Ortho-Directed Lithiation Studies of 3-Carboxy-β-carbolines: A Direct Route to 4-Substituted Derivatives

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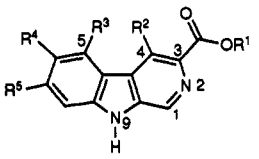
Recent interest in the synthesis of functionalized pyrido[3,4-*b*]indoles (i.e., β-carbolines) has been largely due to the high affinity which some of these compounds possess for the benzodiazepine receptors of the central nervous system and the various pharmacological activities which they display as a result.[1-3] Structure–activity studies have revealed the importance of substitution at the 3 and 4 positions as well as on the aromatic A ring in determining both the affinity and the type of *in vivo* activity demonstrated by these compounds. In particular, the most active β-carboline derivatives have in common a carboxyl group at the C-3 position[4] and an alkyl (e.g., ZK 93426, **1a**; DMCM, **1b**) or alkoxy substituent at C-4 (e.g., ZK 93423, **1c**).[5] Substituted β-carbolines are almost universally synthesized from indoles.[6] While inclusion of appropriate or modifiable substituents at the C-5 and C-6 positions of 3-carboxy-β-carbolines merely requires use of a similarly substituted, generally accessible indole as starting material, the introduction of substituents at the C-4 position other than *via* aldimine chemistry (i.e., condensation of the aldehyde equivalent of the C-4 substituent desired with ethyl nitroacetate and then with indole) is much less satisfactory. No direct method of introducing a C-4 substituent on a preformed 3-carboxy-β-carboline nucleus is known.



1a $R^1 = C_2H_5$; $R^2 = CH_3$; $R^3 = CH(CH_3)_2$; $R^4 = R^5 = H$ (ZK 93426)

1b $R^1 = CH_3$; $R^2 = C_2H_5$; $R^3 = H$; $R^4 = R^5 = OCH_3$ (DMCM)

1c $R^1 = C_2H_5$; $R^2 = CH_2OCH_3$; $R^3 = R^5 = H$; $R^4 = OCH_2Ph$ (ZK 93423)

Since a C-3 carboxyl group (ester or amide) on β-carbolines optimizes their interactions with the receptor, we thought of using this function to direct metalation (i.e., lithiation) and subsequent electrophilic substitution at the C-4 position.[7] Although ortho-lithiation of benzamide-type substrates is a very efficient reaction,[8] the application of this ortho functionalization strategy to π-deficient heteroaromatics (e.g., pyridines, quinolines, diazines) has been hampered by evidence that these substrates, which have low LUMOs, undergo nucleophilic attack instead of proton abstraction by organolithium reagents.[9] However, Meyers, Katritzsky, and others[10] have demonstrated that ortho-metalation techniques can be successful in the pyridine series if suitable, generally nitrogen-containing directing groups are utilized. Since the *N*-benzylcarboxamide group has been shown to be particularly satisfactory in this respect,[10b] we chose to initiate our study of ortho-directed lithiation of β-carbolines using this group at C-3 (i.e., compound **5**, Scheme I). The latter was prepared from ethyl 9-*N*-methyl-β-carboline-3-carboxylate (**4**),[11,12] using the methodology described by Kishi and co-workers.[13] Thus, trimethylaluminum (**2**) was treated with benzylamine in dichloromethane forming dimethylaluminum amide **3** which was then reacted with β-carboline **4** to give **5** in 95% yield. This new method of preparing β-carboline-3-carboxamides is more satisfactory than those previously published in terms of product yield and purity.[14,15]

Treatment of compound **5** with *sec*-butyllithium in dry THF at −78 °C gave a dark purple solution which, when quenched with D_2O,[16] yielded the 4-deuterio derivative **8** (Scheme II), together with starting material **5** (obtained as an inseparable mixture). Product yield (the extent of deuteration) was first established by comparison of the

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(12) Methylation of the N-9 position of β-carboline-3-carboxylates is known to seriously interfere with their binding to the benzodiazepine receptor.[11] It was nevertheless decided to perform preliminary metalation studies using the N-methylated derivative **5** in order to avoid untoward side reactions and electronic effects on the β-carboline nucleus as well as to increase solubility in THF. Although methylation is not generally recognized as a practical way of blocking the indolic nitrogen atom, compound **5** can be efficiently demethylated using sequential benzoyl peroxide–sodium hydroxide treatment. See: Nakatsuka, S.; Asano, O.; Goto, T. *Heterocycles* **1986**, *24*, 2791.

