DOI: 10.1002/ejoc.201000322

Advancing the Morita–Baylis–Hillman Chemistry of 1-Formyl-β-carbolines for the Synthesis of Indolizino-indole Derivatives[‡]

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Keywords: Nitrogen heterocycles / Alkaloids / Morita–Baylis–Hillman reaction / Harmicine / Homofascaplysin

The chemistry of the Morita–Baylis–Hillman adducts of 1-formyl-β-carbolines has been extended for obtaining indolizino-indole derivatives which mimic the harmicine and homofascaplysin frameworks. Adducts of *N*-substituted methyl 1-formyl-9*H*-β-carboline-3-carboxylate yield indolizino-indole derivatives upon bromination followed by aqueous workup. On the other hand, *N*-substituted 1-formyl-9*H*-β-carbolines give rise to similar products in a one-pot DABCO-promoted reaction of activated alkenes. Alternatively, the DMAP-mediated Morita–Baylis–Hillman reaction of *N*-substituted methyl 1-formyl-9*H*-β-carboline-3-carboxylate with cycloalkenones yields adducts that cyclize intramolecularly in the presence of PBr_3 to yield compounds with the homofascaplysin framework. In contrast, the DMAP-mediated reaction of *N*-substituted 1-formyl-β-carboline with cyclohexenone directly gives a product with similar framework in a single step.

Introduction

We have recently reported on the Morita–Baylis–Hillman (MBH) reactions of 1-formyl-9*H*-β-carbolines with alkyl acrylates which resulted in one-pot synthesis of unusual canthin-6-ones.[1] Moreover, adducts derived from acrylonitrile were readily transformed into canthine derivatives via base-promoted intramolecular cyclization. Furthermore, installing an alkene or alkyne chain on the indole NH and generating dipolarophile in the form of nitrile oxide, azide or azomethine ylide from the formyl group allowed us to construct a variety of fused β-carboline-based compounds via cycloaddition reactions.[2] In our efforts to expand the repertoire of fused-carbolines which could be synthesized from substituted 1-formyl-β-carbolines, we became interested in investigating the reactivity of substrates substituted at nitrogen by allyl and alkyne groups for 3+2 cycloaddition reaction. In principle, the allyl bromide obtained from the MBH reaction of such *N*-substituted aldehydes via bromination will lead to an allyl bromide which, under the influence of PPh_3 or PBu_3 may furnish a dipolarophile. This dipolarophile can initiate an intramolecular 3+2 cycloaddition reaction with alkene or alkyne chain on the nitrogen leading to annulated β-carboline (path 1, Figure 1).[3] Alternatively, the nucleophilicity of the N atom of the C-ring of β-carboline may initiate an intramolecular cyclization resulting in an indolizino-indole system (path 2, Figure 1). Indeed, the formation of indolizines from 2-pyridinecarboxaldehyde has been reported to take place following the latter path.[4] More importantly for our study, either pathway would afford new annulated β-carboline system. Investigating this approach, we have discovered that the allyl bromide which is generated via bromination of the MBH adduct of *N*-substituted 1-formyl-β-carboline immediately initiates nucleophilic attack of the nitrogen of the C-ring to furnish an indolizino-indole system which represents the aromatized derivative of the alkaloid harmicine (Figure 2).[5] Similar reactions with cycloalkenones give prod-

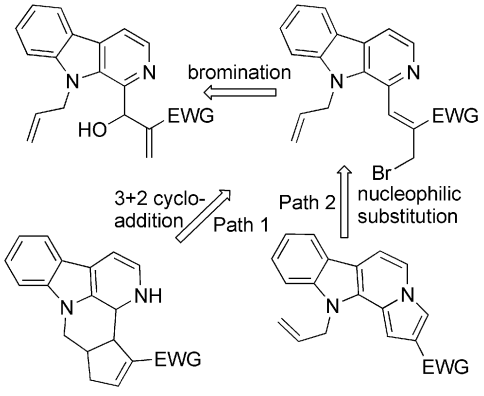

Figure 1. Retrosynthetic pathway.

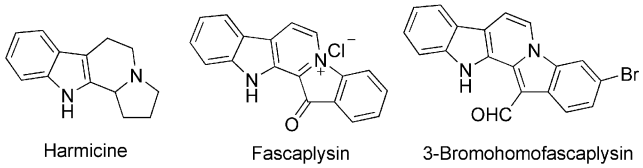

Figure 2. Core structure of alkaloids harmicine and fascaplysin.

[‡] CDRI Communication No. 7935.

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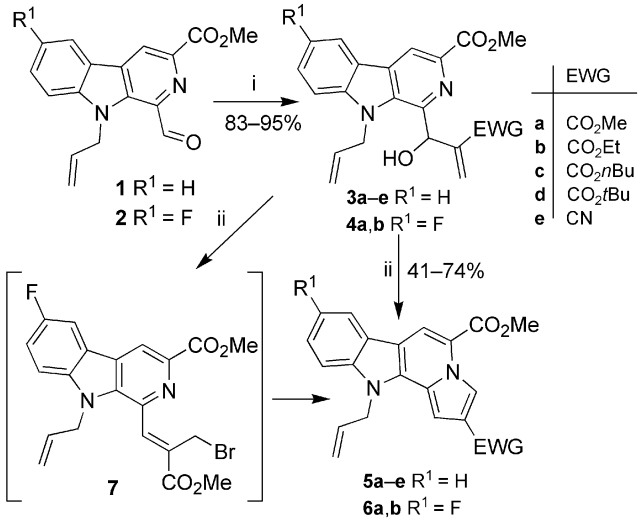
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201000322.

ucts with a homofascaplysin type of ring framework.[6] We provide an update on the results of our study in this direction.

Results and Discussion

The current study commenced with the synthesis of aldehydes **1** and **2** according to reported procedures.[1–2] Optimization studies were initiated by treating **1** with methyl acrylate in the presence of DABCO under neat condition (Scheme 1). This reaction smoothly affords the product **3a** in good yields. In order to generate the allyl bromide, **3a** was treated with PBr_3 in dichloromethane at 0 °C. Although the reaction was complete in 30 min, TLC analysis revealed the presence of three spots out of which the most non-polar spot displayed highly fluorescent green colour under UV light (254 nm). Quenching the reaction mixture with water followed by extraction furnished a residue which displayed two spots on TLC instead of the initial three, thus indicating either loss or transformation of one of the products into other during aqueous work up. However, purification of the residue via column chromatography resulted in a single product as solid which corresponded to the fluorescent spot of TLC. On the basis of this result we presumed that either the polar fraction present in the product could not be eluted, or it was also transformed during chromatographic purification on silica gel. ^{1}H- and ^{13}C NMR analysis of the isolated product revealed the presence of one CH_2 signal instead of the expected two (one for the allyl chain and other for the allyl bromide) and two extra CH signals in the aromatic region. A HMBC spectrum coupled with HRMS data led us to establish the structure of the product as **5a** instead of the anticipated allyl bromide. Perhaps the reaction of PBr_3 has started with the formation of allyl bromide which could have undergone a nucleophilic attack by the nitrogen of C-ring to form a salt that hydrates and rearranges in the presence of water to afford the isolated



Scheme 1. Reagents and conditions: i. DABCO, room temp., 3 h–15 d. ii. PBr_3, 0 °C, 30 min–2 h then left in water for 16–24 h.

product (Figure 3). This plausible mechanism inspired us to perform a few more optimization studies. In one of the experiments, the reaction after quenching with water on completion was allowed to stir for 24 h. TLC analysis of the reaction mixture revealed the presence of only one spot corresponding to the product **5a**.

