a**,**b**,**c** with an internal nucleophile as the π-aromatic or sulfur atom followed by the departure of a proton, a methyl, or a benzyl group.

The related isoindolobenzothiazinones **20a** and **21a** analyzed by GC-MS and separated at the sulfone oxidation state were also formed by reaction of ω-carbinol lactam precursor **14a** with TFA. From **17a**, evidence of the isomerization of the initially formed endocyclic *N*-acyliminium ion **18a** to the corresponding exocyclic one **19a** (not yet known in isoindolone series) leading to cyclized products **20a** and **21a** was observed. On the other hand, compound **21a** was obtained univocally via the model imide **27** in four steps as illustrated in Scheme 7.[6] The generalization of this reaction process was accomplished with *C*-angular substituted ω-carbinol lactam precursors **14b**−**e** (R_2 = Me, Ph, *p*-ClPh, Bn).

Finally, applications of this strategy to the synthesis of more functionalized novel five-, six-, seven-, and eight-membered *N*,*S*-heterocyclic systems are in progress, and the results will be reported in due course.

Experimental Section

General. Melting points are uncorrected. IR spectra of solids (potassium bromide) were recorded on a Perkin-Elmer FTIR paragon 1000 spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured on a Bruker AC-200 instrument (200 MHz), and chemical shifts are reported relative to $CDCl_3$ at δ 7.24 ppm (or to DMSO-d_6 at δ 2.49 ppm) and tetramethylsilane as an internal standard. MS spectral measurements were carried out on a AEI MS 902 S spectrometer (70 eV, electron impact). Reagents were obtained from commercial suppliers and used without further purification. Solvents were dried and purified by standard methods. A Merck silica gel 60 was used for both column chromatography (70−230 mesh) and flash chromatography (230−400 mesh). Ascending TLC was performed on precoated plates of silica gel 60 F 254 (Merck), and the spots were visualized using an ultraviolet lamp or iodine vapor. Elemental analyses (C, H, N) were performed by the microanalysis laboratory of INSA at Rouen, F-76130 Mt-St-Aignan, France.

2,3-Dihydro-3-hydroxy-2-phenylthio-1*H*-isoindol-1-one (2).[12] To a well-stirred solution of *N*-phenylthiophthalimide (2.55 g, 10 mmol) in dry MeOH (30 mL) was added in portions at 0 °C sodium borohydride (1.89 g, 50 mmol) over a period of 10 min. After complete addition of sodium borohydride, 3 drops of ethanolic hydrochloric acid solution was added at regular intervals (10 min) (prepared from 9 drops of concentrated hydrochloric acid in 15 mL of EtOH) until the reaction was complete (40 min) (monitored by TLC using CH_2Cl_2 as eluent). The excess of sodium borohydride was decomposed by careful addition of 10% HCl solution to pH = 3. After removal of the solvent, the residue was diluted with H_2O (40 mL) and extracted with 30 mL of CH_2Cl_2. After a classical workup, the resulting solid was recrystallized from EtOH to give 1.6 g (60%) of the expected ω-carbinol lactam **2**: mp 152 °C (decomposition); IR (KBr) 3302, 3015, 1701 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 5.91 (d, 1H exchangeable with D_2O, J = 8.9 Hz), 6.39 (d, 1H, J = 8.9 Hz), 7.32−7.48 (m, 5H), 7.51−7.71 (m, 4H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 78.1 (CH), 122.3 (CH), 123.6 (CH), 127.1 (2CH), 127.6 (CH), 129 (CH), 129.3 (2CH), 131.8 (CH), 131.9 (C), 135.7 (C), 146.8 (C), 168.4 (CO); MS (*m*/*z*) 257 ($M^{+\bullet}$). Anal. Calcd for $C_{14}H_{11}NO_2S$: C, 65.35; H, 4.31; N, 5.44. Found: C, 65.12; H, 4.28; N, 5.32.

Isoindolo[2,1-*b*]benzoisothiazol-7(11b*H*)-one (4). To 257 mg (1 mmol) of hydroxylactam **2** was added 5 mL of TFA. After 12 h of reaction at room temperature under stirring, the reaction mixture was concentrated in vacuo and diluted with CH_2Cl_2 (10 mL). The organic layer was neutralized with 10% $NaHCO_3$ solution, separated, dried over $MgSO_4$, and evaporated to give after recrystallization from EtOH the expected bicyclic product **4** as a yellow solid (196 mg, 82%): mp 155 °C (decomposition); IR (KBr) 3029, 1688 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 5.72 (s, 1H), 7.15−7.35 (m, 5H), 7.39−7.89 (m, 3H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 58.9 (CH), 122.9 (CH), 123.4 (CH), 127.2 (2CH), 127.5 (CH), 127.7 (CH), 129.4 (2CH), 131.3 (C), 135.8 (C), 139.2 (C), 147.7 (C), 169.6 (CO); MS (*m*/*z*) 239 ($M^{+\bullet}$). Anal. Calcd for $C_{14}H_9NOS$: C, 70.27; H, 3.79; N, 5.85. Found: C, 70.21; H, 3.75; N, 5.78.