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(16) Spectroscopic-grade D_2O (>99.95% pure) must be used for this quenching experiment if deuterium incorporation is to be assured. The use of D_2O of lower purity (i.e., having a greater percentage of HDO) gave very poor yields of deuterated compound **8** due to unfavorable isotope effects.

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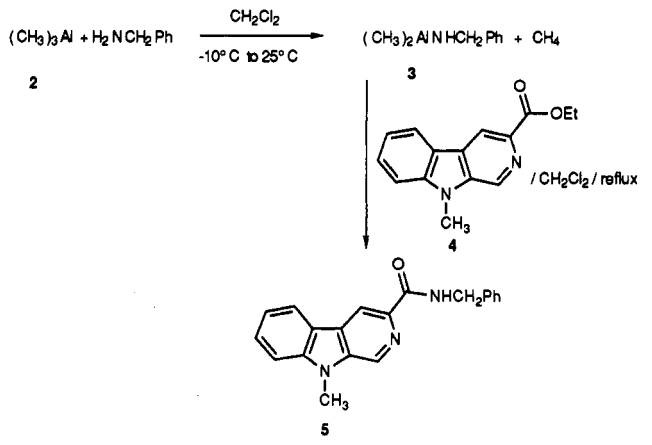
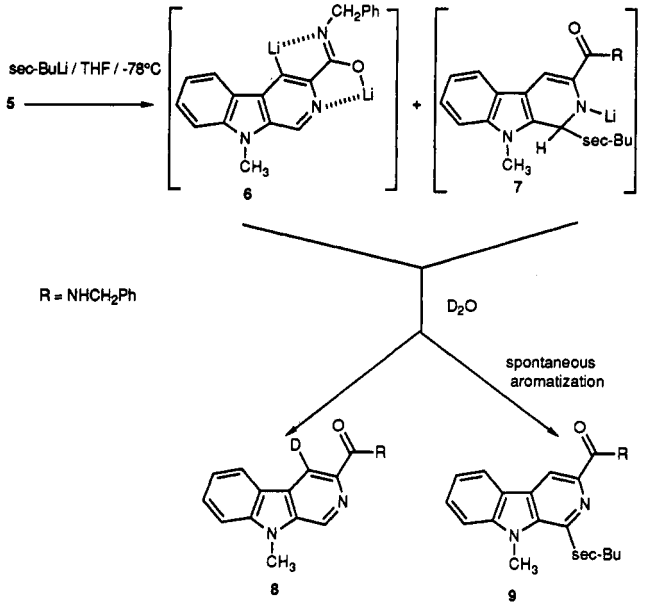
Scheme I



Scheme II



mass spectrum of starting material **5** with that of the reaction product (i.e., **5** + **8**). While the former showed a strong molecular ion peak at m/z = 315, the product displayed, in addition to the 315 peak, a larger peak at m/z = 316, corresponding to the monodeuterated species. The ratio of these two peaks was 75:25 in favor of the deuterated compound. Moreover, strong peaks at m/z = 183 (deuterated heterocycle) and 182 (nondeuterated heterocycle) indicated that deuteration had indeed occurred on the ring rather than on the side chain. Confirmation of both the extent and regioselectivity of deuteration at C-4 was obtained by NMR.[17] A second product, **9** (18%), was also formed by treatment of **5** with *sec*-butyllithium. This compound results from competitive nucleophilic addition of the metalating agent to the C-1 position of the β-carboline (to give intermediate **7**) followed by spontaneous aromatization of the dihydro derivative formed after quenching.[9]

Although the above experiment demonstrated that C-4-directed ortho-metalation of 3-carboxy-β-carbolines was possible, complex mixtures of products were obtained when electrophiles other than D_2O (i.e., anisaldehyde, alkyl halides) were used. While other lithiated bases such as *n*-butyllithium, *tert*-butyllithium, or lithium diisopropylamide (with or without addition of TMEDA[18]) also gave disappointingly low yields of C-4 alkylation products in the presence of various electrophiles,[19] metalation of **5** using methyllithium was much more satisfactory.[10a] Thus, reaction of **5** with methyllithium for 2 h at −78 °C and then 20 min at 0 °C followed by addition of anisaldehyde gave 91% of the C-4 substituted compound **10** (Scheme III) with no traces of side products. Alcohol **10** was easily cyclized[8b] to the lactone **11** using 5% sulfuric acid in acetonitrile or by passage through a silica gel column. This further substantiates that electrophilic attack occurred at the C-4 position of the β-carboline.

