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Preparation and 1,3-Dipolar Cycloaddition Reactions of *β*-Carboline Azomethine Ylides: A Direct Entry into C-1- and/or C-2-Functionalized Indolizino[8,7-*b*]indole Derivatives

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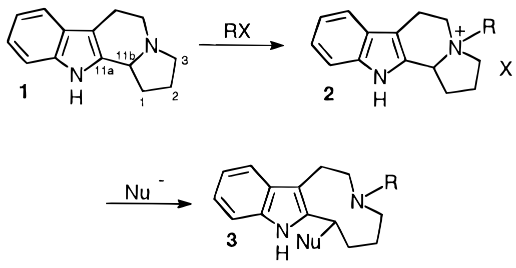
Treatment of norharman with (trimethylsilyl)methyl triflate in dichloromethane gave 2-*N*-[(trimethylsilyl)methyl]-*β*-carboline triflate (**10**). The latter reacted with diethyl acetylenedicarboxylate (**11a**) or ethyl propiolate (**11b**) in the presence of cesium fluoride to afford, via 1,3-dipolar cycloaddition, the indolizino[8,7-*b*]indole derivatives **13a** or **13b**, respectively. In a similar manner, the (trimethylsilyl)methyl triflate salt of ethyl 9-*N*-(*p*-toluenesulfonyl)-*β*-carboline-3-carboxylate (**16**) reacted with **11a** to give the cycloaddition product **17**. The (trimethylsilyl)methyl triflates of 3,4-dihydro-*β*-carbolines were also prepared (**20a**−**c**) and shown to be more reactive than their fully aromatic counterparts **10** and **16** in cycloaddition reactions. Thus, the 9-*N*-benzyl derivative **20b** reacted with **11a** in the presence of cesium fluoride to give the cycloaddition products **21** and **22** as well as the novel azepine derivative **23**. Moreover, unlike **10** and **16**, the azomethine ylides generated from **20a**−**c** reacted with electron-deficient olefins, producing 1,2,3,5,6,11b-hexahydroindolizino[8,7-*b*]indole derivatives. In the case of symmetrically substituted olefins (dimethyl maleate, dimethyl fumarate, fumaronitrile), the cycloaddition reactions were completely stereospecific. However, with unsymmetrically substituted olefins (methyl acrylate, acrylonitrile), cycloaddition reactions were generally neither regio- nor diastereoselective. In the case of **20b**, both the regio- and the diastereoselectivities of the cycloaddition reactions were greatly improved compared to **20a** and **20c**, suggesting that these two stereochemical factors can be controlled by manipulation of the protecting group at the 9-N position of the 3,4-dihydro-*β*-carbolines. The hexahydroindolizino[8,7-*b*]indoles **33** and **37** could be selectively dehydrogenated at the 11b, 1 positions using potassium permanganate in THF to afford the tetrahydro derivatives **58** and **59**, respectively. Treatment of **58** with 1 equiv of DDQ led to further selective dehydrogenation at the 2,3 positions, producing the 5,6-dihydro compound **60**. Alternatively, **33** and **37** could be completely dehydrogenated using 3 equiv of DDQ to give the fully aromatic indolizino[8,7-*b*]indole-1,2-dicarboxylates **56** and **57**, respectively.

Introduction

Indolizino[8,7-*b*]indole derivatives (general formula **1**, Scheme 1) have over several decades been used as synthetic intermediates for the preparation of more complex alkaloids. Most of these preparations have been based on the propensity of the quaternized form of **1** (i.e. **2**) to undergo nucleophile-induced ring opening, yielding an indolic species having a fused 9-membered ring (**3**), a dominant theme found in a good number of naturally occurring substances. This general strategy was used successfully by both Wenkert[2] and Kutney[3] in their approaches to the synthesis of quebrachamine and provided a general entry to iboga and vinca alkaloids.[4] The preparation of dihydrocleavamines was also based on this principle.[5] The 3-oxo derivatives of **1**, in addition to being a newly described class of naturally occurring alkaloids,[6] have proven to be useful as intermediates for the preparation of canthinones[7] and of trichotomine,[8,9] a blue pigment of plant origin, as well as serving as a *β*-turn dipeptide mimic.[10]

Scheme 1



Molecules of general structure **1** have primarily been constructed by reacting a tryptamine or tryptophan derivative with species carrying an aldehyde (or ketone) and a second functional group (usually an ester) sepa-

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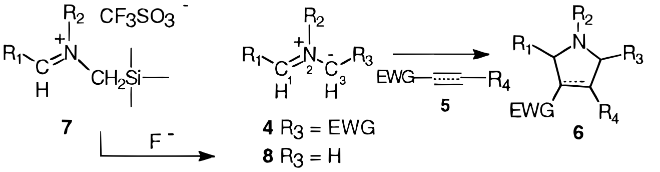
Scheme 2



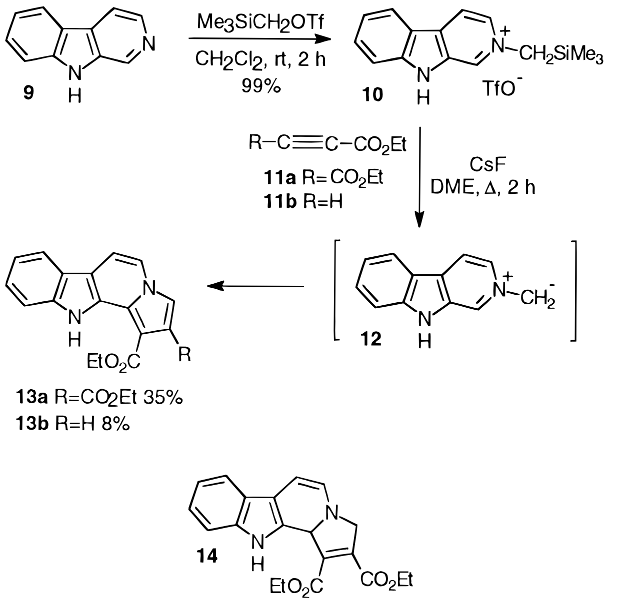
rated by three carbon atoms.[5a,7,9–12] Pictet–Spengler condensation with the aldehyde first gives rise to an intermediate tetrahydro-*β*-carboline derivative. The resulting secondary amine then reacts intramolecularly with the second functional group effecting ring closure. Alternatively, tryptamine or tryptophan can first be converted into their succinimide derivatives and cyclization to a *β*-carboline structure can be accomplished under Bischler–Napieralski conditions[3,8] or *via* mercuric acetate-induced formation of an intermediate iminium species.[4] In nearly all these cases, 3-oxo derivatives of **1** are obtained and reduction of the amide is required to produce a pyrrolidine nucleus. Reaction of a 3,4-dihydro-*β*-carboline with 2-acetoxyacrylates has also been reported to give, among other products, 3-oxo derivatives of **1**.[13]

One of the most powerful methods of forming pyrrolidine rings is the [3 + 2] cycloaddition reaction of azomethine ylides (general formula **4**, Scheme 2) with olefins.[14] The advantages of this approach reside in the high degree of regio- and stereoselectivity observed in these types of reactions as well as the great variety of substituents which can be incorporated on the final pyrrolidine product. This variety is tempered by the necessity of utilizing electron-deficient unsaturated dipolarophiles (i.e., **5**) and, depending on how the ylide **4** is formed, the necessity of stabilizing the negative charge, usually with an electron-withdrawing R^3 group. The introduction by Vedejs and Martinez[15] of *in situ* fluoride ion-induced desilylation of [(trimethylsilyl)methyl]iminium triflates (**7**) as a mild procedure for the generation of nonstabilized azomethine ylides (i.e., **8**) has obviated this last requirement. A large number of multiply substituted pyrrolidine derivatives have been prepared by this methodology which demonstrates the tremendous versatility of the reaction.[16]

The pyridinium nucleus, via a (trimethylsilyl)methyl triflate salt, readily forms an azomethine ylide, and subsequent cycloaddition with electron-deficient acetylenic dipolarophiles affords indolizine derivatives.[17,18] With ethylenic dipolarophiles, this reaction is not useful since the main products observed result from transfer of the methylene group from the pyridinium moiety to the olefin (a process referred to as hydroalkylidenation).[19]

Despite the obvious potential for the preparation of substituted indolizino[8,7-*b*]indole derivatives of type **1**,

Scheme 3



the transformation of a *β*-carboline nucleus into an azomethine ylide has received little attention. Grigg and co-workers[20] have described methods by which tetrahydro-*β*-carbolines are converted into iminium ions by reaction of the secondary amine function with aldehydes. Subsequent azomethine formation can be achieved by an intramolecular proton shift, by base-promoted proton abstraction, or by decarboxylation of an adjacent carboxylate group. Cycloadditions of these *β*-carboline ylides with only one dipolarophile, *N*-methylmaleimide, have been reported.

We have chosen to study the possibility of generating *β*-carboline azomethine ylides using the desilylation procedure. Although, as noted above, ylides produced from pyridine by this method provide cycloaddition products with acetylenic dipolarophiles but not with olefins, this problem could be surmounted by using ylides derived from the easily accessible, and presumably more reactive 3,4-dihydro-*β*-carbolines. We report herein the successful formation of azomethine ylides from fully aromatic *β*-carbolines as well as from 3,4-dihydro-*β*-carbolines via fluoride ion-promoted desilylation techniques and the 1,3-dipolar cycloaddition reactions of these ylides with acetylenic and acetylenic/olefinic dipolarophiles, respectively, to give 1- and/or 2-substituted indolizino[8,7-*b*]indole derivatives.[21]

I. Reactivity of Azomethine Ylides Derived from Fully Aromatic *β*-Carbolines. The feasibility of forming reactive azomethine ylides in the *β*-carboline family of compounds via desilylation of the α-silylmethonium salts was first verified on the simplest representative, norharman **9** (Scheme 3). Following the procedure originally described by Vedejs and Martinez,[15] quater-

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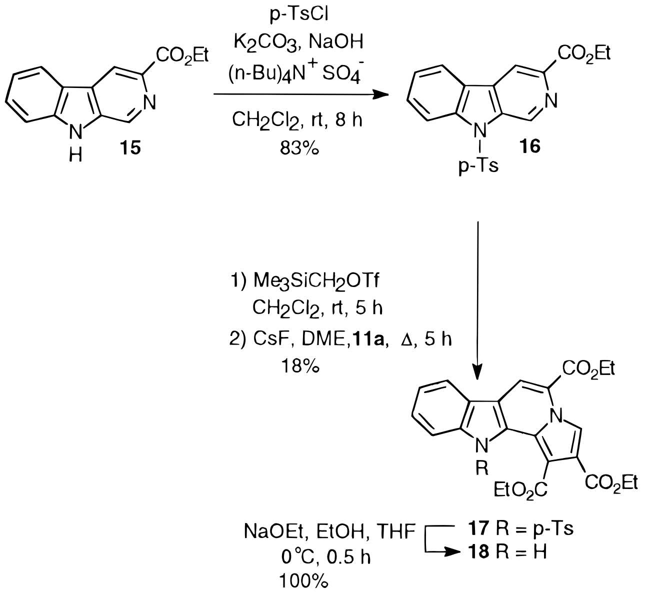
nization of compound **9** with (trimethylsilyl)methyl triflate in dichloromethane for 2 h at room temperature gave the triflate salt **10** in quantitative yield. No competitive N-9 alkylation was observed under the mild conditions of this reaction. Subsequent treatment of **10** with cesium fluoride and diethyl acetylenedicarboxylate (DEAD, **11a**) in refluxing dimethoxyethane afforded the indolizino[8,7-*b*]indole derivative **13a** in 35% yield *via* 1,3-dipolar cycloaddition of **11a** with the β-carboline azomethine ylide **12** formed *in situ*. Although the 3,11b-dihydro derivative **14** would initially be formed by the cycloaddition of DEAD with **12**, only the fully aromatic species **13a** could be isolated from the reaction mixture. This result is analogous to that obtained when acetylene dicarboxylates react with azomethine ylides generated from pyridinium or isoquinolinium *N*-[(trimethylsilyl)-methyl]triflate salts.[17,18,22] In contrast, nonaromatic azomethine ylides react with acetylenic dipolarophiles to give stable dihydropyrrole derivatives,[23-25] but if a leaving group is present (for example, in imidate and thioimidate derived dipoles),[26,27] only pyrroles are isolated.