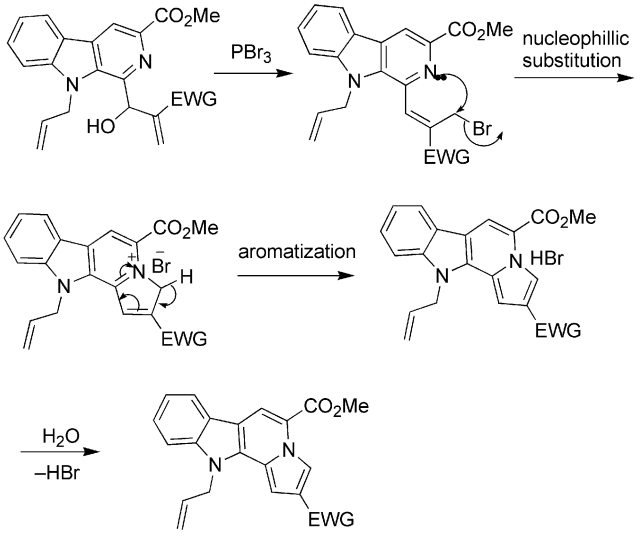
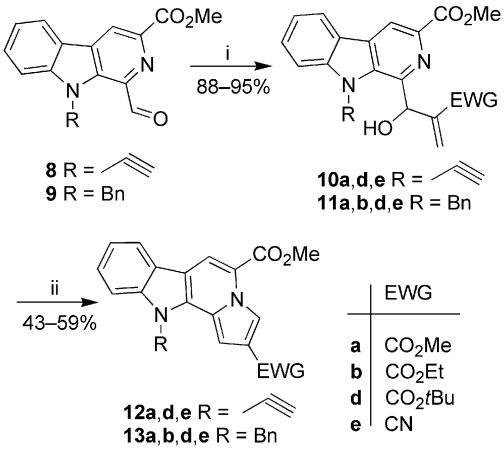


Figure 3. Plausible mechanism for the formation of indolizino-indole via allyl bromide.

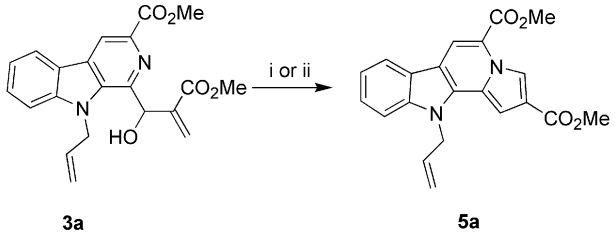
In order to find out more about the general applicability of this sequence we generated **3b–e**, **4a**,**b** by reaction of **1** and **2** with different activated alkenes. Treatment of **3b–e**, **4a**,**b** with PBr_3 for 1–2 h followed by aqueous work up for 24 h resulted in the desired products **5b–e**, **6a**,**b**. In support of the fact that the intramolecular cyclization reaction is preceded by the formation of allyl bromide, during the reaction of **4a** with PBr_3, crude **7** was separated and subjected to ^{1}H NMR and HRMS analysis (Scheme 1). Both data confirm the presence of allyl bromide. Alternating the allyl chain on the nitrogen of indole with propargyl and benzyl groups furnish aldehydes **8** and **9**, respectively, which were then examined for similar reactions. Gratifyingly these substrates too undergo the MBH reaction to afford **10a**,**d**,**e** and **11a**,**b**,**d**,**e** which after bromination yielded the desired products **12a**,**d**,**e** and **13a**,**b**,**d**,**e**, respectively (Scheme 2). These results imply that the intramolecular cyclization is not influenced by the substitution on the nitrogen of the indole subunit.

In previous study with 2-pyridinecarboxaldehyde it has been shown that acetylating the MBH adduct with acetic anhydride leads to the formation of an indolizine derivative.[7] Therefore we decided to probe the effectiveness of acetylation for intramolecular cyclization in compound **3**. Accordingly in a pilot study **3a** was treated with acetyl chloride in the presence of pyridine in MeCN. After screening for optimum conditions it was observed that the reaction of **3a** with 5 equiv. of acetyl chloride in the presence of 2 equiv. of pyridine in dry MeCN at 90 °C in 15 h yielded **5a** in 54% yield (Scheme 3). On the other hand heating **3a**



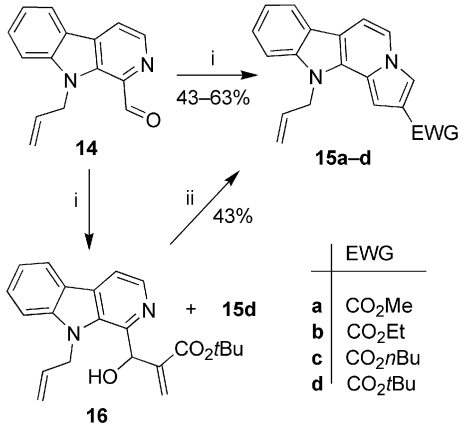
Scheme 2. Reagents and conditions i. DABCO, room temp., 4 h–12 d. ii. PBr_3, 0 °C, 30 min–2 h. then kept in water for 16–24 h.

with 5 equiv. of acetic anhydride in the presence of 2 equiv. of pyridine at 80 °C for 16 h afforded the compound **5a** in 46% yield.



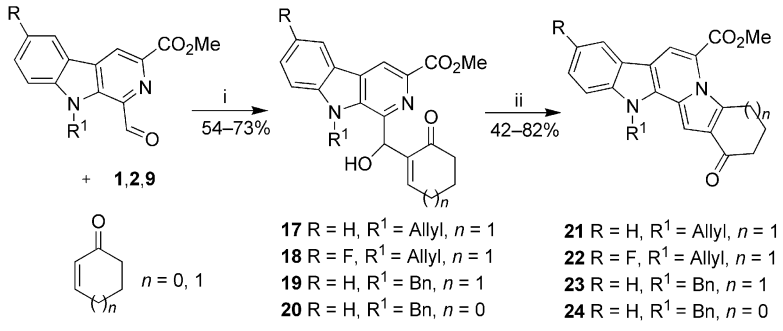
Scheme 3. Reagents and conditions i. AcCl, Py, dry MeCN, 80 °C, 15 h. ii. Ac_2O, Py, dry MeCN, 80 °C, 16 h.

Encouraged by results of the study, we next directed our attention towards analogous *N*-substituted aldehyde originating from tryptamine. Accordingly, **14** was prepared and subjected to MBH reaction with different acrylates at room temperature under neat conditions. As compared to reactions of aldehydes originating from tryptophan ester, reactions of **14** were found to be sluggish. But it was pleasing to note that except for the reaction of *tert*-butyl acrylate, in all cases the isolated products were established to be the indolizino-indoles **15a**–**c** (Scheme 4). For the reaction of **14** with *tert*-butyl acrylate we could isolate adduct **16** in 86% yields beside the indolizino-indole **15d** (5%) as the minor product. Nevertheless **16** upon treatment with PBr_3 furnished the required product **15d** in 43% yield.

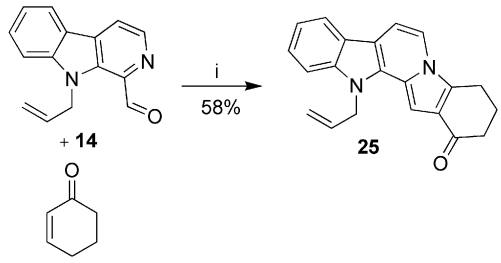


Scheme 4. Reagents and conditions i. alkyl acrylate, DABCO, room temp., 3–15 d. ii. PBr_3, 0 °C, 1 h. then kept in water for 16 h.