The use of benzophenone as electrophile gave lactone **13** in 65% yield after chromatography on silica. In this case, none of the noncyclized precursor **12** could be isolated or detected by TLC. The steric bulk of the benzophenone electrophile may contribute to the somewhat lower yield obtained in this reaction as compared to when anisaldehyde was used.

Similarly, sequential treatment of **5** with methyllithium and DMF gave the cyclized derivative **15** as sole product in 93% yield. The structure of **15** was confirmed by a

(17) The ^1H NMR spectrum of starting β-carboline carboxamide **5** showed two clearly separated singlets at δ 8.64 and 8.92 ppm, each integrating for one proton. These singlets, corresponding to H-1 and H-4, were unambiguously attributed by 1D NOE difference NMR spectroscopy. Thus, irradiation of the NCH_3 resonance at δ 3.89 had an NOE effect on the proton at δ 8.64 but not on that at δ 8.92. H-1, in closer proximity to the NCH_3 group than H-4, can be assigned the δ 8.64 resonance while H-4 must resonate at δ 8.92. Further substantiation of this attribution was obtained by a phase-corrected NOESY experiment which showed an NOE cross peak between NCH_3 at δ 3.89 and the proton at δ 8.64. Furthermore, a long-range coupling experiment (^1H–^{13}C) indicated a cross peak between the carbonyl of the side chain at C-3 and the proton at δ 8.92 proving conclusively that the latter resonance belongs to H-4. Since the ^1H NMR spectrum of the metalation/deuteration product mixture (**5** + **8**) showed that the intensity of the peak at δ 8.92 ppm had diminished by ~75% compared to the singlet at δ 8.64, it can be concluded that ortho-directed metalation did occur exclusively at the C-4 position, as expected. The ratio of **5** to **8**, as determined by NMR, is thus essentially the same as that determined by mass spectrometry (i.e., 25:75). Since the mixture **5** + **8** comprised 60% of the total product that was isolated from this reaction sequence, the overall extent of lithiation was 45%.

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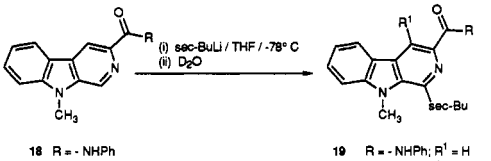
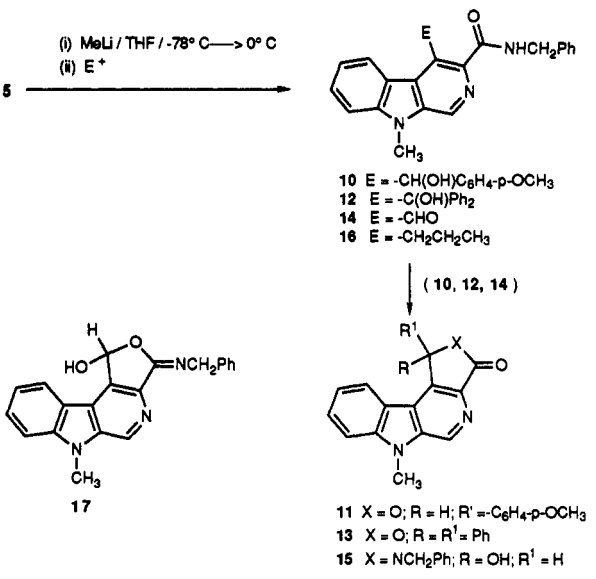
(19) The use of other carboxamides as ortho-directing group was also investigated. Thus, when the anilide **18** was treated sequentially with *sec*-butyllithium and with D_2O, only products arising from nucleophilic addition of the *sec*-butyl group to C-1 of the β-carboline could be isolated. These products included inseparable mixtures of compounds **19** and **20** as well as their unstable dihydro derivatives. The anilide group thus tends to favor C-1 addition to the detriment of C-4 substitution. The diisopropylamide derivative **21** also gave only C-1 addition product **22** under these conditions with this time no evidence of anion formation at C-4. In order to rationalize these observations, the frontier orbital energies of the three β-carboline carboxamides used (i.e., **5**, **18**, and **21**) were calculated using Mopac (version 6.00, MNDO parameters), and their LUMO energies were compared. A correlation was found between the LUMO energies of each compound and the extent of nucleophilic addition of the metalating agent to C-1 (as opposed to proton abstraction at C-4). Thus, the lower the energy of the LUMO of the starting β-carboline, the higher the percentage of product arising from C-1 addition of *sec*-butyllithium (**18**, LUMO = −0.42 eV, 50% nucleophilic addition; **21**, −0.37 eV, 23% addition; **5**, −0.33 eV, 20% addition). Moreover, the LUMO energies of all the β-carboline derivatives were substantially lower than those of the similarly substituted pyridine derivatives (e.g., −0.15 eV for *N*-benzyl-2-pyridinecarboxamide and −0.13 eV for *N*,*N*-diisopropyl-2-pyridinecarboxamide) for which nucleophilic addition of the lithiated base has been shown to be minimal.[18] Details of this work will be given in a forthcoming publication.