[3 + 2]-Dipolar cycloaddition reactions of azomethine ylides with unsymmetrical dipolarophiles have generally been observed to be highly regioselective. This regioselectivity has been rationalized in terms of frontier molecular orbital (FMO) theory whereby the HOMO of the dipole with the highest coefficient interacts with the similar LUMO of the dipolarophile.[14,28-31] Thus, in order to verify the possible regioselectivity of cycloaddition reactions to β-carboline ylides of type **12**, the triflate salt **10** was reacted with ethyl propiolate **11b** in the presence of cesium fluoride. A single compound, corresponding to regioisomer **13b**, was obtained, albeit in low yield (8%). The regiochemistry of **13b** is evident from the ^{1}H NMR spectrum in which the pyrrole hydrogens H-2 and H-3 are observed as coupled doublets (J = 3.0 Hz) at δ 7.22 and 7.33, respectively, a pattern compatible with the presence of the carboxylic ester substituent at C-1 rather than at C-2.[23,27] This regioisomer corresponds to that predicted by FMO theory, but the low yield of product obtained makes it hazardous to draw conclusions regarding regioselectivity of cycloaddition in the case of fully aromatic β-carbolines. However, as will be seen in the dihydro-β-carboline series where cycloaddition product yields are higher (discussed below), lack of regioselectivity appears to be the rule.

Scheme 4



The possibility of forming azomethine ylides from the pharmacologically relevant alkyl esters of β-carboline-3-carboxylic acid (e.g., **15**, Scheme 4) using this methodology was also investigated. However, N-2 alkylation of **15** with (trimethylsilyl)methyl triflate in dichloromethane was somewhat recalcitrant, and only partial quaternization was observed under the same reaction conditions (2 h at room temperature) that afforded complete quaternization of **9**. Increasing reaction times and/or temperatures improved the levels of N-2 alkylation but also led to competitive N-9 alkylation. The increased difficulty of alkylating N-2 of β-carboline **15** may be ascribed to both the steric hindrance and inductive effects provided by the carboxylic ester group at C-3.[32] Consequently, compound **15** was transformed into its N-9 tosylated derivative **16**, thereby allowing subsequent N-2 alkylation with (trimethylsilyl)methyl triflate to proceed over extended reaction periods without overt interference from N-9 alkylation. Though complete N-2 alkylation could not be achieved even after 5 h (decomposition products beginning to appear beyond this time), the mixture of quaternized **16** and unreacted **16** (~9:1 by ^{1}H NMR) was used directly to effect a cycloaddition reaction. Thus, treatment of this crude mixture in dimethoxyethane with cesium fluoride and DEAD yielded cycloaddition product **17** together with unreacted **16**. Compound **17** could then be efficiently de-N-tosylated to provide **18** using a catalytic quantity of sodium ethoxide in ethanol.

II. Reactivity of Azomethine Ylides Derived from 3,4-Dihydro-β-carbolines. Although the preceding experiments prove that β-carboline-derived azomethine ylides are accessible by desilylation techniques, the yields obtained in the cycloaddition reactions of these dipoles with activated alkynes were disappointingly low. We therefore decided to study the reactivity of azomethine ylides generated from 3,4-dihydro-β-carbolines by similar techniques in the hope that cycloadditions would be favored by the nonaromatic character of the dihydropyridinyl ring. For this purpose, the 3,4-dihydro-2-*N*-[(trimethylsilyl)methyl]-β-carbolinium triflate salts **20a–c** were prepared in high yield and in analytically pure form by treatment of 3,4-dihydronorharman (**19a**),[33] 9-*N*-

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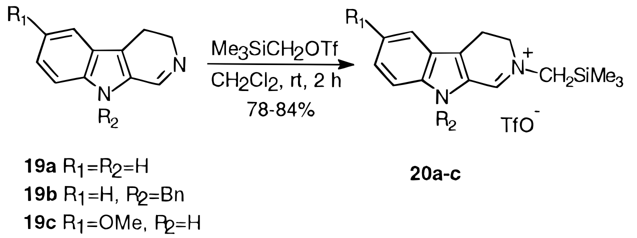
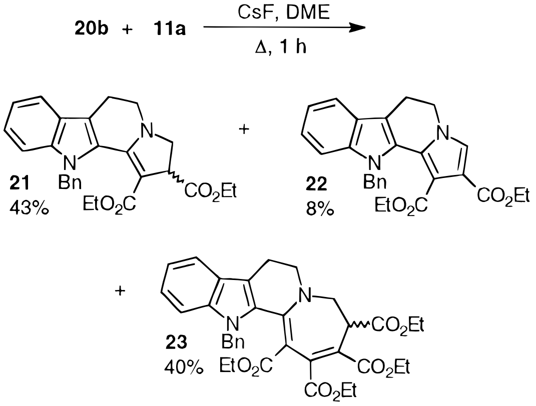
Scheme 5



Scheme 6

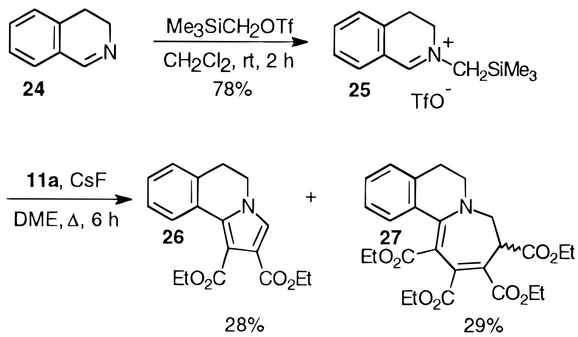


benzyl-3,4-dihydronorharman (**19b**),[34] and 6-methoxy-3,4-dihydronorharman (**19c**) with (trimethylsilyl)methyl triflate (Scheme 5).

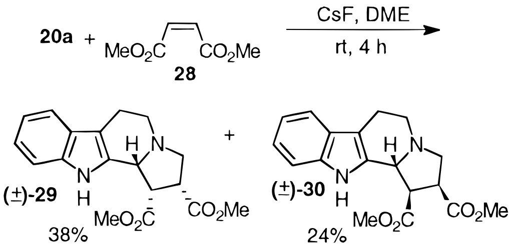
Since the indolic nitrogen atom of **20a** is sensitive to alkylation by acetylenics, cycloadditions were first attempted on the 9-*N*-benzyl triflate salt **20b**. Exposure of the latter to DEAD in the presence of cesium fluoride led to the formation of three compounds, **21**−**23** (Scheme 6), which were separated by chromatography. The major product, **21**, results from the expected cycloaddition of DEAD with the dipole produced by desilylation of dihydro-β-carboline **20b** to give an intermediate of type **14**. The latter undergoes a 1,3 hydrogen migration to the thermodynamically more stable 1,11b-dehydro species **21**. The oxidation level of this molecule was indicated by mass spectroscopy which showed the appropriate molecular ion peak. The migration of the double bond to the 1,11b position was evident from the ^{1}H NMR spectrum in which H-2 and H-3 clearly comprised an ABM system. Compound **22** is the product of partial dehydrogenation of **21**. In contrast to the cycloaddition reaction of DEAD with **10**, where the analogous compound **13a** was the only product observed, formation of **22** represents only a minor reaction pathway. Compound **22** displayed a one-proton singlet at δ 7.48 which corresponds to the uncoupled pyrrolic hydrogen atom at C-3, while H-5 and H-6 showed the typical A_2B_2 triplet pattern at δ 4.18 and 3.18, respectively.

A more unusual product, **23**, is formed by the reaction of DEAD with the dipole generated from **20b**. This 1:2 adduct was produced in almost the same yield as the 1:1 adduct **21**. The incorporation of two molecules of DEAD in **23** was evident from the mass spectrum, which displayed the molecular ion peak, and its ^{1}H NMR spectrum in which the four ethyl ester groups were clearly visible. Moreover, the position of the double bonds in the azepine ring of **23** was evident from the ABM pattern of H-4 and H-5 (analogous to H-2 and H-3 of **21**).

Scheme 7



Scheme 8



A two-dimensional carbon−proton shift NMR of **23** corroborated this structural assignment.

The formation of 1:2 adducts of type **23** is not a particularity of the dihydro-β-carboline family of compounds since reaction of DEAD with the ylide derived from 3,4-dihydro-*N*-[(trimethylsilyl)methyl]isoquinolinium triflate **25** (Scheme 7) also gave an azepine derivative analogous to **23** (i.e., **27**) together with the expected pyrrolo[2,1-*a*]isoquinoline **26** in practically equivalent yields (29% and 28%, respectively).

We next decided to study the stereospecificity of the cycloaddition reaction of the dihydro-β-carboline-derived azomethine ylides with symmetrically substituted electron-poor olefins. Thus, **20a** and dimethyl maleate (**28**) gave, in the presence of cesium fluoride, a mixture of the *cis*-1,2-dicarboxylic ester cycloaddition products (±)-**29** and (±)-**30** in 38% and 24% yield, respectively (Scheme 8). The structures of these compounds were elucidated with the aid of homonuclear ^{1}H−^{1}H two-dimensional NMR spectroscopy. Thus, the H-11b signals of **29** and **30** appeared as doublets at δ 4.62 and δ 4.23, respectively, with $J_{11b,1}$ values of 9.0 Hz (*cis*) and 7.0 Hz (*trans*).[35] Furthermore, the *cis* relationship of the ester functions in **29** and **30** was indicated by H1−H2 coupling constants of 9.0 Hz in both cases. These results demonstrate that the cycloaddition reaction of the ylide derived from **20a** with dimethyl maleate is highly stereospecific, the *cis* geometry of the former being completely retained in the products **29** and **30**.