***o*-Benzylthioaniline (5c).** To a stirred solution under an atmosphere of dry argon of *o*-amino-thiophenol (12.52 g, 0.1 mol) in 60 mL of dry DMF was added 5.94 g (0.11 mol) of sodium methoxide. After stirring for 30 min at room temperature, benzyl chloride (12.66 g, 0.1 mol) was added slowly dropwise over a period of 10 min. The mixture was then allowed to react at the same temperature for 12 h. The solution was filtered and the filtrate was concentrated in vacuo. The oily residue after trituration with a mixture Et_2O/hexane (1/1) was recrystallized from hexane to give amino derivative **5c** (18.06 g, 84% (72%)[15b]) as a yellow solid: mp < 45 °C (oil);[15b] IR (KBr) 3025, 2098, 1305, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.83 (s, 2H), 3.96 (br, 2H exchangeable with D_2O), 6.52−6.60 (m, 2H), 7.00−7.29 (m, 7H); MS (*m*/*z*) 215 ($M^{+\bullet}$). Anal. Calcd for $C_{13}H_{13}NS$: C, 72.51; H, 6.08; N, 6.50. Found: C, 72.46; H, 6.00; N, 6.41.

General Procedure for Preparation of Imides 6a, 6b, and 6c. A mixture of 10 mmol of *o*-amino-thiophenol (*o*-methylthioaniline or *o*-benzylthioaniline (**5c**)), phthalic anhydride (1.48 g, 10 mmol), and two drops of dry triethylamine in toluene (50 mL) was refluxed with a Dean−Stark apparatus for 3 to 5 h. The reaction mixture was cooled and then was concentrated under reduced pressure. The residue was dissolved into CH_2Cl_2 (50 mL) and washed with 5% HCl solution and then with a 10% $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure, and recrystallization of the residue from ethanol gave the desired imide **6a** (96%), **6b** (91%), or **6c** (96%).

S-Methylation (or *S*-benzylation) of imide **6a** leading to imide **6b** in 64% yield (or **6c** in 71% yield) was carried out in standard manner as reported above for *S*-benzylation of **5a** into **5c**.

***N*-(*o*-Mercaptophenyl)phthalimide (6a).** This product was isolated as a green solid: mp 202−206 °C (decomposition); IR (KBr) 3289, 3037, 1715 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 3.37 (s, 1H exchangeable with D_2O), 7.45−7.54 (m, 3H), 7.60−7.69 (m, 1H), 7.89−7.94 (m, 2H), 7.95−8.02 (m, 2H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 148.3 (2CH), 153.6 (CH), 153.9 (CH), 154.7 (CH), 154.9 (CH), 155 (C), 155.7 (2C), 159.5 (C), 159.6 (2CH), 191.2 (2CO); MS (*m*/*z*) 255 ($M^{+\bullet}$). Anal. Calcd for $C_{14}H_9NO_2S$: C, 65.86; H, 3.55; N, 5.48. Found: C, 65.75; H, 3.47; N, 5.31.

***N*-(*o*-Methylthiophenyl)phthalimide (6b).** This product was isolated as a white solid: mp 138 °C; IR (KBr) 3012, 2095, 1702 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.37 (s, 3H), 7.17−7.31 (m, 2H), 7.34−7.47 (m, 2H), 7.70−7.78 (m, 2H), 7.87−7.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 15.9 (CH_3), 123.8 (2CH), 126.1 (CH), 127.5 (CH), 129.5 (CH), 129.7 (C), 130.1 (CH), 131.8 (2C), 134.3 (2CH), 138.4 (C), 167.1 (2CO); MS

(*m*/*z*) 269 ($M^{+\bullet}$). Anal. Calcd for $C_{15}H_{11}NO_2S$: C, 66.89; H, 4.11; N, 5.20. Found: C, 66.75; H, 4.07; N, 5.13.

***N*-(*o*-Benzylthiophenyl)phthalimide (6c).** This product was isolated as a white solid: mp 108−110 °C (decomposition); IR (KBr) 3024, 2092, 1712 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 4.03 (s, 2H), 7.07−7.27 (m, 5H), 7.32−7.39 (m, 4H), 7.72−7.81 (m, 2H), 7.91−7.98 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 39.1 (CH_2), 127.3 (CH), 127.6 (CH), 128.4 (2CH), 128.9 (2CH), 129.6 (CH), 129.8 (CH), 131.5 (CH), 131.9 (C), 134.2 (2CH), 136.3 (C), 136.5 (C), 167.2 (2CO); MS (*m*/*z*) 345 ($M^{+\bullet}$). Anal. Calcd for $C_{21}H_{15}NO_2S$: C, 73.02; H, 4.37; N, 4.05. Found: C, 73.05; H, 4.21; N, 4.00.

***N*-(Phenylthiomethyl)phthalimide (13).**[28] To a stirred solution under an atmosphere of dry argon of thiophenol (11.02 g, 0.1 mol) in 25 mL of dry DMF was added 5.94 g (0.11 mol) of sodium methoxide. After stirring for 20 min at room temperature, *N*-chloromethylphthalimide (19.56 g, 0.1 mol) in 15 mL of dry DMF was added slowly dropwise over a period of 15 min. The mixture was then allowed to react at the same temperature for 5 h and hydrolyzed. The resulting solid was filtered off and recrystallized from EtOH to give the expected imide **13** (24.24 g, 90%) as a white solid: mp 128 °C (127 °C);[19a] IR (KBr) 3031, 2092, 1715 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.03 (s, 2H), 7.24−7.28 (m, 3H), 7.45−7.50 (m, 2H), 7.63−7.67 (m, 2H), 7.77−7.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 42.2 (CH_2), 123.5 (2CH), 128 (CH), 129 (2CH), 131.8 (2C), 132.6 (CH+C), 133.1 (CH), 134.2 (2CH), 166.9 (2CO); MS (*m*/*z*) 269 ($M^{+\bullet}$). Anal. Calcd for $C_{15}H_{11}NO_2S$: C, 66.89; H, 4.11; N, 5.20. Found: C, 66.82; H, 4.04; N, 5.11.