18 R = -NHPh
21 R = -N(CH(CH3)2)2

19 R = -NHPh; R1 = H
20 R = -NHPh; R1 = D
22 R = -N(CH(CH3)2)2; R1 = H

Scheme III



^{1}H–^{1}H COSY experiment which showed a correlation between the two doublets arising from the nonequivalent benzylic protons. Moreover, these protons correlated with the benzylic carbon atom, as indicated by a ^{1}H–^{13}C COSY experiment. An alternative structure (17) in which the oxygen atom of the C-3 carbonyl group of precursor 14 attacks the C-4 aldehyde function was also compatible with these NMR results but was rejected on the basis of both the infrared and ^{13}C-NMR spectra which indicated the presence of a carbonyl group in this compound.

Finally, the anion of 5 generated by methyllithium reacted cleanly with an alkyl halide such as propyl iodide to give 16, the spectral characteristics of which were completely compatible with C-4 alkylation.

In conclusion, the combination of methyllithium as base and 3-*N*-benzylcarboxamide as ortho-directing metalation group allows efficient substitution of 3-carboxy-β-carbolines at the pharmacologically important C-4 position by a variety of electrophiles on a preparative scale. The great superiority of methyllithium over other lithiated bases in this reaction is not altogether clear but may be due to the small size of this reagent which permits more efficient coordination at the sterically encumbered C-4 position of β-carboline 5.[9] Moreover, the fact that methyllithium does not promote competitive side reactions allows β-carboline anion formation at C-4, an apparently slow process, to proceed over several hours, thereby assuring complete conversion. This methodology represents a major improvement over the multistep procedures which have been used until now for the preparation of C-4-substituted β-carbolines and should, moreover, allow easy access to a large number of novel analogues. The use of other electrophiles together with the incorporation of a more easily removed blocking group at N-9[12] are presently under study.

Experimental Section

General Procedures. All melting points were determined in open capillary tubes and are uncorrected. Nuclear magnetic resonance spectra were recorded with a Bruker WP 200-MHz, Bruker WP 250-MHz, or AM 300-MHz spectrometer using $CDCl_3$ as a solvent. Integrations used to report deuterium incorporation were accurate to ±0.03 proton, judging from the accuracy obtained from the integration of protons in pure compound. Chemical shifts are reported in parts per million downfield from internal tetramethylsilane; coupling constants are given in hertz. Electron impact and chemical ionization mass spectra were recorded on an AEI MS-50 and an AEI MS-9 spectrometer, respectively. FAB spectra were recorded on a Kratos MS 80RF instrument. Thin-layer chromatography was performed on Merck silica gel 60 plates with fluorescent indicator. The plates were visualized with UV light (254 nm). All column chromatography was conducted on Merck 60 silica gel (230–400 mesh) at medium pressure (200 mbar). Elemental analyses were performed at the ICSN/CNRS, Gif-sur-Yvette. IR spectra of samples were obtained with a Nicolet 205 FT-IR spectrometer either as KBr pellets or as neat films. THF was dried by distillation under nitrogen from sodium/benzophenone ketyl radical. Commercial *sec*-butyllithium solution in cyclohexane–hexane (Janssen Chimica) and methyllithium in diethyl ether (Aldrich Chemical Co.) were titrated using the Watson–Eastham procedure[20] before use. The alkyllithium solutions were stored at −10 °C in a serum-capped bottle inside a plastic bag containing Drierite. Benzylamine was dried over KOH pellets for 24 h and then distilled. Trimethylaluminum and D_2O (spectroscopic grade, 99.96% pure) were purchased from Aldrich Chemical Co. and were used without further purification. The remaining electrophiles were obtained commercially and were purified before use: Anisaldehyde was washed with aqueous $NaHCO_3$ solution and water, dried over Na_2SO_4 and distilled under reduced pressure; benzophenone was recrystallized from ethyl acetate–heptane; propyl iodide was washed with aqueous Na_2SO_3 solution, dried over silica gel, and distilled under reduced pressure; DMF was dried over silica gel, distilled under reduced pressure, and stored over freshly activated 4-Å molecular sieves for 24 h before use.