Complete stereospecificity was also observed in the cycloaddition reactions of the *trans* olefins dimethyl fumarate (**31**) and fumaronitrile (**32**) with **20a**, yielding the 1,2-*trans*-substituted dicarboxylic esters (**33** and **34**) and dinitriles (**35** and **36**), respectively (Scheme 9). Similarly, the 6-methoxy-5,6-dihydro-β-carboline triflate **20c** reacted with **31** in the presence of cesium fluoride to give the expected *trans* cycloaddition products **37** and **38**. The stereochemical assignments of compounds **33**−

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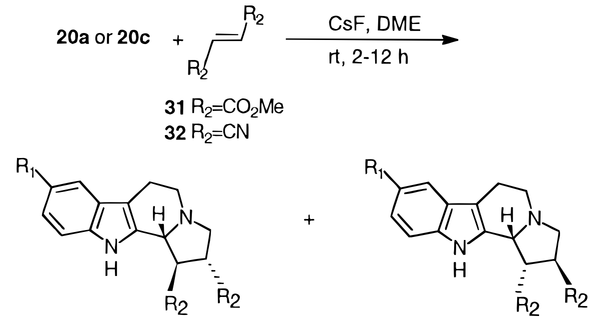
Scheme 9

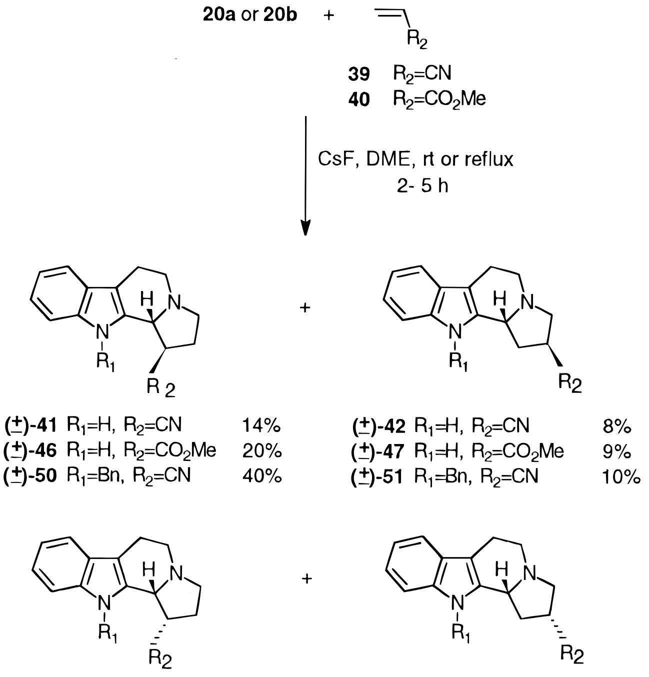


31 $R_2=CO_2Me$
32 $R_2=CN$

(±)-33 $R_1=H$, $R_2=CO_2Me$ 51%
(±)-35 $R_1=H$, $R_2=CN$ 21%
(±)-37 $R_1=OMe$, $R_2=CO_2Me$ 46%

(±)-34 $R_1=H$, $R_2=CO_2Me$ 36%
(±)-36 $R_1=H$, $R_2=CN$ 45%
(±)-38 $R_1=OMe$, $R_2=CO_2Me$ 32%

Scheme 10



39 $R_2=CN$
40 $R_2=CO_2Me$

(±)-41 $R_1=H$, $R_2=CN$ 14%
(±)-46 $R_1=H$, $R_2=CO_2Me$ 20%
(±)-50 $R_1=Bn$, $R_2=CN$ 40%

(±)-42 $R_1=H$, $R_2=CN$ 8%
(±)-47 $R_1=H$, $R_2=CO_2Me$ 9%
(±)-51 $R_1=Bn$, $R_2=CN$ 10%

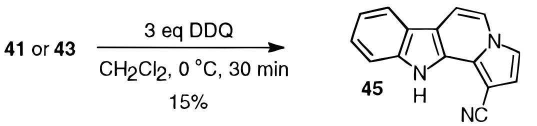
(±)-43 $R_1=H$, $R_2=CN$ 18%
(±)-48 $R_1=H$, $R_2=CO_2Me$ 20%
(±)-52 $R_1=Bn$, $R_2=CN$ 20%
(±)-54 $R_1=Bn$, $R_2=CO_2Me$ 60%

(±)-44 $R_1=H$, $R_2=CN$ 12%
(±)-49 $R_1=H$, $R_2=CO_2Me$ 19%
(±)-53 $R_1=Bn$, $R_2=CN$ 9%
(±)-55 $R_1=Bn$, $R_2=CO_2Me$ 6%

38 were based, as for **29** and **30**, on the coupling constants observed between H-11b and H-1 on one hand and H-1 and H-2 on the other, as determined using $^1H-^1H$ 2-D NMR. Thus, for **33**–**38**, *trans* coupling constants of 7 Hz or less were observed for H-1 and H-2. Moreover, a *trans* relationship between H-11b and H-1 was assigned to **33** and **37** based on the coupling constants of 6–7 Hz, values inferior to the coupling constants of the same protons in **34** and **38** (9 Hz), to which the *cis* geometry was attributed. In the case of the dicyano derivatives **35** and **36**, the H-11b, H-1 coupling constants were too similar to allow unambiguous assignment of their relative geometries. The latter were thus determined by performing NOE experiments.

The regioselectivity of the cycloaddition reactions of unsymmetrical electron-deficient olefins with the 3,4-dihydro-β-carboline ylides was also investigated (Scheme 10). Thus, **20a** reacted with acrylonitrile **39** under the usual conditions to give four compounds, **41**–**44**, which were separated by HPLC and which all displayed identical molecular ion peaks in the mass spectrum and a cyano function in the infrared spectrum. The major products, compounds **41** and **43**, each formed in approximately 20% yield, were shown by NMR and chemical transformations to correspond to the two C-1 regioisomers arising from *exo* and *endo* approaches of the dipole and the dipolarophile, respectively. The identical regiochemistry of **41** and **43** was indicated by ^1H NMR decoupling experiments where H-11b appears as a doublet ($J = 6.0$ and 9.0 Hz, respectively) in both cases. Moreover, both compounds, when treated with DDQ, gave the same 1-cyanoindolizino[8,7-*b*]indole **45** (Scheme 11) in which H-2 and H-3 appeared as coupled, vinylic protons. This pattern is only possible if the cyano function is at C-1. The relative stereochemistry at C-1 and C-11b was confirmed by ^{13}C NMR, both carbons resonating at higher field in the *cis* derivative **43** (δ 31.3 and 60.3, respectively) than in the *trans* derivative **41** (δ 32.3 and 62.5).[36]

Scheme 11



In the case of the minor products **42** and **44**, isolated in 8% and 12% yields, respectively, the appearance of H-11b as a doublet of doublets in their ^1H NMR spectra was consistent with the presence of the cyano group at C-3 while the relative stereochemistries of H-11b and H-2 were determined by NOE difference NMR spectroscopy.[37]

Reaction of **20a** with methyl acrylate (**40**) also gave four products (**46**–**49**) which could be easily separated by chromatography on silica gel. The regioselectivity was similar to that obtained with acrylonitrile, the C-1 regioisomers (**46** + **48**: 40%) being favored over the C-2 regioisomers (**47** + **49**: 28%). Some preference for *endo* products (**48** + **49**: 39%) over *exo* products (**46** + **47**: 29%) was observed, in contrast to the cycloaddition with acrylonitrile where essentially no such selectivity was observed.

Interestingly, the formation of C-2 regioisomers was significantly diminished when the ylide derived from the 9-*N*-benzyldihydro-β-carboline **20b** was used in the cycloaddition reactions. In the case of acrylonitrile as dipolarophile, the ratio of C-1- to C-2-substituted cycloaddition products (**50** + **52**:**51** + **53**) was 3:1 (compared to 1.8:1 for the analogous compounds in the nonbenzylated series) while for methyl acrylate the ratio of these regioisomers (**54**:**55**) was 10:1 (compared to 1.5:1 from **20a**). The *N*-benzyl group also had a favorable effect on the diastereoselectivity of the latter cycloaddition reaction since only the *endo* products (**54**, **55**) were observed.

The reasons why the *N*-benzyl group of the dihydro-β-carboline ylide has such a profound (and favorable) effect on the stereochemical outcome of these cycloaddition reactions remain, for the moment, uncertain. The *N*-benzyl group no doubt modifies the orbital coefficients of the dipole HOMO and, consequently, the regioselectivity. Moreover, regioselectivity may be strongly influenced by the possibility of secondary orbital interactions, for example between the aromatic ring of the benzyl

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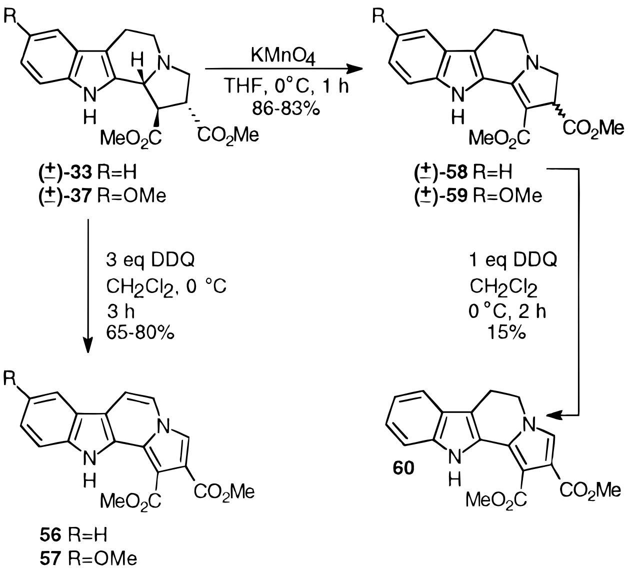
[36] For all C-1-substituted hexahydroindolizino[8,7-*b*]indole derivatives C-11b was always observed at higher field by 0.5–1.1 ppm in the ^{13}C NMR spectra when H-11b was *cis* to H-1 as compared to the *trans* derivatives. The same observation was made for C-1 though in this case the differences in ppm between the *cis* and *trans* isomers were sometimes too small to permit reliable attributions. ^{13}C NMR has been shown to be a reliable method of determining *cis*/*trans* geometries in the cyclopentane series. See: Chin, I. C.; Kohn, H. *J. Org. Chem.* **1983**, *48*, 2857.

[37] The relative configurations of H-11b and H-2 for all the C-2-substituted compounds of Scheme 10 were determined by performing NOE experiments.

Scheme 12



group and the unsaturated bonds of the dipolarophiles (nitrile or carbonyl). Such interactions would also be in favor of C-1 regioselectivity, as observed. The formation of mainly *exo* adducts in the reaction of **20b** with acrylonitrile but of exclusively *endo* adducts with methyl acrylate bears special mention. The latter dipolarophile has also been observed by Plate and co-workers[38] to give mainly *endo* products in 1,3-dipolar cycloaddition reactions with a β-carboline-derived nitrone, contrary to the general predominance of *exo* products in the case of other unsymmetrical olefins. Secondary interactions between dipole and dipolarophile frontier orbitals were invoked by these authors to rationalize this unusual result, although the exact nature of these interactions could not be defined. In our case, it is clear that both the presence of substituents near the reactive centers of the dipole (e.g., the *N*-benzyl group) as well as subtle differences in the steric or electronic nature of the dipolarophiles have substantial influence in directing the regio- and stereochemical course of the cycloaddition reactions.

III. Sequential Dehydrogenation of the Hexahydroindolizino[8,7-*b*]indole Derivatives 33 and 37. The relatively mediocre yields of aromatic cycloaddition products obtained in the reactions of acetylenes with the ylides derived from aromatic β-carbolines **9** and **15** prompted us to investigate the possibility of obtaining these compounds *via* dehydrogenation of their hexahydro counterparts, since the latter can be produced very efficiently from 3,4-dihydro-β-carboline derived ylides (**20a**–**c**) and olefins. Thus, both **33** and the 8-methoxy analogue **37** could be completely dehydrogenated by treatment with 3 equiv of DDQ in methylene chloride at 0 °C (Scheme 12). The products, **56** and **57**, respectively, were obtained in good yield (70–80%) and had spectral characteristics similar to the ethyl ester analogue **13a** formed *via* the acetylenic route.

Compounds **33** and **37** could also be partially and selectively dehydrogenated to the 2,3,5,6-tetrahydro derivatives **58** and **59**, respectively, using potassium permanganate in anhydrous THF as oxidant[39] in ~80% yields. The ^{1}H NMR spectra of **58** and **59** were similar to the NMR spectrum of the *N*-benzyl analogue **21** and clearly indicated that only H-11b and H-1 were absent in these molecules as compared to the starting materials. Compound **58** underwent further partial dehydrogenation to the 5,6-dihydro derivative **60** when exposed to 1 equiv of DDQ in CH_2Cl_2. However, in this case conversion was incomplete and attempts to coax the reaction to completion by slow addition of DDQ led to predominant formation of the completely aromatic product **56**.