General Procedure for Reduction of Imides 6b, 6c, and 13. To a solution of imide **6b**, **6c**, or **13** (10 mmol) in dry MeOH (40 mL) at 0−5 °C was added in portions 6 equiv of sodium borohydride (2.27 g, 60 mmol). After complete addition of sodium borohydride, the mixture was allowed to react under stirring for a required time (monitored by TLC using CH_2Cl_2 as eluent). The excess of sodium borohydride was destroyed carefully by addition of 10% HCl solution and alkalinized by a saturated $NaHCO_3$. After removal of the solvent under reduced pressure, the residue was diluted with cold water (40 mL) and allowed to stir at room temperature for an additional 1 h. The resulting solid was filtered off and recrystallized from EtOH to give pure ω-carbinol lactam **7b**, **7c**, or **14a** in 95%, 62%, or 95% yield, respectively.

2,3-Dihydro-3-hydroxy-2-(*o*-methylthiophenyl)-1*H*-isoindol-1-one (7b). This product was isolated as a white solid: mp 159 °C; IR (KBr) 3299, 3021, 2090, 1692 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.35 (s, 3H), 3.71 (d, 1H exchangeable with D_2O, J = 7.8 Hz), 6.13 (d, 1H, J = 7.8 Hz), 7.09−7.42 (m, 4H), 7.43−7.50 (dd, 1H, J = 4.2 and 7.8 Hz), 7.54−7.63 (m, 2H), 7.72 (d, 1H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 15.2 (CH_3), 83.2 (CH), 123.4 (CH), 123.9 (CH), 125.6 (CH), 126.2 (CH), 129.2 (CH), 129.8 (CH), 130.2 (C), 130.9 (C), 132.5 (CH), 133.1 (C), 138.6 (C), 143.9 (C), 166.7 (CO); MS (*m*/*z*) 271 ($M^{+\bullet}$). Anal. Calcd for $C_{15}H_{13}NO_2S$: C, 66.39; H, 4.82; N, 5.16. Found: C, 66.77; H, 4.69; N, 5.08.

2,3-Dihydro-3-hydroxy-2-(*o*-benzylthiophenyl)-1*H*-isoindol-1-one (7c). This product was isolated as a white solid: mp 142 °C (decomposition); IR (KBr) 3306, 3031, 2089, 1702 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.21 (d, 1H exchangeable with D_2O, J = 7.4 Hz), 4.02 (s, 2H), 5.98 (d, 1H, J = 7.4 Hz), 7.06−7.25 (m, 5H), 7.37−7.45 (m, 4H), 7.52−7.61 (m, 2H), 7.71−7.75 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 38.5 (CH_2), 83.7 (C), 123.4 (CH), 123.9 (CH), 127.3 (CH), 127.4 (CH), 128.5 (2CH), 128.8 (2CH), 129.1 (CH), 129.9 (CH), 130.4 (CH), 130.6 (CH), 131.1 (C), 132.6 (CH), 135.2 (C), 136.5 (C), 136.8 (C), 143.8 (C), 166.9 (CO); MS (*m*/*z*) 347 ($M^{+\bullet}$). Anal. Calcd for $C_{21}H_{17}NO_2S$: C, 72.59; H, 4.93; N, 4.03. Found: C, 72.44; H, 4.88; N, 4.10.

2,3-Dihydro-3-hydroxy-2-(phenylthiomethyl)-1*H*-isoindol-1-one (14a). This product was isolated as a white solid: mp 124 °C; IR (KBr) 3279, 3026, 2089, 1679 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.65 (d, 1H, J = 11.3 Hz), 4.43 (d, 1H, J = 13.8 Hz), 5.07 (d, 1H, J = 13.8 Hz), 5.88 (d, 1H, J = 11.3 Hz), 7.15−7.18 (m, 3H,), 7.36−7.41 (m, 4H), 7.52−7.57 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 42.9 (CH_2), 80.3 (CH), 123.2 (CH), 123.5 (CH), 127.3 (CH), 129.1 (2CH), 129.7 (CH), 130.4 (C), 130.9 (2CH), 132.7 (CH), 133.2 (C), 143.7 (C), 167.0 (CO); MS (*m*/*z*) 271 ($M^{+\bullet}$). Anal. Calcd for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; N, 5.16. Found: C, 66.35; H, 4.67; N, 5.10.

Isoindolo[1,2-*b*]benzothiazolin-6(11b*H*)-one (8). Method A. The unpurified **7a**, obtained by standard borohydride reduction of **6a** as indicated for **6b** and **6c**, was treated with 20% HCl in CH_2Cl_2 (40 mL)[14] or neat TFA (10 mL) at room temperature for 12 h. After concentration in vacuo, the crude solid was extracted with CH_2Cl_2 and the organic layer was washed successively with water, 5% $NaHCO_3$, and saturated brine and then separated. The organic phase was dried over $MgSO_4$ and evaporated under reduced pressure to afford after recrystallization from ethanol the cyclized product **8** in 60% or 62% yield, respectively.