The success of the strategy invoked us to investigate similar reaction employing alkenones as the participating activated alkene. We anticipated that a successful MBH reaction of cycloalkenone with different β-carboline-based aldehydes would lead to adducts which would react with PBr_3 to yield the allyl bromide. The bromide would instantaneously undergo an intramolecular cyclization to afford a product having similar framework as that of alkaloid homofascaplysin. Accordingly, we examined the reaction of **1**–**2** and **9** with cyclohexenone and cyclopentenone under the influence of DMAP in aqueous THF for 36 to 48 h. Gratifyingly for all reactions the corresponding products were furnished in 48–73% yields (Scheme 5). However, **17** could not be isolated in pure form as it undergoes cyclization to afford **21** during purification via silica gel chromatography. Treatment of **17**–**20** with PBr_3 expectedly furnished the desired products **21**–**24**. Encouraged by these results, we then subjected **14** to reaction with cyclohexenone in the presence of DMAP under aqueous condition for 4 d to provide **25** in a one-pot reaction in 58% yield (Scheme 6).



Scheme 5. Reagents and conditions i. DMAP, THF/H_2O (1:1), r.t., 36–48 h. ii. PBr_3, 0 °C, 1 h, 30 min–1 h. then kept in water for 16 h.



Scheme 6. Reagents and conditions i. DMAP, THF/H_2O (1:1), r.t., 4 d.

Conclusions

In summary we have demonstrated a new application of the MBH chemistry with *N*-substituted β-carboline-based electrophiles to generate novel indolizino-indoles. These products are the mimics of the alkaloids harmicine and homofascaplysin. It was found that the presence of an electron-withdrawing substituent on the pyridine ring of 1-formyl-β-carboline originating from tryptophan weakens the nucleophilicity of the pyridine nitrogen. As a consequence the cyclization occurs only after treatment of the MBH adduct with PBr_3 or acetyl chloride (acetic anhydride), thus forming a more reactive allylic electrophile. On the other hand, the 1-formyl-β-carboline originating from tryptamine did not require any activation, cyclized derivatives were furnished during the MBH reaction. The strategy described herein highlights the usefulness of the MBH adduct as valuable source for important structural motifs.

Experimental Section

General: Melting points were determined in capillary tubes on a Precision melting point apparatus containing silicon oil. IR spectra were recorded using a Perkin–Elmer RX I FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded either on a Bruker DPX-200 FT or Bruker Avance DRX-300 spectrometer, using TMS as an internal standard (chemical shifts in δ). The ESMS were recorded on MICROMASS Quadro-II LCMS system. The HRMS spectra were recorded as EI-HRMS on a JEOL system or as DART-HRMS (recorded as ES+) on a JEOL-AccuTOF JMS-T100LC Mass spectrometer having a DART (Direct Analysis in Real Time) source. Elemental analyses were performed on a Carlo–Erba 108 or an Elementar Vario EL III microanalyzer. The room temperature varied between 20 and 35 °C. The ^{13}C NMR spectra of fluoro-substituted derivatives display extra peaks due to C,F couplings.

General Procedure for the Synthesis of 3b–e, 4a,b, 10a,d,e, 11a,b,d,e, 15a–c and 16, Exemplified for 3a: To a mixture of **1** (0.43 g, 1.69 mmol) and DABCO (0.19 g, 1.69 mmol), methyl acrylate (1.53 mL, 16.93 mmol) was added. The mixture was stirred at room temperature for 3 d. After completion of the reaction as monitored by TLC, the content was poured into water (50 mL) and EtOAc (50 mL) was added. The organic layer was partitioned and the aqueous layer was further extracted with EtOAc (3 × 25 mL). The pooled organic layer was washed with brine (40 mL), dried with anhydrous Na_2SO_4 and evaporated to yield a solid residue which was further purified by triturating with hexane/EtOAc, 95:05; R_f = 0.50 (hexane/EtOAc, 60:40) to obtain **3a** as a white solid (0.534 g from 0.43 g, 96%). For analytical grade was purified via silica gel (60–120 mesh) column chromatography by hexane/EtOAc (70:30, v/v) to afford **3a**, m.p. 151–153 °C.

Methyl 9-Allyl-1-[1-hydroxy-2-(methoxycarbonyl)allyl]-9*H*-β-carboline-3-carboxylate (3a): IR (KBr): $\tilde{\nu}_{max}$ = 1722 (CO_2CH_3), 3422 (OH) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.δ = 90 (s, 3 H, CO_2CH_3), 4.02 (s, 3 H, CO_2CH_3), 4.80 (d, J = 17.2 Hz, 1 H, =C*H*H$_{allyl}$), 5.03 (td, J_1 = 2.2, J_2 = 18.3 Hz, 1 H, C*H*HN), 5.18 (d, J = 8.6 Hz, 1 H, =CH*H*$_{allyl}$), 5.25 (td, J_1 = 2.2, J_2 = 18.3 Hz, 1 H, CH*H*N), 5.26 (s, 1 H, CHO*H*), 5.46 (d, J = 8.6 Hz, 1 H, =C*H*H$_{adduct}$), 6.00–6.12 (m, 1 H, =CH), 6.21 (d, J = 8.6 Hz, 1 H, =CH*H*$_{adduct}$), 6.24 (s, 1 H, C*H*OH), 7.40 (t, J = 7.5 Hz, 1 H, ArH), 7.48 (d, J = 8.4 Hz, 1 H, ArH), 7.62–7.67 (m, 1 H, ArH), 8.23 (d, J = 7.9 Hz, 1 H, ArH), 8.88 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 47.2, 52.4, 52.6, 69.6, 110.5, 116.9, 117.6, 121.3, 121.6, 121.8, 126.6, 129.3, 130.4, 132.8, 135.3, 135.7, 142.1, 142.2, 166.2, 167.6 ppm. MS (ES): *m*/*z* (%) = 381.2 (100) [M + 1]$^+$, 403.2 (33) [M + 23]$^+$. $C_{21}H_{20}N_2O_5$ (380.1372): calcd. C 66.31, H 5.30, N 7.36; found C 66.25, H 5.46, N 7.54.

Methyl 11-Allyl-11*H*-indolizino[8,7-*b*]indole-2-carboxylate (15a): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 15:85, v/v, R_f = 0.50 (EtOAc/hexane, 20:80, v/v)] gave a white solid (0.203 g from 0.25 g); yield 63%; m.p. 126–128 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1712 (CO_2CH_3) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.91 (s, 3 H, CO_2CH_3), 4.98 (d, J = 17.2 Hz, 1 H, =C*H*H), 5.19 (t, J = 4.7 Hz, 3 H, CH_2N, =CH*H*), 6.09–6.21 (m, 1 H, =CH), 7.11 (s, 1 H, ArH), 7.26 (q, J = 5.4 Hz, 2 H, ArH), 7.34–7.44 (m, 2 H, ArH), 7.73 (d, J = 7.1 Hz, 1 H, ArH), 7.91 (d, J = 7.8 Hz, 1 H, ArH), 7.95 (s, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 46.8, 51.6, 98.6, 107.1, 109.6, 117.0, 118.2, 118.7, 119.0, 119.1, 120.5, 123.4, 123.8, 124.1, 130.5, 132.6, 138.8, 165.6 ppm. MS (ES): *m*/*z* (%) = 305.2 (100) [M + 1]$^+$. $C_{19}H_{16}N_2O_2$ (304.1212): calcd. C 74.98, H 5.30, N 9.20; found C 74.67, H 5.54, N 9.44.