In conclusion, the present results demonstrate that azomethine ylides derived from β-carbolines can be effectively generated by fluoride ion-induced desilylation of 2-*N*-[(trimethylsilyl)methyl] triflate salts. These ylides undergo *in situ* [3 + 2] dipolar cycloaddition reactions with electron-deficient olefins and acetylenes to give indolizino[8,7-*b*]indoles having functional groups at C-1 and/or C-2. Although yields of cycloaddition products were relatively low when ylides derived from fully aromatic β-carbolines were used, ylides formed from 3,4-dihydro-β-carbolines gave better overall yields. Reactions of the latter with symmetrically substituted olefins were completely stereospecific, but with unsymmetrical olefins, poor regioselectivities and diastereoselectivities were generally observed. Although this may appear to be a complicating factor in the exploitation of cycloaddition reactions with β-carboline ylides generated by the desilylation method, preliminary results with the 9-*N*-benzyl derivatives suggest that these selectivities can be dramatically improved by varying the nature of this protecting group. This possibility is currently being explored.

Experimental Section

General. Melting points are uncorrected. IR spectra of samples were obtained either as KBr pellets or in $CHCl_3$ in an NaCl cell. ^{1}H NMR and ^{13}C NMR chemical shifts are given as δ values with reference to Me_4Si as internal standard. TLC and preparative chromatography were performed on Merck silica gel 60 plates with fluorescent indicator. The plates were visualized with UV light (254 or 366 nm) and, for TLC, with a 3.5% solution of phosphomolybdic acid in ethanol. All column chromatography was conducted on Merck 60 silica gel (230–240 mesh) at medium pressure. All solvents were distilled and stored over 4 Å molecular sieves before use. The various unsaturated dipolarophiles were purchased from Aldrich Chemical Co. and were used without further purification. Elemental analyses were performed at the ICSN, CNRS, Gif-sur-Yvette, France.

2-*N*-[(Trimethylsilyl)methyl]-β-carbolinium Triflate (10). To a solution of norharman (**9**, 0.98 g, 5.95 mmol) in anhydrous CH_2Cl_2 (20 mL) was added dropwise under nitrogen and at rt a solution of (trimethylsilyl)methyl triflate (1.55 mL, 7.14 mmol) in CH_2Cl_2 (3 mL). After completion of the addition, the reaction mixture was stirred for 2 h. The solvent and excess reagent were then removed under reduced pressure, and the residual solid was crystallized from dichloromethane, affording **10** (2.4 g, 99%) as a white solid: mp 174 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.26 (s, 9H), 4.40 (s, 2H), 7.53 (m, 1H), 7.70 (m, 2H), 8.10 (d, 1H, $J = 6.5$ Hz), 8.28 (d, 1H, $J = 8.0$ Hz), 8.45 (d, 1H, $J = 6.5$ Hz), 9.41 (s, 1H), 9.51 (br s, 1H, exchangeable with D_2O); IR (KBr) 1650, 3250 cm^{-1}; mass spectrum (FAB) *m/z* 255 (M^+). Anal. Calcd for $C_{16}H_{19}F_3N_2O_3SSi$: C, 47.51; H, 4.73; N, 6.92; S, 7.93. Found: C, 47.79; H, 4.53; N, 6.65; S, 8.02.

Diethyl Indolizino[8,7-*b*]indole-1,2-dicarboxylate (13a). To a solution of cesium fluoride (0.19 g, 1.25 mmol) (freshly flame-dried) and diethyl acetylenedicarboxylate (**11a**, 198 μL, 1.25 mmol) in anhydrous DME (20 mL), was added compound **10** (0.5 g, 1.23 mmol). The reaction mixture was refluxed under nitrogen for 2 h, cooled, and diluted with CH_2Cl_2 (40 mL). The solution was washed with water (2 × 20 mL), the organic phase was dried over Na_2SO_4, and the solvents were removed under reduced pressure. The crude product was purified by column chromatography on silica gel using CH_2Cl_2–ethanol (10:0.15) as developer, affording **13a** (0.15 g, 35%) as an oil which crystallized in a mixture of ethanol and

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[38] Plate, R.; Hermkens, P. H. H.; Smits, J. M. M.; Ottenheijm, H. C. J. *J. Org. Chem.* **1986**, *51*, 309.

[39] Misztal, S.; Cegla, M. *Synthesis* **1985**, 1134.

hexane: mp 154 °C dec; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.36 (m, 6H), 4.41 (m, 4H), 7.31 (m, 1H, $J = 8.0$ Hz), 7.41 (m, 1H, $J = 8.0$ Hz), 7.48 (d, 1H, $J = 7.0$ Hz), 7.63 (d, 1H, $J = 8.0$ Hz), 7.71 (s, 1H), 7.78 (d, 1H, $J = 7.0$ Hz), 8.00 (d, 1H, $J = 8.0$ Hz), 9.66 (br s, 1H, exchangeable with D_2O); IR (KBr) 1730, 3340 cm^{-1}; mass spectrum (EI) *m/z* 350 (M^+). Anal. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.17; N, 7.99. Found: C, 68.66; H, 5.06; N, 7.98.

Ethyl Indolizino[8,7-*b*]indole-1-carboxylate (13b). Following the same procedure as for the preparation of **13a**, triflate **10** (100 mg, 0.25 mmol) was treated with cesium fluoride (380 mg, 0.25 mmol) and ethyl propiolate (**11b**, 25 μL, 0.25 mmol) in DME (7 mL). After workup, the crude product was purified by column chromatography on silica gel (toluene−ethanol 9:0.25), yielding **13b** (5.5 mg, 8%) as a white powder which was crystallized from ethyl acetate: mp 149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (t, 3H, $J = 8.0$ Hz), 4.46 (q, 2H, $J = 8.0$ Hz), 7.22 (d, 1H, $J = 3.0$ Hz), 7.33 (t, 1H, $J = 7.8$ Hz), 7.38 (d, 1H, $J = 3.0$ Hz), 7.46 (m, 2H), 7.66 (d, 1H, $J = 7.8$ Hz), 7.87 (d, 1H, $J = 7.2$ Hz), 8.05 (d, 1H, 7.8 Hz), 11.52 (br s, 1H, exchangeable with D_2O); IR (KBr) 1730, 3220 cm^{-1}; mass spectrum (EI) *m/z* 278 (M^+). Anal. Calcd for $C_{17}H_{14}N_2O_2$: C, 73.36; H, 5.07; N, 10.06. Found: C, 73.33; H, 5.12; N, 10.14.

Ethyl 9-*N*-(*p*-Toluenesulfonyl)-*β*-carboline-3-carboxylate (16). A mixture of ethyl β-carboline-3-carboxylate (**15**, 2.32 g, 9.66 mmol), *p*-toluenesulfonyl chloride (2.2 g, 11.6 mmol), tetra-*n*-butylammonium sulfate (0.5 g, 1.47 mmol), anhydrous K_2CO_3 (4 g) and powdered NaOH (4 g) in CH_2Cl_2 (200 mL) was vigorously stirred for 8 h at rt. The reaction mixture was then filtered, the filtrate was washed with water (30 mL), and the organic phase was dried over Na_2SO_4. Removal of the solvent under reduced pressure left solid **16** (3.16 g, 83%) which was crystallized from ethanol: mp 206 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.50 (t, 3H, $J = 8.0$ Hz), 2.36 (s, 3H), 4.56 (q, 2H, $J = 8.0$ Hz), 7.25 (d, 1H, $J = 7.8$ Hz), 7.60 (t, 1H, $J = 7.8$ Hz), 7.76 (m, 4H), 8.23 (d, 1H, $J = 7.8$ Hz), 8.46 (d, 1H, $J = 7.8$ Hz), 8.85 (s, 1H), 9.80 (s, 1H); IR (KBr) 1180, 1740 cm^{-1}; mass spectrum (EI) *m/z* 394 (M^+). Anal. Calcd for $C_{21}H_{18}N_2O_4S{\cdot}0.5H_2O$: C, 62.53; H, 4.74; N, 6.94. Found: C, 62.79; H, 4.72; N, 6.55.

Triethyl 11-*N*-(*p*-Toluenesulfonyl)indolizino[8,7-*b*]indole-1,2,5-tricarboxylate (17). A solution of compound **16** (100 mg, 0.25 mmol) in CH_2Cl_2 (10 mL) was treated dropwise with a solution of (trimethylsilyl)methyl triflate (60.8 μL, 0.30 mmol) in CH_2Cl_2 (0.5 mL), and the reaction mixture was stirred for 5 h at rt. The solvent and excess reagent were removed under reduced pressure, the residue was dissolved in DME (10 mL), and cesium fluoride (39 mg, 0.26 mmol) followed by diethyl acetylenedicarboxylate (**11a**, 41.4 μL, 0.26 mmol) were added. The solution was refluxed for 5 h and then cooled, diluted with CH_2Cl_2 (10 mL), and washed with water (2 × 10 mL). The organic phase was dried over Na_2SO_4, and the solvents were removed under reduced pressure leaving an oily residue which crystallized in ethanol to give **17** (26 mg, 18%) as a bright yellow powder: mp 265 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.39 (t, 3H, $J = 6.8$ Hz), 1.51 (m, 6H), 2.16 (s, 3H), 4.43 (q, 2H, $J = 6.8$ Hz), 4.60 (m, 4H), 6.86 (d, 2H, $J = 8.0$ Hz), 7.03 (d, 2H), 7.40 (m, 2H), 7.68 (d, 1H, $J = 7.0$ Hz), 8.13 (s, 1H), 8.26 (d, 1H, $J = 7.3$ Hz), 8.33 (s, 1H); IR (KBr) 1190, 1710 cm^{-1}; mass spectrum (EI) *m/z* 576 (M^+), 421 (M^+ − tos). Anal. Calcd for $C_{30}H_{28}N_2O_8S{\cdot}0.5H_2O$: C, 61.53; H, 4.99; N, 4.78. Found: C, 61.46; H, 4.86; N, 4.76.

Triethyl Indolizino[8,7-*b*]indole-1,2,5-tricarboxylate (18). A solution of sodium hydride (5 mg, 0.125 mmol) (60% dispersion in oil) and ethanol (0.01 mL) in anhydrous THF (8 mL) was stirred for 1 h at 0 °C. Compound **17** (50 mg, 0.09 mmol) was then added, and stirring was continued for 0.5 h. The reaction mixture was quenched with ice-cold water (6 mL) and extracted with $CHCl_3$ (2 × 10 mL). The organic extracts were combined and dried over Na_2SO_4, and the solvents were removed under reduced pressure affording **18** (37 mg, 100%) as a pale yellow solid which was crystallized from ethanol−hexane: mp 137 °C; ^{1}H NMR (200 MHz, acetone-d_6) δ 1.58 (m, 9H), 4.60 (m, 6H), 7.58 (dt, 1H, $J = 8.0$, 1.0 Hz), 7.72 (dt, 1H, $J = 8.0$, 1.0 Hz), 8.13 (d, 1H, $J = 8.0$ Hz), 8.40 (d, 1H, $J = 8.0$ Hz), 8.93 (s, 1H), 9.37 (s, 1H), 12.05 (br s, 1H, exchangeable with D_2O); IR (KBr) 1690, 1715, 1735, 3360 cm^{-1}; mass spectrum (EI) *m/z* 422 (M^+). Anal. Calcd for $C_{23}H_{22}N_2O_6$: C, 65.39; H, 5.24; N, 6.63. Found: C, 65.33; H, 5.24; N, 6.48.