Method B. To a stirred solution of hydroxylactam **7b** or **7c** (10 mmol) was added neat TFA (10 mL). After 12 h of reaction at room temperature under stirring, the reaction mixture was diluted with water (30 mL) and neutralized with 10% NaOH aqueous solution. The solution was extracted twice with CH_2Cl_2 (20 mL). The organic layer was washed with water, separated, dried over $MgSO_4$, and evaporated. The resulting crude residue was purified by flash chromatography (SiO_2, CH_2Cl_2/hexane (4/1)) to give the tricyclic product **8** as white crystals in 95% (2.27 g) or 62% (1.48 g) yield, respectively: mp 168−171 °C (decomposition) (172−174 °C);[13a] IR (KBr) 3015, 1692 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 6.97 (s, 1H), 7.06−7.25 (m, 4H), 7.50−7.67 (m, 3H), 7.95 (d, 1H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 69.2 (CH), 118.4 (CH), 123.0 (CH), 123.5 (CH), 125.1 (CH), 125.7 (CH), 125.8 (CH), 129.8 (CH), 132.6 (C), 133.1 (CH), 135.7 (C), 136.5 (C), 143.1 (C), 168.5 (CO); MS (*m*/*z*) 239 ($M^{+\bullet}$). Anal. Calcd for $C_{14}H_9NOS$: C, 70.27; H, 3.79; N, 5.85. Found: C, 70.19; H, 3.80; N, 5.75.

General Procedure for Grignard Addition onto *N*-(Phenylthiomethyl)phthalimide (13). To a well stirred and cold solution of imide **13** (10 mmol) under dry nitrogen atmosphere in anhydrous CH_2Cl_2 (20 mL) was added slowly in dropwise a 0.5 M solution of Grignard reagent (methylmagnesium iodide, phenylmagnesium bromide, *p*-chlorophenylmagnesium bromide, or benzylmagnesium chloride (11 to 15 mmol)) freshly prepared according to the classical procedure in dry ether over a period of 30 min. After 1 h of reaction at 0−5 °C, the reaction was allowed to stir for an additional 2 h at room temperature. After hydrolysis under stirring with water (30 mL) and then with 0.5 M NH_4Cl solution (40 mL), the solution was passed through Celite. After separation, the organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Recrystallization of the reaction residue from a mixture of ether/hexane gave suitable α-hydroxylactams in yields of 96% (**14b**), 98%, (**14c**), 96% (**14d**), and 69% (**14e**), respectively.

2,3-Dihydro-3-hydroxy-3-methyl-2-(phenylthiomethyl)-1*H*-isoindol-1-one (14b). This product was obtained as yellow needles: mp 124 °C; IR (KBr) 3290, 3018, 2085, 1675 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.67 (s, 3H), 3.94 (s, 1H exchangeable with D_2O), 4.59 (d, 1H, J = 14 Hz), 4.74 (d, 1H, J = 14 Hz), 7.23−7.28 (m, 2H), 7.38−7.43 (m, 4H), 7.50−7.56 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 24.7 (CH_3), 43.2 (CH_2), 88.7 (C), 121.7 (CH), 123.5 (CH), 127.3 (CH), 129.1 (2CH), 129.5 (C), 129.6 (CH), 131.6 (2CH), 132.9 (CH), 134.6 (C), 148.1 (C), 167.9 (CO); MS (*m*/*z*) 285 ($M^{+\bullet}$). Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.29; N, 4.91. Found: C, 67.15; H, 5.27; N, 4.94.

2,3-Dihydro-3-hydroxy-3-phenyl-2-(phenylthiomethyl)-1*H*-isoindol-1-one (14c). This compound was obtained as a yellow solid: mp 166 °C; IR (KBr) 3329, 3020, 2096, 1709 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.77 (s, 1H exchangeable with D_2O), 4.27 (d, 1H, J = 13.5 Hz), 5.22 (d, 1H, J = 13.5 Hz), 7.20−7.24 (m, 5H), 7.28−7.34 (m, 5H), 7.42−7.46 (m, 3H), 7.75−7.79 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 44.1 (CH_2), 91.5 (C), 122.7 (CH), 123.6 (CH), 126.2 (2CH), 127.2 (CH),

(28) Hucher, N.; Daïch, A.; Decroix, B. *Org. Lett.* **2000**, *2*, 1201.

128.6 (2CH), 128.7 (CH), 128.9 (2CH), 129.4 (C), 129.5 (CH), 131.2 (2CH), 133.2 (CH), 134.5 (C), 137.8 (C), 148.8 (C), 167.4 (CO); MS (*m*/*z*) 347 ($M^{+\bullet}$). Anal. Calcd for $C_{21}H_{17}NO_2S$: C, 72.60; H, 4.93; N, 4.03. Found: C, 72.54; H, 4.88; N, 4.10.