Ethyl 11-Allyl-11*H*-indolizino[8,7-*b*]indole-2-carboxylate (15b): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 15:85, v/v, R_f = 0.54 (EtOAc/hexane, 20:80, v/v)] gave a yellow solid (0.068 g from 0.15 g); yield 48%; m.p. 128–129 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1707 (CO_2Et) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.41 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 4.38 (q, J = 7.1 Hz, 2 H, OCH_2CH_3), 4.97 (d, J = 16.4 Hz, 1 H, =C*H*H), 5.19 (d, J = 4.8 Hz, 3 H, CH_2N and =CH*H*), 6.09–6.21 (m, 1 H, =CH), 7.11 (s, 1 H, ArH), 7.23–7.29 (m, 2 H, ArH), 7.35–7.44 (m, 2 H, ArH), 7.73 (d, J = 7.0 Hz, 1 H, ArH), 7.91 (d, J = 7.8 Hz, 1 H, ArH), 7.95 (d, J = 1.2 Hz, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.6, 46.8, 60.3, 98.6, 107.1, 109.6, 109.8, 117.0, 118.2, 119.0, 119.1, 120.5, 123.4, 123.8, 124.1, 125.6, 130.5, 132.7, 138.8 ppm. MS (ES): *m*/*z* (%) = 305.2 (100) [M + 1]$^+$. DART-HRMS (ES+): calcd. for $C_{20}H_{18}N_2O_2$ 319.1436; found 319.1446.

Butyl 11-Allyl-11*H*-indolizino[8,7-*b*]indole-2-carboxylate (15c): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 08:92, v/v, R_f = 0.75 (EtOAc/hexane, 20:80, v/v)] gave a yellow oil (0.126 g from 0.20 g); yield 43%. IR (neat): $\tilde{\nu}_{max}$ = 1705 ($CO_2CH_2CH_2CH_2CH_3$) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, J = 7.3 Hz, 3 H, $CO_2CH_2CH_2CH_2CH_3$), 1.44–1.54 (m, 2 H, $CO_2CH_2CH_2CH_2CH_3$), 1.72–1.82 (m, 2 H, $CO_2CH_2CH_2CH_2CH_3$), 4.33 (t, J = 6.7 Hz, 2 H, $CO_2CH_2CH_2CH_2CH_3$), 4.98 (d, J = 16.4 Hz, 1 H, =C*H*H), 5.18–5.22 (m, 3 H, =CH*H* and CH_2N),

6.09–6.21 (m, 1 H, =CH), 7.11 (s, 1 H, ArH), 7.22–7.30 (m, 2 H, ArH), 7.34–7.40 (m, 1 H, ArH), 7.42 (d, J = 8.0 Hz, 1 H, ArH), 7.73 (d, J = 6.7 Hz, 1 H, ArH), 7.90 (d, J = 7.7 Hz, 1 H, ArH), 7.94 (d, J = 1.4 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 19.4, 29.8, 31.0, 46.9, 64.3, 98.7, 107.1, 109.6, 109.8, 117.0, 118.1, 119.0, 119.1, 120.5, 123.3, 123.8, 124.1, 130.6, 132.6, 138.7, 165.3 ppm. MS (ES): m/z (%) = 347.2 (100) $[M + 1]^+$. $C_{22}H_{22}N_2O_2$ (346.1681): calcd. C 76.28, H 6.40, N 8.09; found C 76.45, H 6.38, N 7.98.

General Procedure for the Synthesis of 5b–e, 6a,b, 12a,d,e, 13a,b,d,e, 15d and 21–24, Exemplified for 5a: To a solution of **3a** (0.13 g, 0.34 mmol) in dry dichloromethane (6 mL), PBr_3 (0.07 mL, 0.68 mmol) was added and the reaction was stirred at 0 °C for 30 min. After completion, the content was poured into crushed ice and left for 16 h. Thereafter, the mixture was neutralized with $NaHCO_3$. The organic layer was separated and the aqueous layer was further extracted with $CHCl_3$ (3 × 25 mL). The organic layers were combined and washed with brine (50 mL), dried with anhydrous Na_2SO_4 and concentrated to yield a crude product which was further purified via silica gel (60–120 mesh) column chromatography by [hexane/EtOAc, 90:10, R_f = 0.60 (hexane/EtOAc, 80:20, v/v)] to yield **5a** as a yellow solid (with green tinge) (0.092 g from 0.13 g); yield 74%; m.p. 146–148 °C.

Dimethyl 11-Allyl-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (5a): IR (KBr): $\tilde{\nu}_{max}$ = 1704 (CO_2CH_3) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.90 (s, 3 H, CO_2CH_3), 3.96 (s, 3 H, CO_2CH_3), 4.92 (d, J = 17.2 Hz, 1 H, =C*H*H), 5.00 (t, J = 2.9 Hz, 2 H, CH_2N), 5.18 (d, J = 10.4 Hz, 1 H, =CH*H*), 6.01–6.13 (m, 1 H, =CH), 7.17 (d, J = 1.4 Hz, 1 H, $ArH_{pyrrole}$), 7.25–7.41 (m, 3 H, ArH), 7.87 (d, J = 7.7 Hz, 1 H, ArH), 8.21 (s, 1 H, ArH), 9.31 (d, J = 1.4 Hz, 1 H, $ArH_{pyrrole}$) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ = 46.8, 51.6, 52.3, 100.7, 109.0, 109.8, 116.4, 117.4, 117.8, 119.0, 119.2, 121.5, 123.6, 124.0, 124.6, 131.9, 133.7, 139.5, 163.1, 165.5 ppm. MS (ES): m/z (%) = 363.2 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{21}H_{19}N_2O_4$ 363.1345; found 363.1331.

2-Ethyl 5-Methyl 11-Allyl-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (5b): The title compound was prepared following the above-described general procedure. Purification by triturating [EtOAc/hexane, 05:95, R_f = 0.62 (EtOAc/hexane, 20:80, v/v)] gave a yellow solid with a green tinge (0.094 g from 0.21 g); yield 45%; m.p. 160–161 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1704 (CO_2CH_3 and $CO_2CH_2CH_3$) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.42 (t, J = 7.1 Hz, 3 H, $CO_2CH_2CH_3$), 4.03 (s, 3 H, CO_2CH_3), 4.40 (q, J = 7.1 Hz, 2 H, $CO_2CH_2CH_3$), 4.99 (d, J = 17.2 Hz, 1 H, =C*H*H), 5.19–5.25 (s, 3 H, CH_2N and = CH*H*), 6.09–6.21 (m, 1 H, =CH), 7.31–7.36 (m, 2 H, ArH), 7.43 (t, J = 2.6 Hz, 2 H, ArH), 7.96 (d, J = 7.7 Hz, 1 H, ArH), 8.40 (s, 1 H, ArH), 9.41 (d, J = 1.2 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6, 46.8, 52.2, 60.4, 100.7, 108.9, 109.8, 116.3, 117.4, 117.8, 119.1, 119.4, 121.4, 123.5, 124.0, 124.6, 131.9, 133.7, 139.5, 163.2, 165.1 ppm. MS (ES): m/z (%) = 377.2 (100) $[M + 1]^+$. $C_{22}H_{20}N_2O_4$ (376.1423): calcd. C 78.15, H 6.89, N 4.56; found C 78.10, H 6.81, N 4.46.