3,4-Dihydro-2-*N*-[(trimethylsilyl)methyl]-*β*-carbolinium Triflate (20a). Following the same procedure as for the preparation of **10**, compound **20a** was prepared from 3,4-dihydro-β-carboline (**19a**)[33] in 73% yield: mp 136 °C (ethanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.20 (s, 9H), 3.32 (t, 2H, $J = 8.0$ Hz), 3.58 (s, 2H), 4.00 (t, 2H, $J = 8.0$ Hz), 7.15 (t, 1H, $J = 7.2$ Hz), 7.42 (m, 2H), 7.55 (d, 1H, $J = 7.2$ Hz), 8.86 (br s, 1H, exchangeable with D_2O), 9.03 (s, 1H); IR (KBr) 1640, 3300 cm^{-1}; mass spectrum (FAB) *m/z* 257 (M^+). Anal. Calcd for $C_{16}H_{21}F_3N_2O_3SSi$: C, 47.28; H, 5.20; N, 6.89; S, 7.88. Found: C, 47.60; H, 5.03; N, 6.78; S, 7.79.

9-*N*-Benzyl-3,4-dihydro-2-*N*-[(trimethylsilyl)methyl]-*β*-carbolinium Triflate (20b). This compound was prepared as above in 84% yield from **19b**:[34] mp 193−194 °C (ethanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.12 (s, 9H), 3.33 (t, 2H, $J = 9.0$ Hz), 3.82 (s, 2H), 3.96 (t, 2H, $J = 9.0$ Hz), 5.66 (s, 2H), 7.11 (m, 8H), 7.63 (d, 1H, $J = 7.8$ Hz), 9.05 (s, 1H); IR (KBr) 1640 cm^{-1}; mass spectrum (FAB) *m/z* 347 (M^+). Anal. Calcd for $C_{23}H_{27}F_3N_2O_3SSi$: C, 55.62; H, 5.48; N, 5.64; S, 6.45. Found: C, 55.87; H, 5.23; N, 5.38; S, 6.32.

3,4-Dihydro-6-methoxy-2-*N*-[(trimethylsilyl)methyl)-*β*-carbolinium Triflate (20c). This compound was prepared as above in 78% yield from **19c**: mp 173 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.26 (s, 9H), 3.13 (t, 2H, $J = 8.0$ Hz), 3.45 (s, 2H), 3.68 (s, 3H), 3.82 (t, 2H, $J = 8.0$ Hz), 6.58 (d, 1H, $J = 2.3$ Hz), 6.84 (dd, 1H, $J = 7.8$, 2.3 Hz), 7.55 (d, 1H, $J = 7.8$ Hz), 8.74 (s, 1H), 9.68 (br s, 1H, exchangeable with D_2O); IR (KBr) 1640, 3250 cm^{-1}; mass spectrum (FAB) *m/z* 287 (M^+). Anal. Calcd for $C_{17}H_{23}F_3N_2O_4SSi$: C, 46.77; H, 5.31; N, 6.41; S, 7.34. Found: C, 46.47; H, 5.57; N, 6.31; S, 7.20.

Diethyl (2*RS*)-11-*N*-Benzyl-2,3,5,6-tetrahydroindolizino-[8,7-*b*]indole-1,2-dicarboxylate (21), Diethyl 5,6-Dihydro-11-*N*-benzylindolizino[8,7-*b*]indole-1,2-dicarboxylate (22) and Tetraethyl (4*RS*)-11-*N*-Benzyl-4,5,7,8-tetrahydroazepino[1′,2′:1,2]pyrido[3,4-*b*]indole-1,2,3,4-tetracarboxylate (23). Following the same procedure as for the preparation of **13a**, compound **20b** (500 mg, 1.01 mmol) was refluxed for 1 h in DME (20 mL) in the presence of diethyl acetylenedicarboxylate (**11a**, 162 μL, 1.01 mmol) and cesium fluoride (154 mg, 1.01 mmol) affording, after the usual workup, three products which were separated by column chromatography on silica gel using CH_2Cl_2−ethyl acetate (10:0.5) as eluent. Compound **22** (36 mg, 8%), obtained as an oil, was the first product to be eluted: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.18 (t, 3H, $J = 8.0$ Hz), 1.30 (t,3H, $J = 8.0$ Hz), 3.18 (t, 2H, $J = 7.0$ Hz), 3.88 (q, 2H, $J = 8.0$ Hz), 4.18 (t, 2H, $J = 7.0$ Hz), 4.30 (q, 2H, $J = 8.0$ Hz), 5.50 (s, 2H), 7.00−7.34 (m, 8H), 7.48 (s, 1H), 7.60 (d, 1H, $J = 7.8$ Hz); IR ($CHCl_3$) 1720 cm^{-1}; mass spectrum (EI) *m/z* 442 (M^+). Anal. Calcd for $C_{27}H_{26}N_2O_4$: C, 73.28; H, 5.92; N, 6.33. Found: C, 73.20; H, 6.01; N, 6.23.

Continued elution of the column afforded compound **23** (248 mg, 40%) as an oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (m, 9H), 1.31 (t, 3H, $J = 8.2$ Hz), 2.49 (dd, 1H, $J = 11.0$, 13.0 Hz), 2.85 (m, 1H), 3.11 (m, 1H), 3.21 (dd, 1H, $J = 11.0$, 13.0 Hz), 3.26 (m, 1H), 3.35 (m, 1H), 4.05−4.31 (m, 9H), 5.43 (d, 1H, $J = 16.0$ Hz), 5.53 (d, 1H, $J = 16.0$ Hz), 6.96 (m, 2H), 7.11−7.27 (m, 5H), 7.44 (d, 1H, $J = 7.0$ Hz), 7.58 (d, 1H, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 14.9, 23.2, 32.2, 44.0, 45.2, 50.8, 59.7, 61.0, 61.2, 61.9, 112.3, 119.8, 120.3, 120.6, 124.5, 125.2, 127.1, 127.2, 128.2, 164.2, 168.1, 170.7; IR ($CHCl_3$) 1660, 1730 cm^{-1}; mass spectrum (EI) *m/z* 614 (M^+). Anal. Calcd for $C_{35}H_{38}N_2O_8$: C, 68.39; H, 6.23; N, 4.55. Found: C, 68.58; H, 6.22; N, 4.35.

Compound **21** (193 mg, 43%), also obtained as an oil, was the last to be eluted from the column: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, 3H, $J = 8.0$ Hz), 1.26 (t, 3H, $J = 8.0$ Hz), 3.02 (t, 2H, $J = 6.0$ Hz), 3.26 (t, 2H, $J = 6.0$ Hz), 3.83 (dd, 1H, $J = 6.0$, 10.0 Hz), 3.88 (t, 1H, $J = 10.0$, 10.0 Hz), 4.08 (dd, 1H, $J = 6.0$, 10.0 Hz), 4.17 (m, 4H), 5.44 (d, 1H, $J = 16.0$ Hz), 5.66 (d, 1H, $J = 16.0$ Hz), 6.85 (m, 2H), 7.09−7.20 (m, 4H), 7.34 (d, 1H, $J = 7.8$ Hz), 7.56 (d, 1H, $J = 7.8$ Hz); IR ($CHCl_3$) 1660, 1720 cm^{-1}; mass spectrum (EI) *m/z* 444 (M^+). Anal. Calcd for $C_{27}H_{28}N_2O_4{\cdot}0.5H_2O$: C, 73.28; H, 5.92; N, 6.33. Found: C, 73.20; H, 6.01; N, 6.23.

3,4-Dihydro-2-*N*-[(trimethylsilyl)methyl]isoquinolinium Triflate (25). Compound **25** was prepared in 78% yield from 3,4-dihydroisoquinoline (**24**)[40] and (trimethylsilyl)methyl triflate following the same procedure as for **20a**–**c**: mp 88 °C (ethanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.25 (s, 9H), 3.80 (t, 2H, $J = 8.0$ Hz), 3.95 (s, 2H), 4.03 (t, 2H, $J = 8.0$ Hz), 7.41 (d, 1H, $J = 7.2$ Hz), 7.53 (t, 1H, $J = 7.2$ Hz), 7.77 (m, 1H), 7.95 (d, 1H, $J = 7.0$ Hz), 9.21 (s, 1H); IR (KBr) 1650 cm^{-1}; mass spectrum (FAB) *m/z* 218 (M^+). Anal. Calcd for $C_{14}H_{20}F_3NO_3SSi$: C, 45.76; H, 5.48; N, 3.81; S, 8.72. Found: C, 45.76; H, 5.42; N, 3.84; S, 8.99.

Diethyl 5,6-Dihydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarboxylate (26) and Tetraethyl (4*RS*)-7,8-Dihydroazepino[2,1-*a*]isoquinoline-1,2,3,4-tetracarboxylate (27). Following the same procedure as for the preparation of **13a**, compound **25** (300 mg, 0.8 mmol) was refluxed for 6 h in DME (20 mL) in the presence of diethyl acetylenedicarboxylate (**11a**, 136 μL, 0.8 mmol) and cesium fluoride (122 mg, 0.8 mmol). After the usual workup, two products, **26** (70 mg, 28%) and **27** (112 mg, 29%), were isolated as oils following column chromatography on silica gel using ethyl acetate–CH_2Cl_2 (8:0.4) as developer. Compound **26**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.33 (t, 3H, $J = 7.2$ Hz), 1.41 (t, 3H, $J = 7.2$ Hz), 3.08 (t, 2H, $J = 5.8$ Hz), 4.10 (t, 2H, $J = 5.8$ Hz), 4.31 (q, 2H, $J = 7.2$ Hz), 4.45 (q, 2H, $J = 7.2$ Hz), 7.25 (m, 3H), 7.30 (s, 1H), 7.70 (d, 1H, $J = 6.9$ Hz); IR ($CHCl_3$) 1745 cm^{-1}; mass spectrum (EI) *m/z* 313 (M^+). Anal. Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.81; H, 6.28; N, 4.29.

Compound **27**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (m, 9H), 1.32 (t, 3H, $J = 7.8$ Hz), 2.74 (dd, 1H, $J = 10.0$, 13.0 Hz), 2.85 (m, 1 H), 3.04 (m, 1H), 3.23 (dd, 1H, $J = 10.0$, 13.0 Hz), 3.23 (m, 1H), 3.36 (m, 1H), 4.08–4.29 (m, 9H), 7.21 (d, 1H, $J = 6.8$ Hz), 7.34 (d, 1H, $J = 6.8$ Hz), 7.40 (d, 1H, $J = 6.8$ Hz), 8.56 (d, 1H, $J = 6.8$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.2, 14.4, 31.2, 31.5, 42.5, 44.8, 59.1, 61.2, 61.4, 62.3, 126.1, 127.3, 131.1, 131.7, 164.5, 170.9; IR ($CHCl_3$) 1670, 1720 cm^{-1}; mass spectrum (EI) *m/z* 485 (M^+). Anal. Calcd for $C_{26}H_{31}NO_8$: C, 64.31; H, 6.43; N, 2.88. Found: C, 64.06; H, 6.43; N, 2.70.

General Procedure for 1,3-Dipolar Cycloaddition of Activated Ethylenic Derivatives with the β-Carboline Azomethine Ylides Generated from 20a–c. Solutions of equimolar quantities of the *N*-[(trimethylsilyl)methyl]-3,4-dihydro-β-carbolinium triflates **20a**, **20b**, or **20c**, cesium fluoride, and ethylenic dipolarophiles (**28**, **31**, **32**, **39**, and **40**) in anhydrous DME were stirred at rt or at reflux under nitrogen for 2–12 h. At the end of the reaction period (as determined by TLC monitoring), the mixtures were concentrated *in vacuo* to one-quarter of their volume, the residues were taken up in 5 volumes of ethyl acetate, and the solutions were washed with water (2×). The combined aqueous washings were extracted with ethyl acetate, the organic extracts were combined and dried over Na_2SO_4, and the solvents were removed under vacuum. Addition of ethanol to the residue sometimes led to precipitation of one of the diastereomers which was collected by filtration. The other diastereomer(s) could then be purified by chromatography of the mother liquor on silica gel. In other cases, the residue was immediately purified by chromatography on silica gel and/or by HPLC. Reaction times, yields, and purification procedures are given for each compound.