3-*p*-Chlorophenyl-2,3-dihydro-3-hydroxy-2-(phenylthiomethyl)-1*H*-isoindol-1-one (14d). This compound was a obtained as yellow solid: mp 182 °C; IR (KBr) 3331, 3018, 2098, 1713 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.12 (s, 1H exchangeable with D_2O), 4.33 (d, 1H, J = 13.7 Hz), 5.06 (d, 1H, J = 13.7 Hz), 7.18−7.21 (m, 5H), 7.35−7.38 (m, 4H), 7.44−7.49 (m, 3H), 7.72−7.75 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 44.1 (CH_2), 91.1 (C), 122.7 (CH), 123.7 (CH), 127.3 (CH), 127.7 (2CH), 128.8 (2CH), 128.9 (2CH), 129.3 (C), 129.8 (CH), 131.2 (2CH), 133.3 (CH), 134.3 (C), 134.7 (C), 136.5 (C), 148.4 (C), 167.2 (CO); MS (*m*/*z*) 381 ($M^{+\bullet}$). Anal. Calcd for $C_{21}H_{16}ClNO_2S$: C, 66.05; H, 4.22; N, 3.67. Found: C, 66.01; H, 4.13; N, 3.59.

3-Benzyl-2,3-dihydro-3-hydroxy-2-(phenylthiomethyl)-1*H*-isoindol-1-one (14e). This compound was obtained as yellow needles: mp 133 °C; IR (KBr) 3314, 3016, 2082, 1678 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.05 (s, 1H exchangeable with D_2O), 3.09 (d, 1H, J = 14.1 Hz), 4.08 (d, 1H, J = 14.1 Hz), 4.78 (d, 1H, J = 13.5 Hz), 5.16 (d, 1H, J = 13.5 Hz), 6.91−6.94 (m, 2H,), 7.11−7.15 (m, 4H), 7.24−7.28 (m, 3H), 7.37−7.42 (m, 2H), 7.54−7.59 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 43.7 (CH_2), 44.1 (CH_2), 90.9 (C), 123.2 (2CH), 126.9 (CH), 127.3 (CH), 127.8 (2CH), 128.9 (2CH), 129.4 (CH), 130.1 (C), 130.4 (2CH), 131.6 (2CH), 132.0 (CH), 134.5 (C), 134.8 (C), 146.1 (C), 166.7 (CO); MS (*m*/*z*) 361 ($M^{+\bullet}$). Anal. Calcd for $C_{22}H_{19}NO_2S$: C, 73.10; H, 5.29; N, 3.87. Found: C, 72.95; H, 5.19; N, 3.79.

2,3-Dihydro-3-acetyloxy-2-(phenylthiomethyl)-1*H*-isoindol-1-one (16a). A stirred solution of 2,3-dihydro-3-hydroxy-2-(phenylthiomethyl)-1*H*-isoindol-1-one (**14a**) (271 mg, 1 mmol) in 20 mL of acetic acid was allowed to react at room temperature. After 3 h of reaction at room temperature, the reaction mixture was concentrated in vacuo and diluted with CH_2Cl_2 (15 mL). The organic layer was neutralized with 10% $NaHCO_3$ solution, separated, dried over $MgSO_4$, and evaporated to give after recrystallization from EtOH the title product **16a** as a yellow solid (147 mg, 47%): mp 151 °C (decomposition); IR (KBr) 1681, 1652 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.11 (s, 3H), 5.41 (d, 1H, J = 11 Hz), 5.62 (d, 1H, J = 11 Hz), 6.95 (s, 1H), 7.16−7.32 (m, 5H), δ 7.51−7.56 (m, 3H), 7.78 (d, 1H, J = 6.7 Hz); MS (*m*/*z*) 313 ($M^{+\bullet}$). Anal. Calcd for $C_{17}H_{15}NO_3S$: C, 65.15; H, 4.82; N, 4.47. Found: C, 65.14; H, 4.77; N, 4.45.

2,3-Dihydro-3-phenylthio-2-(phenylthiomethyl)-1*H*-isoindol-1-one (17a). This product was obtained as a white solid in similar manner as for **16a**, using 257 mg (1 mmol) of hydroxylactam **14a** and 10 mL of TFA, 10% HCl, or 10% H_2SO_4 solution, in 32% (116 mg), 30% (109 mg) or 27% (98 mg) yield, respectively: mp 130 °C (ethanol); IR (KBr) 3009, 1715 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 4.83 (d, 1H, J = 13.7 Hz), 5.71 (d, 1H, J = 13.7 Hz), 5.91 (s, 1H), 6.98−7.03 (m, 5H), 7.19−7.31 (m, 5H), 7.44−7.61 (m, 4H); MS (*m*/*z*) 363 ($M^{+\bullet}$). Anal. Calcd for $C_{21}H_{17}NOS_2$: C, 69.38; H, 4.71; N, 3.58. Found: C, 69.31; H, 4.68; N, 3.88.

6,12b-Dihydroisoindolo[2,1-*c*][1,3]benzothiazin-8-one (20a) and 6,12b-Dihydroisoindolo[1,2-*b*][1,3]benzothiazin-7-one (21a). Method A. A solution containing 271 mg (1 mmol) of 2,3-dihydro-3-hydroxy-2-(phenylthiomethyl)-1*H*-isoindol-1-one (**14a**) and 5 mL of TFA was allowed to react at room temperature under stirring. After 12 h of reaction at same temperature, the mixture was concentrated in vacuo and diluted with CH_2Cl_2 (20 mL). The organic layer was neutralized with 10% $NaHCO_3$ solution, separated, dried over $MgSO_4$, and evaporated to give 243 mg (96%) of an inseparable **20a**/**21a** (5.5/4.5) mixture.