2-Butyl 5-Methyl 11-Allyl-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (5c): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 10:90, R_f = 0.55 (EtOAc/hexane, 10:90, v/v)] gave a light yellow solid with a green tinge (0.35 g from 0.50 g); yield 73%; m.p. 161–163 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1707 ($CO_2CH_2CH_2CH_2CH_3$) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.00 (t, J = 7.3 Hz, 3 H, $CO_2CH_2CH_2CH_2CH_3$), 1.53 (q, J = 7.4 Hz, 2 H, $CO_2CH_2CH_2CH_2CH_3$), 1.77 (q, J = 6.8 Hz, 2 H, $CO_2CH_2CH_2CH_2CH_3$), 4.03 (s, 3 H, CO_2CH_3), 4.35 (t, J = 6.7 Hz, 2 H, $CO_2CH_2CH_2CH_2CH_3$), 4.99 (d, J = 17.2 Hz, 1 H, =C*H*H), 5.19 (s, 2 H, CH_2N), 5.22 (d, J = 17.2 Hz, 1 H, =CH*H*), 6.08–6.20 (m, 1 H, =CH), 7.31–7.36 (m, 2 H, ArH), 7.43 (d, J = 2.4 Hz, 2 H, ArH), 7.96 (d, J = 7.7 Hz, 1 H, ArH), 8.40 (s, 1 H, ArH), 9.40 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 19.5, 31.1, 46.9, 52.3, 64.4, 100.8, 109.0, 109.8, 116.4, 117.4, 117.9, 119.2, 119.5, 121.4, 121.5, 123.6, 124.0, 124.6, 131.9, 133.8, 139.6, 163.2, 165.2 ppm. MS (ES): m/z (%) = 405.2 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{24}H_{25}N_2O_4$: 405.1814; found 405.1804.

2-(*tert*-Butyl) 5-Methyl 11-Allyl-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (5d): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 10:90, R_f = 0.58 (EtOAc/hexane, 10:90, v/v)] gave a yellow solid (0.11 g from 0.20 g); yield 58%; m.p. 98–100 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1708 ($CO_2C_4H_9$) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.63 (s, 9 H, $CO_2C_4H_9$), 4.03 (s, 3 H, CO_2CH_3), 5.00 (d, J = 17.2 Hz, 1 H, =C*H*H), 5.18–5.25 (m, 3 H, CH_2N and = CH*H*), 6.08–6.20 (m, 1 H, =CH), 7.29 (d, J = 1.4 Hz, 1 H, ArH), 7.30–7.35 (m, 1 H, ArH), 7.43 (d, J = 7.7 Hz, 2 H, ArH), 7.96 (d, J = 7.7 Hz, 1 H, ArH), 8.40 (s, 1 H, ArH), 9.35 (s, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 28.6, 46.9, 52.3, 80.6, 100.9, 108.9, 109.8, 116.4, 117.5, 117.9, 119.2, 121.2, 121.4, 123.7, 123.9, 124.6, 134.0, 133.9, 139.5, 163.3, 164.7 ppm. MS (ES): m/z (%) = 405.1 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{24}H_{25}N_2O_4$: 405.1794; found 405.1814.

Methyl 11-Allyl-2-cyano-11*H*-indolizino[8,7-*b*]indole-5-carboxylate (5e): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 10:90, R_f = 0.55 (EtOAc/hexane, 10:90, v/v)] gave a light yellow solid with a green tinge (0.183 g from 0.44 g); yield 44%; m.p. 183–185 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1697 (CO_2CH_3), 2223 (CN) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.03 (s, 3 H, CO_2CH_3), 4.97 (d, J = 17.2 Hz, 1 H, =C*H*H), 5.14 (t, J = 1.4 Hz, 2 H, CH_2N), 5.26 (d, J = 10.5 Hz, 1 H, =CH*H*), 6.06–6.19 (m, 1 H, =CH), 7.10 (d, J = 1.4 Hz, 1 H, ArH), 7.34–7.39 (m, 1 H, ArH), 7.47 (d, J = 3.7 Hz, 2 H, ArH), 7.99 (d, J = 7.8 Hz, 1 H, ArH), 8.45 (s, 1 H, ArH), 9.36 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.9, 52.5, 96.9, 102.2, 109.8, 109.9, 116.5, 116.7, 117.7, 119.4, 121.8, 123.2, 123.3, 124.0, 125.3, 131.5, 132.8, 133.5, 139.6, 162.9 ppm. MS (ES): m/z (%) = 330.1 (100) $[M + 1]^+$. $C_{20}H_{15}N_3O_2$ (329.1164): calcd. C 72.94, H 4.59, N 12.76; found C 73.09, H 4.73, N 12.54.

Dimethyl 11-Allyl-8-fluoro-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (6a): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 20:80, v/v, R_f = 0.60 (EtOAc/hexane, 30:70, v/v)] gave a yellow solid (0.421 g from 0.70 g); yield 63%; m.p. 195–197 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1713 (CO_2CH_3) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.93 (s, 3 H, CO_2CH_3), 4.03 (s, 3 H, CO_2CH_3), 4.94 (d, J = 17.0 Hz, 1 H, =C*H*H), 5.15–5.18 (s, 2 H, CH_2N), 5.24 (d, J = 10.3 Hz, 1 H, =CH*H*), 6.08–6.20 (m, 1 H, =CH), 7.11–7.18 (m, 1 H, ArH), 7.30 (d, J = 1.4 Hz, 1 H, ArH), 7.33–7.37 (m, 1 H, ArH), 7.61 (dd, J_1 = 2.4, J_2 = 8.8 Hz, 1 H, ArH), 8.33 (s, 1 H, ArH), 9.42 (d, J = 1.4 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 47.1, 51.6, 52.4, 101.1, 104.6, 105.0, 108.6, 108.7, 110.5, 110.7, 112.4, 112.7, 116.2, 117.6, 118.0, 119.2, 121.8, 123.8, 124.1, 124.2, 131.7, 134.7, 135.9, 157.3, 160.5, 163.0, 165.4 ppm. MS (ES): m/z (%) = 381.1 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{21}H_{18}FN_2O_4$ 381.1251; found 381.1232.

3-Ethyl 5-Methyl 11-Allyl-8-fluoro-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (6b): The title compound was prepared following the above-described general procedure. Purification by column

chromatography [EtOAc/hexane, 20:80, v/v, R_f = 0.65 (EtOAc/hexane, 30:70, v/v)] gave a yellow solid with a green tinge (0.20 g from 0.50 g); yield 41%; m.p. 168–170 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1709 (CO_2CH_3) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.42 (t, J = 7.1 Hz, 3 H, $CO_2CH_2CH_3$), 4.02 (s, 3 H, CO_2CH_3), 4.40 (q, J = 7.1 Hz, 2 H, $CO_2CH_2CH_3$), 4.97 (d, J = 17.1 Hz, 1 H, =CHH), 5.16 (d, J = 2.0 Hz, 2 H, CH_2N), 5.24 (d, J = 10.4 Hz, 1 H, =CHH), 6.08–6.17 (m, 1 H, =CH), 7.11–7.17 (m, 1 H, ArH), 7.30–7.36 (m, 2 H, ArH), 7.59 (dd, J_1 = 2.1, J_2 = 8.8 Hz, 1 H, ArH), 8.30 (s, 1 H, ArH), 9.40 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6, 47.1, 52.3, 60.5, 101.1, 104.6, 104.9, 108.6, 108.7, 110.5, 110.7, 112.3, 112.7, 116.1, 117.6, 118.0, 119.6, 121.7, 123.8, 124.1, 124.3, 131.7, 134.7, 135.9, 157.3, 160.5, 163.1, 165.0 ppm. MS (ES): m/z (%) = 395.2 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{22}H_{20}FN_2O_4$: C, 395.1381; found 395.1377.