Dimethyl (1*S*,2*S*,11b*R*)- and (1*R*,2*R*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-1,2-dicarboxylate [(±)-29] and Dimethyl (1*R*,2*R*,11b*R*)- and (1*S*,2*S*,11b*S*)-1,2,3,5,6,-11b-Hexahydroindolizino[8,7-*b*]indole-1,2-dicarboxylate [(±)-30]. These compounds were obtained from **20a** and dimethyl maleate (**28**) after a reaction period of 4 h. Compound **29** (38%) was isolated by crystallization of the crude reaction mixture in ethanol: mp 152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (m, 1H), 2.94 (m, 2H), 3.06 (dd, 1H, $J = 7.0$, 10.0 Hz), 3.25 (m, 1H), 3.46 (t, 1H, $J = 10.0$ Hz), 3.52 (m, 1H), 3.59 (s, 3H), 3.75 (s, 3H), 3.90 (t, 1H, $J = 9.0$ Hz), 4.62 (d, 1H, $J = 9.0$ Hz), 7.10 (t, 1H, $J = 7.8$ Hz), 7.16 (t, 1H, $J = 7.8$ Hz), 7.32 (d, 1H, $J = 7.8$ Hz), 7.49 (d, 1H, $J = 7.8$ Hz), 8.21 (s, 1H, exchangeable with D_2O); IR (KBr) 1720, 3350 cm^{-1}; mass spectrum (EI) *m/z* 328 (M^+). Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.95; H, 5.98; N, 8.23.

Compound **30** (24%) was isolated as an oil after chromatography of the mother liquor on silica gel (toluene–ethanol 9:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.80 (m, 1H), 2.93 (m, 2H), 3.15 (m, 1H), 3.29 (t, 1H, $J = 10.0$ Hz superimposed on dd, 1H, $J = 7.0$, 10.0 Hz), 3.53 (m, 1H), 3.64 (dd, 1H, $J = 9.0$, 7.0 Hz), 3.73 (s, 3H), 3.90 (s, 3H), 4.23 (d, 1H, $J = 7.0$ Hz), 7.15 (t, 1H, $J = 7.8$ Hz), 7.20 (t, 1H, $J = 7.8$ Hz), 7.45 (d, 1H, $J = 7.8$ Hz), 7.58 (d, 1H, $J = 7.8$ Hz), 8.68 (s, 1H, exchangeable with D_2O); IR ($CHCl_3$) 1725, 3450 cm^{-1}; mass spectrum (EI) *m/z* 328 (M^+). Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.69; H, 6.10; N, 7.72.

Dimethyl (1*R*,2*S*,11b*R*)- and (1*S*,2*R*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-1,2-dicarboxylate [(±)-33] and Dimethyl (1*S*,2*R*,11b*R*)- and (1*R*,2*S*,11b*S*)-1,2,3,5,6,-11b-Hexahydroindolizino[8,7-*b*]indole-1,2-dicarboxylate [(±)-34]. These compounds were obtained from **20a** and dimethyl fumarate (**31**) after a reaction period of 4 h. Compound **33** (51%) was isolated by crystallization of the crude reaction mixture in ethanol: mp 169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.59 (m, 1H), 3.00 (m, 2H), 3.28 (m, 4H), 3.30 (t, 1H, $J = 11.0$ Hz), 3.41 (m, 2H), 3.60 (s, 3H), 3.62 (t, 1H, $J = 7.0$ Hz), 4.65 (d, 1H, $J = 7.0$ Hz), 6.95 (t, 1H, $J = 7.8$ Hz), 7.05 (t, 1H, $J = 7.8$ Hz), 7.30 (d, 1H, $J = 7.8$ Hz), 7.38 (d, 1H, $J = 7.8$ Hz), 8.83 (br s, 1H, exchangeable with D_2O); IR (KBr) 1725, 3450 cm^{-1}; mass spectrum (EI) *m/z* 328 (M^+). Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.54; H, 6.24; N, 8.23.

Compound **34** (36%) was isolated as an oil after chromatography of the mother liquor on silica gel (CH_2Cl_2–ethyl acetate 7:3): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.85 (m, 3H), 3.10 (t superimposed on m, 2H, $J = 10.0$ Hz), 3.18 (dd, 1H, $J = 6.0$, 10.0 Hz), 3.45 (dd, 1H, $J = 9.0$, 7.0 Hz), 3.51 (m, 1H), 3.73 (s, 3H), 3.78 (s, 3H), 4.51 (d, 1H, $J = 9.0$ Hz), 7.09 (t, 1H, $J = 8.0$ Hz), 7.16 (t, 1H, $J = 8.0$ Hz), 7.35 (d, 1H, $J = 8.0$ Hz), 7.50 (d, 1H, $J = 8.0$ Hz), 8.71 (br s, 1H, exchangeable with D_2O); IR ($CHCl_3$) 1720, 3400 cm^{-1}; mass spectrum (EI) *m/z* 328 (M^+). Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.58; H, 6.08; N, 8.51.

(1*R*,2*R*,11b*R*)- and (1*S*,2*S*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-1,2-dicarbonitrile [(±)-35] and (1*S*,2*S*,11b*R*)- and (1*R*,2*R*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-1,2-dicarbonitrile [(±)-36]. These compounds were obtained from **11a** and fumaronitrile (**32**) after a reaction period of 12 h. After the usual workup, the crude reaction mixture was purified by HPLC on a silica gel column (15–20 μm, 15 × 20 cm) using heptane–2-propanol 92:8 as eluent (flow rate = 50 mL/min). Compound **36** (45%) was first eluted: mp 169 °C (methanol); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.88 (m, 2H), 3.07 (m, 1H), 3.17 (m, 1H), 3.32 (t, 1H, $J = 8.0$ Hz), 3.43 (m, 2H), 3.47 (m, 1H), 4.38 (d, 1H, $J = 8.0$ Hz), 7.14 (dd, 1H, $J = 7.2$ Hz), 7.22 (dd, 1H, $J = 7.2$ Hz), 7.40 (d, 1H, $J = 7.2$ Hz), 7.53 (d, 1H, $J = 7.2$ Hz), 8.05 (br s, 1H, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.9, 31.7, 36.7, 45.4, 53.7, 61.3, 108.0, 110.6, 116.0, 117.6, 118.1, 118.8, 125.6, 128.9, 135.9; IR ($CHCl_3$) 2246, 3361 cm^{-1}; mass spectrum (EI) *m/z* 262 (M^+). Anal. Calcd for $C_{16}H_{14}N_4\cdot 0.1H_2O$: C, 72.78; H, 5.38; N, 21.23. Found: C, 72.53; H, 5.46; N, 21.55.

Continued elution of the column afforded compound **35** (21%): mp 198 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.89 (m, 3H), 3.13 (m, 1H, $J = 7.5$, 9.8 Hz), 3.18 (m, 1H), 3.56 (m, 1H), 3.64 (dd, 1H, $J = 8.0$, 9.0 Hz), 3.78 (dd, 1H, $J = 5.0$, 6.7 Hz), 4.32 (d, 1H, $J = 6.8$ Hz), 6.64 (dd, 1H, $J = 8.0$ Hz), 6.72 (dd, 1H, $J = 8.0$ Hz), 7.03 (d, 1H, $J = 8.0$ Hz), 7.18 (d, 1H, $J = 8.0$ Hz), 8.50 (br s, 1H, exchangeable with D_2O); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 20.2, 31.4, 36.7, 46.3, 55.8, 60.2, 108.0, 110.7, 117.5, 117.7, 118.4, 118.7, 121.4, 127.8, 128.1, 136.0; IR ($CHCl_3$) 2246, 3381 cm^{-1}; mass spectrum (EI) *m/z* 262 (M^+). Anal. Calcd for $C_{16}H_{14}N_4$: C, 73.28; H, 5.34; N, 21.37. Found: C, 73.21; H, 5.49; N, 21.10.

Dimethyl (1*R*,2*S*,11b*R*)- and (1*S*,2*R*,11b*S*)-1,2,3,5,6,11b-Hexahydro-8-methoxyindolizino[8,7-*b*]indole-1,2-dicarboxylate [(±)-37] and Dimethyl (1*S*,2*R*,11b*R*)- and (1*R*,2*S*,-11b*S*)-1,2,3,5,6,11b-Hexahydro-8-methoxyindolizino[8,7-*b*]indole-1,2-dicarboxylate [(±)-38]. These compounds were

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(40) Dale, W. J.; Starr, L.; Strobel, C. W. *J. Org. Chem.* **1961**, *26*, 2225.

obtained from **20c** and dimethyl fumarate (**31**) after a reaction period of 2 h. Compound **37** (46%) was isolated by crystallization of the crude reaction mixture in ethanol: mp 129 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.60 (m, 1H), 2.84 (m, 2H), 3.00 (dd, 1H, $J = 7.0, 9.0$ Hz), 3.16 (m, 1H), 3.44 (m, 2H), 3.51 (s, 3H), 3.63 (s, 3H), 3.76 (s, 4H), 4.48 (d, 1H, $J = 9.0$ Hz), 6.63 (dd, 1H, $J = 8.0, 2.0$ Hz), 6.76 (d, 1H, $J = 2.0$ Hz), 7.03 (d, 1H, $J = 8.0$ Hz), 7.84 (br s, 1H, exchangeable with D_2O); IR (KBr) 1720, 3360 cm^{-1}; mass spectrum (EI) m/z 358 (M^+). Anal. Calcd for $C_{19}H_{22}N_2O_5$: C, 63.67; H, 6.18; N, 7.81. Found: C, 63.56; H, 6.14; N, 7.82.

Compound **38** (32%) was isolated as an oil after chromatography of the mother liquor on silica gel (toluene−ethanol 9:1): ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.77 (m, 3H), 3.16 (m, 3H), 3.49 (m, 2H), 3.52 (s, 3H), 3.79 (s, 6H), 4.11 (d, 1H, $J = 6.0$ Hz), 6.69 (dd, 1H, $J = 8.0, 2.0$ Hz), 6.80 (d, 1H, $J = 2.0$ Hz), 7.11 (d, 1H, $J = 8.0$ Hz), 8.36 (br s, 1H, exchangeable with D_2O); IR ($CHCl_3$) 1720, 3450 cm^{-1}; mass spectrum (EI) m/z 358 (M^+). Anal. Calcd for $C_{19}H_{22}N_2O_5$: C, 63.67; H, 6.18; N, 7.81. Found: C, 63.76; H, 6.01; N, 7.68.

(1*R*,11b*R*)- and (1*S*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-1-carbonitrile [(±)-41], (2*S*,11b*R*)- and (2*R*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-2-carbonitrile [(±)-42], (1*S*,11b*R*)- and (1*R*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-1-carbonitrile [(±)-43], and (2*R*,11b*R*)- and (2*S*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-2-carbonitrile [(±)-44]. These compounds were obtained from **20a** and acrylonitrile (**39**) after a reaction period of 5 h. After the usual workup, the crude reaction product was partially purified by column chromatography on silica gel using ethyl acetate−heptane (30:70) followed by ethyl acetate. Two fractions were obtained, the first corresponding to a mixture of **41** and **42**, the second to **43** and **44**. Each fraction was in turn purified by HPLC either on a silica gel column (15−20 μm, 250 mm, heptane−ethyl acetate gradient with a flow rate of 50 mL/min) (for **41** and **42**) or a C18 column (47 × 300 mm, methanol−water 60:40, 40 mL/min) (for **43** and **44**):

Compound **41** (foam, 19%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.26 (m, 1H), 2.44 (m, 1H), 2.79 (m, 1H), 2.88 (m, 1H), 2.98 (m, 2H), 3.11 (m, 3H), 4.27 (d, 1H, $J = 6.0$ Hz), 7.17 (dd, 1H, $J = 7.8$ Hz), 7.24 (dd, 2H, $J = 7.8$ Hz), 7.37 (d, 1H, $J = 7.8$ Hz), 7.52 (d, 1H, $J = 7.8$ Hz), 8.20 (br s, 1H, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.2, 29.2, 32.3, 47.2, 51.4, 62.5, 108.1, 111.4, 117.7, 118.6, 119.4, 122.4, 126.7, 131.5, 136.5; IR ($CHCl_3$) 2240, 3448 cm^{-1}; mass spectrum (EI) m/z 237 (M^+). Anal. Calcd for $C_{15}H_{15}N_3$: C, 75.95; H, 6.33; N, 17.72. Found: C, 75.82; H, 75.82; H, 6.32; N, 17.75.