Method B. A solution containing 728 mg (2 mmol) of 2,3-dihydro-3-phenylthio-2-(phenylthi*o*-methyl)-1*H*-isoindol-1-one (**17a**), 5 mL of TFA, and 2−5 equiv of H_2O was refluxed for 12 h. After identical workup as described above, 466 mg (92%) of a mixture of **20a**/**21a** in a 5.5/4.5 ratio was obtained.

6,12b-Dihydroisoindolo[2,1-*c*][1,3]benzothiazin-8-one (20a). This product was obtained by fractional recrystallization from a mixture of ether/hexane (9.5/0.5) as a white solid: mp 142 °C (decomposition); IR (KBr) 3021, 1701 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 4.63 (d, 1H, J = 12.4 Hz), 5.29 (d, 1H, J = 12.4 Hz), 5.86 (s, 1H), 7.19−7.25 (m, 4H), 7.56−7.61 (m, 2H), 7.82−7.86 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 41.3 (CH_2), 59.6 (CH), 123.6 (CH), 124.1 (CH), 126.1 (CH), 127.0 (CH), 127.6 (CH), 128.8 (CH), 129.4 (CH), 131.8 (C), 132.0 (C), 132.2 (CH), 132.4 (C), 144.0 (C), 175.6 (CO); MS (*m*/*z*) 253 ($M^{+\bullet}$). Anal. Calcd for $C_{15}H_{11}NOS$: C, 71.12; H, 4.38; N, 5.53. Found: C, 71.08; H, 4.34; N, 5.50.

6,12b-Dihydroisoindolo[1,2-*b*][1,3]benzothiazin-7-one (21a). This product was obtained in pure form univocally by a strategy developed in Scheme 7 (see text and Supporting Information part for more details) as a white solid: mp 159 °C (decomposition); IR (KBr) 3011, 1702 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 4.62 (d, 1H, J = 17.5 Hz), 5.31 (d, 1H, J = 17.5 Hz), 5.80 (s, 1H), 7.16−7.26 (m, 4H), 7.50−7.64 (m, 2H), 7.77−7.96 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 38.7 (CH_2), 62.1 (CH), 121.8 (CH), 123.9 (CH), 125.8 (CH), 127.2 (CH), 127.5 (CH), 128.3 (CH), 130.4 (CH), 130.9 (C), 131.2 (C), 132.7 (CH), 135.1 (C), 148.0 (C), 166.3 (CO); MS (*m*/*z*) 253 ($M^{+\bullet}$). Anal. Calcd for $C_{15}H_{11}NOS$: C, 71.12; H, 4.38; N, 5.53. Found: C, 71.05; H, 4.29; N, 5.48.

General Procedure for Cyclization of Hydroxylactams 14a−e. These products were prepared according to the method A as described above for synthesis of **20a** and **21a**. But after a standard workup, the mixture was purified by chromatography on silica gel column using CH_2Cl_2 as eluent to give pure enamides **16b**, **31** (*Z*/*E*) and the title products **20b−e** and **21b−e** as inseparable mixtures (see text for more details). In the cases of Ph (**20c**, **21c**) and *p*-ClPh (**20d**, **21d**) as angular groups, the major products **21c** and **21d** were isolated in pure form by fractional recrystallization.

6,12b-Dihydro-12b-methylisoindolo[2,1-*c*][1,3]benzothiazin-8-one (20b) and 5,11b-Dihydro-11b-methylisoindolo[1,2-*b*][1,3]benzothiazin-7-one (21b). These products were obtained as an inseparable mixture in 5.5/4.5 ratio in 85% yield and were accompanied with **16b** which was isolated in pure form.

Product 20b: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.87 (s, 3H), 4.65 (d, 1H, J = 12.6 Hz), 5.41 (d, 1H, J = 12.6 Hz), 7.02−7.27 (m, 4H), 7.37−7.54 (m, 2H), 7.58−7.89 (m, 2H); MS (*m*/*z*) 267 ($M^{+\bullet}$).

Product 21b: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.88 (s, 3H), 4.45 (d, 1H, J = 17.7 Hz), 5.50 (d, 1H, J = 17.7 Hz), 7.02−7.27 (m, 4H), 7.37−7.54 (m, 2H), 7.58−7.89 (m, 2H); MS (*m*/*z*) 267 ($M^{+\bullet}$).

1,2-Dihydro-3-methylidene-2-(phenylthiomethyl)-1*H*-isoindol-1-one (16b). This product was obtained in pure form as a white solid: mp 115 °C; IR (KBr) 3011, 1716, 1624 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 4.88 (d, 1H, J = 2.5 Hz), 5.13 (s, 2H), 5.22 (d, 1H, J = 2.5 Hz), 7.17−7.37 (m, 5H), 7.39−7.57 (m, 4H); MS (*m*/*z*) 267 ($M^{+\bullet}$). Anal. Calcd for $C_{16}H_{13}NOS$: C, 71.88; H, 4.90; N, 5.24. Found: C, 71.73; H, 4.87; N, 5.31.

6,12b-Dihydro-12b-phenylisoindolo[2,1-*c*][1,3]benzothiazin-8-one (20c) and 5,11b-Dihydro-11b-phenylisoindolo[1,2-*b*][1,3]benzothiazin-7-one (21c). These products were obtained as a mixture in 0.6/9.4 ratio in 92% yield. Compound **21c** was isolated in pure form by fractional recrystallization from ethanol.