Dimethyl 11-(Prop-2-ynyl)-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (12a): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 15:85, v/v, R_f = 0.40 (EtOAc/hexane, 30:70, v/v)] gave a yellow solid with a green tinge (0.134 g from 0.30 g); yield 47%; m.p. 242–244 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1712 (CO_2CH_3) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.39 (d, J = 2.6 Hz, 1 H, CCH), 3.94 (d, J = 3.4 Hz, 3 H, CO_2CH_3), 4.03 (d, J = 3.4 Hz, 3 H, CO_2CH_3), 5.31 (d, J = 2.8 Hz, 2 H, CH_2N), 7.33–7.39 (m, 1 H, ArH), 7.44–7.57 (m, 3 H, ArH), 7.96 (q, J = 3.8 Hz, 1 H, ArH), 8.38 (d, J = 3.5 Hz, 1 H, ArH), 9.43 (dd, J_1 = 1.3, J_2 = 3.4 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 39.3, 56.7, 57.6, 81.3, 84.4, 106.2, 114.1, 115.6, 121.6, 122.9, 123.8, 124.9, 125.6, 126.9, 128.1, 128.8, 130.1, 137.8, 144.0, 167.9, 169.5 ppm. MS (ES): m/z (%) = 361.2 (100) $[M + 1]^+$. $C_{21}H_{16}N_2O_4$ (360.1110): calcd. C 69.99, H 4.48, N 7.77; found C 70.30, H 4.54, N 7.56.

2-*tert*-Butyl 5-Methyl 11-(Prop-2-ynyl)-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (12d): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 15:85, v/v, R_f = 0.50 (EtOAc/hexane, 20:80, v/v)] gave a yellowish solid with a green tinge (0.143 g from 0.30 g); yield 50%; m.p. 201–203 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1708 ($CO_2CC_3H_9$) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.64 (s, 9 H, $CO_2CC_3H_9$), 2.39 (t, J = 2.4 Hz, 1 H, CCH), 4.02 (s, 3 H, CO_2CH_3), 5.29 (d, J = 2.5 Hz, 2 H, CH_2N), 7.32–7.37 (m, 1 H, ArH), 7.43–7.48 (m, 2 H, ArH), 7.54 (d, J = 8.2 Hz, 1 H, ArH), 7.94 (d, J = 7.7 Hz, 1 H, ArH), 8.35 (s, 1 H, ArH), 9.33 (d, J = 1.4 Hz, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 28.6, 34.2, 52.3, 74.1, 80.6, 100.9, 109.1, 109.5, 115.9, 118.1, 119.2, 121.2, 121.4, 123.6, 123.7, 124.7, 133.3, 138.8, 163.1, 164.5 ppm. MS (ES): m/z (%) = 403.1 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{24}H_{23}N_2O_4$ 403.1658; found 403.1644.

Methyl 2-Cyano-11-(prop-2-ynyl)-11*H*-indolizino[8,7-*b*]indole-5-carboxylate (12e): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 25:75, v/v, R_f = 0.42 (EtOAc/hexane, 20:80, v/v)] gave a white solid (0.144 g from 0.30 g); yield 51%; m.p. 212–214 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1724 (CO_2CH_3), 2224 (CN) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.44 (t, J = 2.4 Hz, 1 H, CCH), 4.04 (s, 3 H, CO_2CH_3), 5.25 (d, J = 2.5 Hz, 2 H, CH_2N), 7.34 (s, 1 H, ArH), 7.36–7.42 (m, 1 H, ArH), 7.49–7.58 (m, 2 H, ArH), 7.98 (d, J = 7.8 Hz, 1 H, ArH), 8.43 (s, 1 H, ArH), 9.39 (d, J = 1.4 Hz, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, [D_6]-DMSO): δ = 29.4, 53.0, 76.6, 79.0, 96.5, 103.6, 110.0, 111.0, 117.2, 118.0, 119.6, 120.3, 122.3, 123.1, 123.9, 125.6, 132.2, 134.8, 139.2, 162.8 ppm. MS (ES): m/z (%) = 328.1 (100) $[M + 1]^+$. $C_{20}H_{13}N_3O_2$ (327.1008): calcd. C 73.38, H 4.00, N 12.84; found C 73.44, H 4.23, N 12.78.

Dimethyl 11-Benzyl-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (13a): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 15:85, v/v, R_f = 0.50 (EtOAc/hexane, 25:75, v/v)] gave a yellow solid (0.23 g from 0.40 g); yield 59%; m.p. 209–211 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1713 (CO_2CH_3) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, CO_2CH_3), 4.04 (s, 3 H, CO_2CH_3), 5.81 (s, 2 H, CH_2N), 7.15 (t, J = 6.3 Hz, 2 H, ArH), 7.22–7.32 (m, 1 H, ArH), 7.33–7.36 (m, 3 H, ArH), 7.36–7.40 (m, 3 H, ArH), 7.99 (d, J = 6.7 Hz, 1 H, ArH), 8.45 (s, 1 H, ArH), 9.41 (d, J = 1.3 Hz, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 29.8, 48.4, 51.6, 52.4, 100.7, 109.3, 110.2, 116.5, 118.2, 119.2, 119.3, 121.6, 121.7, 123.8, 124.2, 124.8, 126.3, 127.9, 129.2, 134.1, 136.2, 139.9, 163.2, 165.5 ppm. MS (ES): m/z (%) = 413.2 (100) $[M + 1]^+$. $C_{25}H_{20}N_2O_4$ (412.1423): calcd. C 72.80, H 4.89, N 6.79; found C 72.96, H 4.78, N 6.83.

2-Ethyl 5-Methyl 11-Benzyl-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (13b): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 15:85, v/v, R_f = 0.52 (EtOAc/hexane, 20:80, v/v)] gave a yellow solid with a green tinge (0.346 g from 0.80 g); yield 45%; m.p. 185–187 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1710 ($CO_2CH_2CH_3$ and CO_2CH_3) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.36 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 4.06 (s, 3 H, CO_2CH_3), 4.34 (q, J = 7.1 Hz, 2 H, OCH_2CH_3), 5.82 (s, 2 H, CH_2), 7.14 (d, J = 6.3 Hz, 2 H, ArH), 7.23–7.33 (m, 4 H, ArH), 7.35–7.42 (m, 3 H, ArH), 7.99 (d, J = 6.7 Hz, 1 H, ArH), 8.44 (s, 1 H, ArH), 9.40 (d, J = 1.4 Hz, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.6, 48.3, 52.3, 60.4, 109.2, 110.1, 116.4, 118.1, 119.2, 119.6, 121.5, 121.7, 123.8, 124.1, 124.8, 126.3, 127.9, 129.2, 134.1, 136.2, 139.9, 163.2, 165.0 ppm. MS (ES): m/z (%) = 427.2 (100) $[M + 1]^+$. $C_{26}H_{22}N_2O_4$ (426.1580): calcd. C 73.23, H 5.20, N 6.57; found C 73.47, H 5.04, N 6.69.