Compound **42** (oil, 8%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.29 (m, 1H), 2.59 (m, 1H), 2.71 (m, 1H), 2.90 (m, 1H), 3.09 (m, 2H), 3.19 (m, 1H), 3.27 (m, 2H), 4.42 (dd, 1H, $J = 6.0, 9.0$ Hz), 7.11 (t, 1H, $J = 8.0$ Hz), 7.18 (t, 1H, $J = 8.0$ Hz), 7.33 (d, 1H, $J = 8.0$ Hz), 7.49 (d, 1H, $J = 8.0$ Hz), 7.97 (br s, 1H, exchangeable with D_2O); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 18.4, 26.6, 34.9, 46.0, 53.9, 56.8, 108.6, 111.1, 118.4, 119.9, 122.2, 127.1, 130.8, 136.3; IR ($CHCl_3$) 2240, 3269, 3462 cm^{-1}; mass spectrum (HREI) calcd for $C_{15}H_{15}N_3$ m/z 237.1266, found 237.1264.

Compound **43** (18%): mp 169 °C (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17 (m, 1H), 2.31 (m, 1H), 2.80 (t, 1H), 2.85 (t, 1H), 3.01 (dd, 1H), 3.17 (m, 2H), 3.35 (m, 1H), 3.60 (t, 1H, $J = 8.0$ Hz), 4.58 (d, 1H, $J = 9.0$ Hz), 6.97 (t, 1H, $J = 8.0$ Hz), 7.03 (t, 1H, $J = 8.0$ Hz), 7.25 (d, 1H, $J = 8.0$ Hz), 7.38 (d, 1H, $J = 8.0$ Hz), 8.74 (br s, 1H, exchangeable with D_2O); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 19.2, 28.6, 31.3, 46.7, 49.7, 60.3, 110.7, 111.4, 118.5, 119.6, 121.2, 122.3, 126.8, 129.7, 136.6; IR ($CHCl_3$) 2240, 3265, 3452 cm^{-1}; mass spectrum (EI) m/z 237 (M^+). Anal. Calcd for $C_{15}H_{15}N_3 \cdot 0.4H_2O$: C, 73.71; H, 6.47; N, 17.20. Found: C, 73.94; H, 6.22; N, 17.93.

Compound **44** (foam, 12%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.18 (m, 1H), 2.73 (m, 2H), 2.93 (m, 1H), 3.07 (dd, 2H), 3.18 (m, 2H), 3.33 (m, 1H), 4.36 (dd, 1H, $J = 7.5, 4.5$ Hz), 7.14 (t, 1H, $J = 7.2$ Hz), 7.18 (t, 1H, $J = 7.2$ Hz), 7.38 (d, 1H, $J = 7.2$ Hz), 7.50 (d, 1H, $J = 7.2$ Hz), 7.85 (br s, 1H, exchangeable with D_2O); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 18.1, 26.5, 34.7, 45.8, 53.4, 56.3, 107.9, 111.1, 118.4, 119.8, 121.4, 122.0, 127.1, 133.3, 136.4; IR ($CHCl_3$) 2240, 3303, 3471 cm^{-1}; mass spectrum (HREI) calcd for $C_{15}H_{15}N_3$ m/z 237.1266, found 237.1280.

Methyl (1*R*,11b*R*)- and (1*S*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-1-carboxylate [(±)-46], Methyl (2*S*,11b*R*)- and (2*R*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-2-carboxylate [(±)-47], Methyl (1*S*,11b*R*)- and (1*R*,11b*S*)-1,2,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-1-carboxylate [(±)-48], and Methyl (2*R*,11b*R*)- and (2*S*,11b*S*)-1,2,3,5,6,11b-Hexahydroindolizino[8,7-*b*]indole-2-carboxylate [(±)-49]. These compounds were obtained from **20a** and methyl acrylate (**40**) after a 2 h reaction period at reflux. After the usual workup, the crude reaction mixture was purified by column chromatography on silica gel using first CH_2Cl_2 as eluent followed by a CH_2Cl_2−ethanol gradient (9:0.1 to 9:1). The following compounds, listed in order of their elution from the column, were obtained as foams:

Compound **46** (20%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30 (q, 2H), 2.88 (m, 2H), 3.02 (m, 1H), 3.12 (m, 3H), 3.21 (m, 1H), 3.86 (s, 3H), 4.29 (d, 1H, $J = 9.0$ Hz), 7.10 (t, 1H, $J = 7.0$ Hz), 7.17 (t, 1H, $J = 7.0$ Hz), 7.36 (d, 1H, $J = 7.0$ Hz), 7.48 (d, 1H, $J = 7.0$ Hz), 8.76 (br s, 1H, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.6, 26.8, 47.8, 48.5, 51.8, 52.4, 60.7, 111.1, 118.3, 119.5, 121.7, 175.1; IR ($CHCl_3$) 1737, 3262 cm^{-1}; mass spectrum (EI) m/z 270 (M^+). Anal. Calcd for $C_{16}H_{18}N_2O_2 \cdot 0.17CCl_4$: C, 64.82; H, 6.07; N, 9.45. Found: C, 64.68; H, 6.05; N, 9.98.

Compound **47** (9%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.61 (m, 2H), 2.70 (m, 1H), 2.97 (m, 1H), 3.07 (m, 2H), 3.15 (t, 1H), 3.24 (m, 2H), 3.73 (s, 3H), 4.31 (t, 1H), 7.10 (t, 1H, $J = 7.0$ Hz), 7.17 (t, 1H, $J = 7.0$ Hz), 7.33 (d, 1H, $J = 7.0$ Hz), 7.49 (d, 1H, $J = 7.0$ Hz), 7.89 (br s, 1H, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.4, 33.1, 41.8, 46.3, 52.1, 53.3, 57.7, 107.8, 111.1, 118.2, 119.9, 121.7, 127.2, 133.8, 136.4, 175.1; IR ($CHCl_3$) 1731, 3262 cm^{-1}; mass spectrum (HREI) calcd for $C_{16}H_{18}N_2O_2$ m/z 270.1347, found 270.1358.

Compound **48** (20%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.15 (m, 2H), 2.61 (m, 1H), 2.81 (m, 1H), 3.00 (m, 1H), 3.12 (m, 1H), 3.22 (m, 2H), 3.40 (m, 1H), 3.58 (s, 3H), 3.69 (q, 1H, $J = 8.0$ Hz), 4.78 (d, 1H, $J = 8.0$ Hz), 7.07 (t, 1H, $J = 7.0$ Hz), 7.16 (t, 1H, $J = 7.0$ Hz), 7.33 (d, 1H, $J = 7.0$ Hz), 7.44 (d, 1H, $J = 7.0$ Hz), 8.97 (br s, 1H, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.7, 26.1, 46.7, 47.2, 49.8, 52.3, 60.0, 111.3, 118.4, 119.7, 122.4, 173.5; IR ($CHCl_3$) 1737, 3294 cm^{-1}; mass spectrum (HREI) calcd for $C_{16}H_{18}N_2O_2$ m/z 270.1347, found 270.1358.

Compound **49** (19%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.24 (m, 1H), 2.59 (m, 1H), 2.69 (m, 1H), 2.94 (m, 1H), 3.06 (m, 1H), 3.17 (m, 3H), 3.32 (m, 1H), 3.57 (s, 3H), 4.38 (dt, 1H), 7.09 (t, 1H, $J = 7.0$ Hz), 7.25 (t, 1H, $J = 7.0$ Hz), 7.32 (d, 1H, $J = 7.0$ Hz), 7.47 (d, 1H, $J = 7.0$ Hz), 8.06 (br s, 1H, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.7, 32.9, 42.5, 52.0, 52.2, 56.8, 107.5, 110.9, 118.2, 119.5, 121.1, 127.1, 133.4, 136.3, 174.2; IR ($CHCl_3$) 1731, 3125 cm^{-1}; mass spectrum (HREI) calcd for $C_{16}H_{18}N_2O_2$ m/z 270.1347, found 270.1359.

Indolizino[8,7-*b*]indole-1-carbonitrile (45). A solution of compound **41** (20.5 mg, 0.09 mmol) in anhydrous CH_2Cl_2 was treated at 0 °C with DDQ (61.4 mg, 0.27 mmol). After 30 min, the reaction mixture was filtered through a pad of alumina, and the filtrate was evaporated to dryness under reduced pressure. The residue was purified by preparative TLC on silica gel (CH_2Cl_2−ethanol 99:1), affording **45** (2.9 mg, 15%) as an unstable solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (d, 1H, $J = 3.0$ Hz), 7.31 (d, 1H, $J = 6.2$ Hz), 7.35 (d, 1H, $J = 3.0$ Hz), 7.45 (t, 1H, $J = 9.0$ Hz), 7.48 (t, 1H, $J = 9.0$ Hz), 7.60 (d, 1H, $J = 8.0$ Hz), 7.87 (d, 1H, $J = 6.2$ Hz), 7.99 (d, 1H, $J = 8.0$ Hz), 9.20 (br s, 1H, exchangeable with D_2O); IR ($CHCl_3$) 3289, 2221 cm^{-1}; mass spectrum (HREI) calcd for $C_{15}H_9N_3$ m/z 231.0796, found 231.0791.

Similar treatment of compound **43** also gave **45** (18%).

(1*R*,11b*R*)- and (1*S*,11b*S*)-11-*N*-Benzyl-1,2,3,5,6,11b-hexahydroindolizino[8,7-*b*]indole-1-carbonitrile [(±)-50], (2*S*,11b*R*)- and (2*R*,11b*S*)-11-*N*-Benzyl-1,2,3,5,6,11b-hexahydroindolizino[8,7-*b*]indole-2-carbonitrile [(±)-51], (1*S*,-11b*R*)- and (1*R*,11b*S*)-11-*N*-Benzyl-1,2,3,5,6,11b-hexahydroindolizino[8,7-*b*]indole-1-carbonitrile [(±)-52], and (2*R*,11b*R*)- and (2*S*,11b*S*)-11-*N*-Benzyl-1,2,3,5,6,11b-hexahydroindolizino[8,7-*b*]indole-2-carbonitrile [(±)-53]. These compounds were obtained from **20b** and acrylonitrile (**39**) after a reaction period of 1 h. After the usual workup, the crude reaction mixture was purified by column chromatography on silica gel using an ethyl acetate−heptane gradient (20:80 to 60:40) as eluent. The following compounds, listed in order of their elution from the column, were obtained as oils:

Compound **51** (10%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.08 (m, 1 H), 2.40 (m, 1H), 2.85 (m, 1H), 2.93 (m, 1H), 2.98 (m, 1H), 3.07 (m, 1H), 3.12 (m, 1H), 3.17 (m, 1H), 3.39 (m, 1H), 4.25 (t, 1H), 5.29 (pseudo q, 2H, $J = 18.0, 2.0$ Hz), 6.95 (m, 2H), 7.18 (m, 3H), 7.29 (m, 3H), 7.58 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.0, 26.5, 35.2, 46.5, 47.2, 55.9, 63.6, 108.2, 109.5, 118.4, 119.6, 121.9, 122.0, 125.7, 126.6, 127.5, 128.9, 134.8, 137.2, 137.3; IR ($CHCl_3$) 2231 cm^{-1}; mass spectrum (HREI) calcd for $C_{22}H_{21}N_3$ m/z 327.1735, found 327.1730.