Product 20c: ^1H NMR ($CDCl_3$, 200 MHz) δ 4.34 (d, 1H, J = 12.4 Hz), 5.27 (d, 1H, J = 12.4 Hz), 7.06−7.38 (m, 6H), 7.41−7.54 (m, 7H); MS (*m*/*z*) 329 ($M^{+\bullet}$).

Product 21c: This product was obtained in pure form as a white solid: mp 161 °C (ethanol); IR (KBr) 3013, 1709 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 4.22 (d, 1H, J = 17.8 Hz), 5.51 (d, 1H, J = 17.8 Hz), 7.06−7.17 (m, 4H), 7.25−7.31 (m, 5H), 7.47−7.51 (m, 3H), 7.91−7.96 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 39.4 (CH_2), 71.4 (C), 121.9 (CH), 124.1 (CH), 125.6 (CH), 126.6 (2CH), 127 (CH), 127.1 (CH), 127.6 (CH), 128.1 (C), 128.3 (CH), 128,7 (2CH), 128.9 (CH), 129.1 (C), 129.2 (C), 132.1 (CH), 137.3 (C), 148.3 (C), 166.4 (CO); MS (*m*/*z*) 329 ($M^{+\bullet}$). Anal. Calcd for $C_{21}H_{15}NOS$: C, 76.56; H, 4.59; N, 4.25. Found: C, 76.49; H, 4.53; N, 4.23.

12b-*p*-Chlorophenyl-6,12b-dihydroisoindolo[2,1-*c*][1,3]-benzothiazin-8-one (20d) and 11b-*p*-Chlorophenyl-5,11b-dihydroisoindolo[1,2-*b*][1,3]benzothiazin-7-one (21d). These products were obtained as a mixture in 0.4/9.6 ratio in 98% yield. Compound **21d** was isolated in pure form by fractional recrystallization from ethanol.

Product 20d: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.33 (d, 1H, J = 12.5 Hz), 5.28 (d, 1H, J = 12.5 Hz), 6.80−7.38 (m, 7H), 7.41−7.58 (m, 5H); MS (*m*/*z*) 364 ($M^{+\bullet}$).

Product 21d: This product was obtained in pure form as a white solid: mp 172 °C (ethanol); IR (KBr) 3019, 1712 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.25 (d, 1H, J = 17.8 Hz), 5.53 (d, 1H, J = 17.8 Hz), 7.08−7.29 (m, 8H), 7.41−7.45 (m, 1H), 7.50−7.57 (m, 2H), 7.97 (d, 1H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 39.8 (CH_2), 71.2 (C), 122.1 (CH), 124.5 (CH), 126.1 (CH), 127.4 (CH), 127.5 (CH), 127.9 (CH), 128.3 (C), 128.5 (2CH), 128.9 (C), 129.2 (2CH), 129.4 (CH), 129.6 (C), 132.7 (CH), 134.7 (C), 136.3 (C), 148.1 (C), 166.7 (CO); MS (*m*/*z*) 363 ($M^{+\bullet}$). Anal. Calcd for $C_{21}H_{14}ClNOS$: C, 69.32; H, 3.88; N, 3.85. Found: C, 69.29; H, 3.90; N, 3.82.

12b-Benzyl-6,12b-dihydroisoindolo[2,1-*c*][1,3]benzothiazin-8-one (20e) and 11b-Benzyl-5,11b-dihydroisoindolo[2,1-*d*][1,3]benzothiazin-7-one (21e). These products were obtained as an inseparable mixture **20e**/**21e** (3/1) in 92% yield and were accompanied with the enamide **31** as a *Z*/*E* mixture which was separated easily by chromatography on silica gel column using CH_2Cl_2 as eluent.

Product 20e: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.57 (d, 1H, J = 14.2 Hz), 3.74 (d, 1H, J = 14.2 Hz), 4.56 (d, 1H, J = 12.4 Hz), 5.39 (d, 1H, J = 12.4 Hz), 6.73−7.42 (m, 7H), 7.51−8.01 (m, 6H); MS (*m*/*z*) 343 ($M^{+\bullet}$).

Product 21e: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.48 (d, 1H, J = 14.5 Hz), 3.69 (d, 1H, J = 14.5 Hz), 4.61 (d, 1H, J = 18.1 Hz), 5.51 (d, 1H, J = 18.1 Hz), 6.73−7.42 (m, 7H), 7.51−8.01 (m, 6H); MS (*m*/*z*) 343 ($M^{+\bullet}$).

(*Z*)-3-Benzylidene-1,2-dihydro-2-(phenylthiomethyl)-1*H*-isoindol-1-one (31). This product was obtained in pure form as a yellow solid: mp 158 °C; IR (KBr) 3022, 1690, 1656 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.13 (s, 2H), 6.48 (s, 1H), 7.17−7.30 (m, 10H), 7.50−7.65 (m, 2H), 7.76 (d, 1H, J = 7.1 Hz), 7.89 (d, 1H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 42.9 (CH_2), 103.4 (=CH), 120.1 (CH), 123.1 (CH), 126.7 (CH), 127.3 (CH), 127.8 (2CH), 127.9 (CH), 128.0 (2CH), 129.1 (CH), 129.2 (C), 129.3 (2CH), 130.2 (C), 130.5 (C), 131.4 (2CH), 133.9 (C), 134.5 (C), 166.1 (CO); MS (*m*/*z*) 343 ($M^{+\bullet}$). Anal. Calcd for $C_{22}H_{17}NOS$: C, 76.94; H, 4.99; N, 4.08. Found: C, 76.85; H, 5.03; N, 4.06.