2-(*tert*-Butyl) 5-Methyl 11-Benzyl-11*H*-indolizino[8,7-*b*]indole-2,5-dicarboxylate (13d): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 15:85, v/v, R_f = 0.80 (EtOac/hexane, 20:80, v/v)] gave a yellow solid with a green tinge (0.452 g from 1.00 g); yield 47%; m.p. 179–181 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1707 ($CO_2CC_3H_9$ and CO_2CH_3) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.59 (s, 9 H, $CO_2CC_3H_9$), 4.03 (d, J = 1.9 Hz, 3 H, CO_2CH_3), 5.81 (s, 2 H, CH_2N), 7.16 (t, J = 8.4 Hz, 3 H, ArH), 7.26–7.33 (m, 3 H, ArH), 7.34–7.40 (m, 3 H, ArH), 7.99 (d, J = 6.7 Hz, 1 H, ArH), 8.43 (t, J = 6.7 Hz, 1 H, ArH), 9.30 (d, J = 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.6, 48.3, 52.3, 80.5, 100.9, 109.1, 110.1, 116.3, 118.0, 119.2, 121.2, 123.7, 123.9, 124.7, 126.2, 127.8, 129.1, 134.1, 136.2, 139.9, 163.3, 164.5 ppm. MS (ES): m/z (%) = 455.1 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{28}H_{27}N_2O_4$ 454.1971; found 454.1959.

Methyl 11-Benzyl-2-cyano-11*H*-indolizino[8,7-*b*]indole-5-carboxylate (13e): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 10:90, v/v, R_f = 0.60 (EtOAc/hexane, 10:90, v/v)] gave a white solid with a green tinge (0.071 g from 0.17 g); yield 43%; m.p. 227–229 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1707 (CO_2CH_3), 2231 (CN) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.04 (s, 3 H, CO_2CH_3), 5.76 (s, 2 H, CH_2N), 6.94 (d, J = 0.8 Hz, 1 H, ArH), 7.08–7.11 (m, 2 H, ArH), 7.26–7.33 (m, 3 H, ArH), 7.36–7.41 (m, 1 H, ArH), 7.45 (t, J = 2.5 Hz, 2 H, ArH), 8.02 (d, J = 7.5 Hz, 1 H, ArH), 8.48 (s, 1 H, ArH), 9.33 (d, J = 1.4 Hz, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 29.8, 48.3, 52.6, 97.0, 102.3, 110.0, 110.1, 116.7, 117.9, 119.5, 122.0, 123.4, 124.0, 125.5, 125.9,

128.1, 129.4, 135.8, 140.1, 162.9 ppm. MS (ES): *m*/*z* (%) = 380.1 (100) $[M + 1]^+$. $C_{24}H_{17}N_3O_2$ (379.1321): calcd. C 75.97, H 4.52, N 11.08; found C 75.88, H 4.64, N 10.94.

***tert*-Butyl 11-Allyl-11*H*-indolizino[8,7-*b*]indole-2-carboxylate (15d):** The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 10:90, v/v, R_f = 0.60 (EtOAc/hexane, 10:90, v/v)] was obtained as a yellow oil (0.128 g from 0.30 g); yield 45%. IR (neat): $\tilde{\nu}_{max}$ = 1701 ($CO_2CC_3H_9$) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.62 (s, 9 H, $CO_2CC_3H_9$), 4.99 (d, *J* = 17.5 Hz, 1 H, =C*H*H), 5.19 (t, *J* = 7.4 Hz, 3 H, CH_2N and =CH*H*), 6.07–6.19 (m, 1 H, =CH), 7.06 (s, 1 H, ArH), 7.19–7.28 (m, 2 H, ArH), 7.33–7.43 (m, 2 H, ArH), 7.70 (d, *J* = 7.1 Hz, 1 H, ArH), 7.86 (d, *J* = 1.3 Hz, 1 H, ArH), 7.89 (d, *J* = 7.8 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.5, 46.8, 80.4, 98.7, 106.9, 109.5, 109.7, 117.0, 118.0, 119.0, 119.1, 120.4, 120.8, 123.4, 123.7, 123.9, 130.6, 132.7, 138.7, 164.6 ppm. MS (ES): *m*/*z* (%) = 347.1 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{22}H_{23}N_2O_2$ 347.1760; found 347.1744.

Methyl 12-Allyl-1-oxo-2,3,4,12-tetrahydro-1*H*-benzo[2,3]indolizino-[8,7-*b*]indole-6-carboxylate (21): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 20:80, v/v, R_f = 0.40 (EtOAc/hexane, 50:50, v/v)] gave a white solid (0.576 g from 0.70 g); yield 65%; m.p. 228–230 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1670 (CO), 1718 (CO_2CH_3) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.20 (q, *J* = 6.3 Hz, 2 H, CH_2), 2.65 (t, *J* = 5.8 Hz, 2 H, CH_2), 2.86 (t, *J* = 6.0 Hz, 2 H, CH_2), 4.04 (s, 3 H, CO_2CH_3), 4.95 (d, *J* = 17.0 Hz, 1 H, =C*H*H), 5.21 (t, *J* = 5.0 Hz, 3 H, =CH*H* and CH_2N), 6.08–6.20 (m, 1 H, =CH), 7.30–7.35 (m, 2 H, ArH), 7.39–7.46 (m, 2 H, ArH), 7.94 (d, *J* = 7.7 Hz, 1 H, ArH), 8.10 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.0, 26.6, 38.4, 46.9, 52.6, 97.0, 108.8, 109.9, 117.0, 117.3, 119.2, 119.8, 121.4, 123.6, 123.7, 124.6, 124.8, 131.9, 133.7, 138.4, 139.5, 163.5, 196.4 ppm. MS (ES): *m*/*z* (%) = 373.2 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{23}H_{21}N_2O_3$ 373.1552; found 373.1534.

Methyl 12-Allyl-9-fluoro-1-oxo-2,3,4,12-tetrahydro-1*H*-benzo[2,3]-indolizino[8,7-*b*]indole-6-carboxylate (22): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 30:70, v/v, R_f = 0.38 (EtOAc/hexane, 50:50, v/v)] gave a white solid (0.06 g from 0.15 g); yield 42%; m.p. >250 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1655 (CO), 1713 (CO_2CH_3) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.18 (t, *J* = 6.2 Hz, 2 H, CH_2), 2.68 (t, *J* = 6.3 Hz, 2 H, CH_2), 2.87 (t, *J* = 6.1 Hz, 2 H, CH_2), 4.03 (s, 3 H, CO_2CH_3), 4.92 (d, *J* = 17.1 Hz, 1 H, =C*H*H), 5.15–5.23 (m, 3 H, =CH*H* and CH_2N), 6.05–6.17 (m, 1 H, =CH), 7.10–7.16 (m, 1 H, ArH), 7.31–7.39 (m, 2 H, ArH), 7.56 (dd, J_1 = 2.4, J_2 = 8.8 Hz, 1 H, ArH), 8.00 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 24.9, 26.2, 33.6, 47.0, 53.1, 97.7, 105.4, 105.8, 108.1, 108.4, 111.7, 112.2, 116.9, 120.5, 124.3, 133.6, 136.3, 138.6, 170.8, 174.7, 195.9 ppm. MS (ES): *m*/*z* (%) = 391.2 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{23}H_{20}FN_2O_3$ 391.1458; found 391.1454.