Compound **50** (40%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.24 (m, 1H), 2.38 (m, 1H), 2.84 (m, 1H), 2.92 (m, 2H), 3.05 (m, 1H), 3.12 (m, 3H), 4.52 (d, 1H, $J = 6.0$ Hz), 5.50 (pseudo q, 2H, $J = 18.0, 3.0$ Hz), 6.93 (dd, 2H), 7.17 (m, 2H), 7.25 (m, 4H), 7.57 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.9, 30.1, 32.8, 46.2, 47.4, 51.2, 61.3, 109.5, 109.9, 118.6, 119.8, 121.9, 122.8, 125.8, 126.5, 127.3, 128.9, 133.2, 137.2, 137.7; IR ($CHCl_3$) 2240 cm^{-1}; mass spectrum (EI) m/z 327 (M^+). Anal. Calcd for $C_{22}H_{21}N_3 \cdot 0.06CCl_4$: C, 78.51; H, 6.24; N, 12.49. Found: C, 78.51; H, 6.26; N, 12.25.

Compound **53** (9%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.07 (m, 1H), 2.60 (m, 1H), 2.86 (m, 1H), 2.95 (m, 2H), 3.02 (m, 1H), 3.11 (m, 1H), 3.21 (m, 3H), 4.25 (t, 1H), 5.25 (pseudo q, 2H, $J = 18.0, 3.0$ Hz), 6.94 (m, 2H), 7.15 (m, 3H), 7.26 (m, 3H), 7.55 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2, 26.7, 35.4, 46.6, 47.3, 54.9, 56.4, 107.9, 109.7, 118.6, 119.8, 121.3, 122.1, 126.7, 127.7, 129.0, 134.9, 137.3; IR ($CHCl_3$) 2253 cm^{-1}; mass spectrum (HREI) calcd for $C_{22}H_{21}N_3$ m/z 327.1735, found 327.1733.

Compound **52** (20%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.41 (m, 2H), 3.10 (m, 3H), 3.26 (m, 3H), 3.36 (m, 1H), 4.47 (d, 1H, $J = 8.3$ Hz), 5.04 (d, 2H, $J = 18.0$ Hz), 7.02 (m, 2H), 7.17 (m, 2H), 7.26 (m, 4H), 7.58 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 29.3, 33.0, 47.1, 48.2, 52.6, 60.1, 109.9, 118.8, 119.8, 119.9, 122.8, 126.1, 127.7, 129.0; IR ($CHCl_3$) 2243 cm^{-1}; mass spectrum (HREI) calcd for $C_{22}H_{21}N_3$ m/z 327.1735, found 327.1697.

Methyl (1*S*,11b*R*)- and (1*R*,11b*S*)-11-*N*-Benzyl-1,2,3,5,6,-11b-hexahydroindolizino[8,7-*b*]indole-1-carboxylate [(±)-54] and Methyl (2*R*,11b*R*)- and (2*S*,11b*S*)-11-*N*-Benzyl-1,2,3,5,6,11b-hexahydroindolizino[8,7-*b*]indole-1-carboxylate [(±)-55]. These compounds were obtained from **20b** and methyl acrylate (**40**) after a reaction period of 2 h. After the usual workup, the crude reaction mixture was purified by column chromatography on silica gel using an ethyl acetate−heptane gradient (10−100% ethyl acetate) as eluent. Compound **55** (oil, 6%) was eluted first: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.01 (m, 1H), 2.53 (m, 1H), 2.95 (m, 2H), 3.01 (m, 1H), 3.11 (m, 1H), 3.20 (m, 2H), 3.26 (m, 1H), 3.70 (s, 3H), 4.26 (dd, 1H), 5.31 (pseudo q, 2H, $J = 18.0, 3.0$ Hz), 6.96 (m, 1H), 7.14 (m, 3H), 7.26 (m, 4H), 7.55 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 33.5, 41.8, 47.2, 47.5, 52.5, 55.3, 57.6, 107.5, 109.9, 118.6, 119.8, 122.2, 126.0, 126.1, 127.7, 129.1, 134.2, 137.5, 174.3; IR ($CHCl_3$) 1737 cm^{-1}; mass spectrum (HREI) calcd for $C_{22}H_{24}N_2O_2$ m/z 361.1915, found 361.1887.

Continued elution of the column afforded compound **54** as an oil (60%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.22 (m, 1H), 2.56 (m, 1H), 2.99 (m, 2H), 3.08 (m, 2H), 3.27 (s, 3H), 3.36 (m, 1H), 3.45 (m, 2H), 4.43 (d, 1H, $J = 9.0$ Hz), 5.36 (pseudo q, 2H, $J = 18.0, 3.0$ Hz), 6.94 (m, 1H), 7.13 (m, 3H), 7.25 (m, 4H), 7.55 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.5, 27.7, 45.8, 46.8, 48.2, 51.7, 53.7, 60.3, 109.6, 118.1, 119.4, 121.7, 125.4, 127.0, 127.2, 128.4, 137.1, 137.4, 169.0; IR ($CHCl_3$) 1737 cm^{-1}; mass spectrum (HREI) calcd for $C_{22}H_{24}N_2O_2$ m/z 361.1915, found 361.1890.

Dimethyl Indolizino[8,7-*b*]indole-1,2-dicarboxylate (56). A solution of compound **33** (50 mg, 0.152 mmol) in CH_2Cl_2 (5 mL) was treated at 0 °C and under nitrogen with DDQ (104 mg, 0.46 mmol). After 2 h, the reaction mixture was filtered through Celite, the filtrate was evaporated to dryness under reduced pressure, and the residue was crystallized in ethanol, affording compound **56** (31.8 mg, 65%): mp 163 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.05 (s, 3H), 4.10 (s, 3H), 7.43 (t, 1H, $J = 8.0$ Hz), 7.61 (m, 2H), 7.78 (d, 1H, $J = 8.0$ Hz), 7.86 (s, 1H), 7.91 (d, 1H, $J = 7.2$ Hz), 8.14 (d, 1H, $J = 8.0$ Hz), 11.62 (br s, 1H, exchangeable with D_2O); IR (KBr) 1640, 1725, 3340 cm^{-1}; mass spectrum (EI) m/z 322 (M^+). Anal. Calcd for $C_{18}H_{14}N_2O_4 \cdot 1/4H_2O$: C, 65.25; H, 4.56; N, 8.45. Found: C, 65.11; H, 4.58; N, 8.42.

Dimethyl 8-Methoxyindolizino[8,7-*b*]indole-1,2-dicarboxylate (57). This compound was prepared from **37** in 80% yield following the same procedure as for the preparation of **56**: mp 181 °C (ethanol); ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.92 (s, 6H), 4.00 (s, 3H), 7.08 (dd, 1H, $J = 8.0, 3.2$ Hz), 7.38 (m, 2H), 7.48 (d, 1H, $J = 7.2$ Hz), 7.66 (s, 1H), 7.69 (d, 1H, $J = 8.0$ Hz), 11.31 (br s, 1H, exchangeable with D_2O); IR (KBr) 1640, 1660, 1720, 3325 cm^{-1}; mass spectrum (EI) m/z 354 (M^+). Anal. Calcd for $C_{19}H_{16}N_2O_5$: C, 64.76; H, 4.57; N, 7.95. Found: C, 64.66; H, 4.62; N, 7.90.

Dimethyl (2*R*,*S*)-2,3,5,6-Tetrahydroindolizino[8,7-*b*]-indole-1,2-dicarboxylate (58). A mixture of compound **33** (177 mg, 0.54 mmol) and potassium permanganate (1 g) in THF was stirred for 1 h at 0 °C under nitrogen. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. Chromatography of the residue on silica gel using CH_2Cl_2 as developer afforded compound **58** as a yellow syrup (152 mg, 86%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.08 (m, 2H), 3.18 (m, 1H), 3.28 (m, 1H), 3.58 (dd, 1H, $J_{gem} = 10.0$ Hz, $J_{vic} = 7.0$ Hz superimposed on a pseudo t, 1H, $J_{vic} = 10.0$ Hz), 3.71 (s, 6H), 3.98 (dd, 1H, $J = 7.0, 10.0$ Hz), 7.06 (t, 1H, $J = 8.0$ Hz), 7.23 (t, 1H, $J = 8.0$ Hz), 7.39 (d, 1H, $J = 8.0$ Hz), 7.51 (d, 1H, $J = 8.0$ Hz), 11.80 (br s, 1H, exchangeable with D_2O); IR ($CHCl_3$) 1600, 1645, 1740, 3250 cm^{-1}; mass spectrum (EI) m/z 326 (M^+). Anal. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.25; H, 5.56; N, 8.58. Found: C, 66.20; H, 5.55; N, 8.23.

Dimethyl (2*R*,*S*)-8-Methoxy-2,3,5,6-tetrahydroindolizino[8,7-*b*]indole-1,2-dicarboxylate (59). This compound was prepared from **37** following the same procedure as for the preparation of **58**. The crude reaction product was purified by chromatography on silica gel using CH_2Cl_2−ethanol (9:0.5) as developer, affording **59** (83%) as a yellow syrup: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.04 (m, 2H), 3.22 (m, 2H), 3.60 (dd, 2H, $J = 9.0$ Hz), 3.68 (s, 6H), 3.79 (s, 3H), 3.95 (dd, 1H, $J = 9.0, 10.0$ Hz), 6.87 (m, 2H), 7.30 (d, 1H, $J = 8.0$ Hz), 9.15 (br s, 1H, exchangeable with D_2O); IR ($CHCl_3$) 1600, 1660, 1745, 3180 cm^{-1}; mass spectrum (EI) m/z 356 (M^+). Anal. Calcd for $C_{19}H_{20}N_2O_5$: C, 64.03; H, 5.65; N, 7.86. Found: C, 64.14; H, 5.50; N, 7.61.

Dimethyl 5,6-Dihydro[8,7-*b*]indole-1,2-dicarboxylate (60). A solution of compound **58** (100 mg, 0.31 mmol) in CH_2Cl_2 (10 mL) was maintained at 0 °C under nitrogen while DDQ (70 mg, 0.31 mmol) was added in small portions over a period of 2 h. The reaction mixture was then filtered through Celite, the filtrate was evaporated to dryness under reduced pressure, and the residue was purified by chromatography on silica gel (CH_2Cl_2−ethanol 20:0.5), affording compound **60** (143 mg, 15%) as a white solid: mp 193 °C (ethanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.08 (t, 2H, $J = 7.0$ Hz), 3.65 (s, 3H), 3.79 (s, 3H), 4.06 (t, 2H, $J = 7.0$ Hz), 6.91 (m, 2H), 7.01 (s, 1H), 7.19 (d, 1H, $J = 8.0$ Hz), 7.27 (d, 1H, $J = 8.0$ Hz), 10.27 (br s, 1H, exchangeable with D_2O); IR (KBr) 1600, 1670, 1710, 3380 cm^{-1}; mass spectrum (EI) m/z 324 (M^+). Anal. Calcd for $C_{18}H_{16}N_2O_4$: C, 66.65; H, 4.97; N, 8.63. Found: C, 66.48; H, 4.85; N, 8.56.

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