(*E*)-3-Benzylidene-1,2-dihydro-2-(phenylthiomethyl)-1*H*-isoindol-1-one (31). This product was obtained in pure form as a yellow solid: mp 163 °C; IR (KBr) 3016, 1686, 1641 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.30 (s, 2H), 6.54 (s, 1H), 7.10−7.14 (m, 1H), 7.23−7.30 (m, 3H), 7.34−7.43 (m, 6H), 7.50−7.57 (m, 3H), 7.74 (d, 1H, J = 7.8 Hz); MS (*m*/*z*) 343 ($M^{+\bullet}$). Anal. Calcd for $C_{22}H_{17}NOS$: C, 76.94; H, 4.99; N, 4.08. Found: C, 76.90; H, 4.91; N, 4.00.

Other Method for Preparation of Benzylidene Derivative 31*Z*. To 905 mg (2.5 mmol) of α-benzyl-α-hydroxylactam **14e** in dry CH_2Cl_2 (20 mL) was added 10 mg of *p*-toluenesulfonic acid. After 12 h of reaction at room temperature under stirring, the reaction mixture was concentrated in vacuo and diluted with CH_2Cl_2 (10 mL). The organic layer was neutralized with 5% NaOH solution, separated, dried over $MgSO_4$, and evaporated to give after recrystallization from EtOH a yellow solid in 86% yield (738 mg) identical to the benzylidene derivative **31*Z*** described above.

***m*-CPBA Oxidation of the Mixture of Isoindolo[1,3]-benzothiazines 20a and 21a.** To a cold solution at 0 °C of the mixture of thiazines **20a** and **21a** (1 g, 3.95 mmol) in dry CH_2Cl_2 (20 mL) was added in portionwise *m*-chloroperbenzoic acid (86% pure, 1.32 g, 7 mmol) in dry CH_2Cl_2 over a period of 20 min under vigorous stirring. After 10 min of reaction at this temperature, the reaction was allowed to stir for an additional 4 h at room temperature. The reaction was hydrolyzed carefully with saturated solution of $NaHCO_3$ and separated. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Recrystallization of the residue from dry dichloromethane or dry ethanol afforded pure sulfone **22a**. Sulfone **23a** was isolated in pure form from the mother liquor after concentration in vacuo and recrystallization from the mixture ether/hexane (9.5/0.5). These sulfones were obtained in 96% yield.

6,12b-Dihydro-5,5-dioxyisoindolo[2,1-*c*][1,3]benzothiazin-8-one (22a). This compound was obtained as yellow needles: mp 206 °C (decomposition); IR (KBr) 3020, 1712 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 5.05 (d, 1H, J = 14.2 Hz), 5.65 (d, 1H, J = 14.2 Hz), 6.81 (s, 1H), 7.58−8.10 (m, 6H), 8.12−8.17 (m, 1H), 8.40−8.44 (m, 1H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.5 (CH_2), 73.3 (CH), 123.6 (CH), 124.8 (CH), 125.7 (CH), 128.2 (C), 130.6 (C), 131.4 (CH), 131.9 (CH), 132.2 (C), 134.8 (CH), 135.2 (CH), 135.6 (CH), 138.7 (C), 164.8 (CO); MS (*m*/*z*) 285 ($M^{+\bullet}$). Anal. Calcd for $C_{15}H_{11}NO_3S$: C, 63.14; H, 3.88; N, 4.91. Found: C, 63.06; H, 3.92; N, 5.03.

6,12b-Dihydro-12,12-dioxyisoindolo[2,1-*b*][1,3]benzothiazin-7-one (23a). This compound was obtained as white needles: mp 197−199 °C (decomposition); IR (KBr) 3032, 1717 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 4.94 (d, 1H, J = 13.7 Hz), 5.72 (d, 1H, J = 13.7 Hz), 6.14 (s, 1H), 7.46−8.01 (m, 8H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 58.3 (CH_2), 56.6 (CH), 123.5 (CH), 123.7 (CH), 124.3 (CH), 127.8 (CH), 128.8 (CH), 129.3 (CH), 129.9 (C), 133.2 (CH), 133.3 (CH), 134.7 (C), 137.1 (C), 143.8 (CH), 166.8 (CO); MS (*m*/*z*) 285 ($M^{+\bullet}$). Anal. Calcd for $C_{15}H_{11}NO_3S$: C, 63.14; H, 3.88; N, 4.91. Found: C, 63.09; H, 3.81; N, 4.87.

Acknowledgment. Financial support by "Region of Haute Normandy, France" (Regional Scholarship: **1996**−**99**) and Scientific Council of University of Le Havre are gratefully acknowledged. The helpful discussions rendered by Dr. Jean C. Plaquevent, UMR 6014, CNRS, IRCOF, University of Rouen, Faculty of Sciences, F-76821 Mont-Saint-Aignan, France, is greatly appreciated.

Supporting Information Available: Physical data of all other products not described herein (**6c** and **25**−**30**) and detailed descriptions of experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org. The data may also be obtained at the following e-mail address: Adam.Daich@univ-lehavre.fr.

JO0156316