Methyl 12-Benzyl-1-oxo-2,3,4,12-tetrahydro-1*H*-benzo[2,3]indolizino[8,7-*b*]indole-6-carboxylate (23): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 20:80, v/v, R_f = 0.50 (EtOAc/hexane, 40:60, v/v)] gave a yellow solid with a green tinge (0.277 g from 0.35 g); yield 82%; m.p. 198–200 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1717 (CO and CO_2CH_3) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.17 (t, *J* = 5.8 Hz, 2 H, CH_2), 2.65 (t, *J* = 5.8 Hz, 2 H, CH_2), 2.86 (t, *J* = 5.6 Hz, 2 H, CH_2), 4.05 (s, 3 H, CO_2CH_3), 5.82 (s, 2 H, CH_2N), 7.11 (d, *J* = 7.0 Hz, 2 H, ArH), 7.23–7.30 (m, 4 H, ArH), 7.33–7.40 (m, 3 H, ArH), 7.97 (d, *J* = 6.8 Hz, 1 H, ArH), 8.13 (d, *J* = 1.5 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.0, 26.6, 38.4, 48.4, 52.6, 97.0, 109.0, 110.2, 117.0, 119.2, 120.0, 121.6, 123.7, 123.8, 124.7, 124.9, 126.2, 127.8. 129.1, 133.9, 136.1, 138.4, 139.8, 163.5, 196.2 ppm. MS (ES): *m*/*z* (%) = 423.3 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{27}H_{23}N_2O_3$ 423.1709; found 423.1689.

Methyl 12-Benzyl-1-oxo-2,3,4,12-tetrahydro-1*H*-benzo[2,3]indolizino[8,7-*b*]indole-6-carboxylate (24): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 25:75, v/v, R_f = 0.60 (EtOAc/hexane, 50:50, v/v)] was obtained as a yellow solid (0.098 g from 0.20 g); y ield: 51%; m.p. >250 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1703 (CO_2CH_3), 1711 (CO) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.95–2.99 (m, 2 H, CH_2), 3.34–3.37 (m, 2 H, CH_2), 4.03 (s, 3 H, CO_2CH_3), 5.79 (s, 2 H, CH_2N), 6.90 (s, 1 H, ArH), 7.09 (t, *J* = 3.4 Hz, 2 H, ArH), 7.24–7.28 (m, 4 H, ArH), 7.34–7.42 (m, 2 H, ArH), 7.99 (d, *J* = 7.0 Hz, 1 H, ArH), 8.22 (s, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.7, 41.4, 48.2, 52.6, 93.1, 109.3, 110.1, 116.2, 119.3, 119.8, 121.8, 123.5, 125.0, 125.9, 127.9, 129.2, 130.6, 130.9, 134.0, 136.0, 140.0, 153.0, 162.7 ppm. MS (ES): *m*/*z* (%) = 409.3 (100) $[M + 1]^+$. $C_{26}H_{20}N_2O_3$ (408.1474): calcd. C 76.45, H 4.94, N 6.86; found C 76.81, H 5.06, N 6.73.

General Procedure for the Synthesis of 17–18, 20, 25, Exemplified for 19: To a solution of **9** (0.50 g, 1.45 mmol) was added DMAP (0.071 g, 0.58 mmol) and cyclohexenone (2.66 mL, 29.5 mmol) in a THF/water mixture (10 mL, 1:1, v/v). The reaction mixture was stirred at room temperature for 48 h. After completion of the reaction as monitored by TLC, the content was extracted with EtOAc (3 × 40 mL). The organic layer was washed with brine (70 mL), dried with anhydrous Na_2SO_4 and evaporated to yield a solid residue which was further purified via silica gel column chromatography using [hexane/EtOAc, 40:60, R_f = 0.50 (hexane/EtOAc, 50:50)] to obtain **19** as a yellow solid (0.344 g from 0.50 g); yield 54%; m.p. 185–187 °C.

Methyl 9-Benzyl-1-[hydroxy(6-oxocyclohex-1-en-1-yl)methyl]-β-carboline-3-carboxylate (19): IR (KBr): $\tilde{\nu}_{max}$ = 1665 (CO), 1701 (CO_2CH_3), 3448 (OH) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.57–1.63 (m, 1 H, C*H*H), 1.85–1.96 (m, 2 H, CH_2), 2.04–2.14 (m, 2 H, CH_2), 2.44–2.50 (m, 1 H, CH*H*), 4.03 (s, 3 H, CO_2CH_3), 5.64 (d, *J* = 18.0 Hz, 2 H, =CH and CHO*H*), 5.87 (d, *J* = 18.0 Hz, 1 H, C*H*OH), 6.27 (t, *J* = 4.2 Hz, 2 H, CH_2Ph), 6.79 (t, *J* = 4.2 Hz, 2 H, ArH), 7.20–7.24 (m, 3 H, ArH), 7.33 (d, *J* = 8.3 Hz, 1 H, ArH), 7.40 (t, *J* = 7.4 Hz, 1 H, ArH), 7.54–7.60 (m, 1 H, ArH), 8.26 (d, *J* = 7.8 Hz, 1 H, ArH), 8.91 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.1, 25.8, 38.1, 48.3, 52.6, 67.5, 111.1, 117.5, 121.5, 121.7, 121.8, 125.6, 127.6, 129.0, 129.4, 130.5, 135.3, 135.6, 136.9, 140.7, 142.4, 143.1, 148.3, 166.3 ppm. MS (ES): *m*/*z* (%) = 441.2 (100) $[M + 1]^+$, 464.2 (60) $[M + 23]^+$. $C_{27}H_{24}N_2O_4$ (440.1736): calcd. C 73.62, H 5.49, N 6.36; found C 73.59, H 5.67, N 6.57.

12-Allyl-2,3,4,12-tetrahydro-1*H*-benzo[2,3]indolizino[8,7-*b*]indol-1-one (25): The title compound was prepared following the above-described general procedure. Purification by column chromatography [EtOAc/hexane, 15:85, v/v, R_f = 0.40 (EtOAc/hexane, 30:70, v/v)] gave a white solid (0.241 g from 0.31 g); yield 58%; m.p. 135–137 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1660 (CO) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.31–2.39 (m, 2 H, CH_2), 2.66 (t, *J* = 5.8 Hz, 2 H, CH_2), 3.04 (t, *J* = 6.2 Hz, 2 H, CH_2), 4.93 (d, *J* = 16.5 Hz, 1 H, =C*H*H), 5.16–5.18 (m, 3 H, =CH*H* and CH_2N), 6.06–6.18 (m, 1 H, =CH), 7.06 (s, 1 H, ArH), 7.26–7.30 (m, 2 H, ArH), 7.34–7.44

(m, 2 H, ArH), 7.51 (d, J = 7.2 Hz, 1 H, ArH), 7.91 (d, J = 7.7 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7, 23.6, 38.5, 46.8, 93.6, 107.2, 109.6, 109.8, 115.7, 116.9, 119.0, 120.5, 122.6, 123.4, 123.9, 124.4, 130.8, 132.6, 134.4, 138.8, 195.9 ppm. MS (ES): m/z (%) = 315.3 (100) $[M + 1]^+$. DART-HRMS (ES^+): calcd. $C_{21}H_{18}N_2O$ 315.1485; found 315.1497.

Supporting Information (see also the footnote on the first page of this article): Experimental details, spectroscopic data for remaining compounds and copies of ^{1}H and ^{13}C NMR spectra for all new compounds are provided.

Acknowledgments

Two of the authors (V. S. and S. H.) gratefully acknowledge financial support from the Council of Scientific and Industrial Research, New Delhi. The authors also acknowledge SAIF, CDRI for recording of the spectroscopic and analytical data of all compounds. This work was sponsored by the Department of Science and Technology, New Delhi under a grant (SR/SI/OC-01/2010).

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Received: March 9, 2010
Published Online: May 19, 2010