Preparation of 9-*N*-Methyl-3-*N*-benzyl-β-carboline-3-carboxamide (5). To a solution of trimethylaluminum (2) (7.9 mL of a 2 M solution in hexane; 15.8 mmol) in anhydrous dichloromethane (100 mL) held under nitrogen at −10 °C was slowly added benzylamine (0.86 mL, 7.9 mmol). The cooling bath was removed 20 min after completion of the addition, and the reaction mixture (i.e., of 3) was allowed to come to room temperature over 45 min. A solution of ethyl 9-*N*-methyl-β-carboline-3-carboxylate (4)[11] (2.01 g, 7.9 mmol) in dichloromethane (20 mL) was then added to the reaction mixture, and the latter was refluxed for 9 h. The solution was cooled to room temperature, and aqueous HCl (0.67 M) was added cautiously until a solid began to precipitate. The mixture was allowed to stir for 30 min after which the solid was collected by filtration and crystallized from ethyl acetate–heptane to give β-carbolinecarboxamide 5 in 95% yield, mp 162 °C: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.89 (3H, s), 4.73 (2H, d, J = 6.0 Hz), 7.32 (7H, m), 7.58 (1H, t, J = 8 Hz), 8.17 (1H, d, J = 8 Hz), 8.47 (1H, bs, exchangeable with D_2O), 8.64 (1H, s), 8.92 (1H, s); IR (KBr) 1628, 1662, 2937 cm^{-1}; EIMS m/z 315 (M^+), 272 ($M - NH=CO)^+$, 210 ($M - PhCH=NH)^+$, 182. Anal. Calcd for $C_{20}H_{17}N_3O_3 \cdot 0.5H_2O$: C, 74.07; H, 5.24; N, 12.96. Found: C, 73.37; H, 5.46; N, 12.67.

Deuteration of 5 Using *sec*-Butyllithium and D_2O. To a flame-dried, septum-capped, and nitrogen-flushed round-bottom flask was added β-carbolinecarboxamide 5, dissolved in anhydrous THF. A continuous flow of nitrogen was maintained over the stirred mixture which was cooled externally with a dry ice–acetone bath. When an internal temperature of −78 °C was attained, a 1.3 M solution of *sec*-butyllithium in cyclohexane–hexane (5 molar equiv) was added by syringe over a period of 10 min. The deep purple solution was allowed to stir for 15 min at −78 °C after which D_2O[16] (5 molar equiv) was added dropwise. The solution was then stirred for 2 h at −78 °C, the cooling bath was removed, and stirring was continued for 20 min before distilled water was added. The organic layer was separated from the aqueous layer, the latter was extracted with ethyl acetate, and the combined organic extracts were concentrated under vacuum. The residue was dissolved in ethyl acetate and washed with water. The organic phase was dried with magnesium sulfate, the solvents were removed under reduced pressure at 20 °C, and the resulting crude product was purified by flash chromatography on silica gel using ethyl acetate–heptane (2:3) as developer. Compounds 5 and 8 were first eluted together (60% yield). The ^{1}H NMR spectrum

(20) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

of the mixture was identical to that of pure **5**, except that the integration of the one proton singlet at δ 8.92 (H-4) had diminished by 75%:[17] EIMS *m/z* 316 (M^+ of **8**, 75), 315 (M^+ of **5**, 25), 273 (316 $NH{=}C{=}O^+$, 75), 272 (315 - $NH{=}C{=}O^+$, 25), 183 (316 - $PhCH_2NHCO)^+$, 182 (315 - $PhCH_2NHCO)^+$.

Further elution gave compound **9** as a colorless oil which crystallized on standing in the cold (18%), mp 125 °C: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.91 (3H, t, J = 7.5 Hz), 1.70 (3H, d, J = 7.5 Hz), 1.95 (2H, m), 2.22 (1H, m), 3.95 (3H, s), 4.70 (2H, d, J = 6.0 Hz), 7.29–7.44 (6H, m), 7.51 (1H, d, J = 8.0 Hz), 7.63 (1H, t, J = 8.0 Hz), 8.01 (1H, bs, exchangeable with D_2O), 8.40 (1H, d, J = 8.0 Hz), 8.64 (1H, s); IR (KBr) 1656, 1619, 1579 cm^{-1}; EIMS *m/z* 371 (M^+). Anal. Calcd for $C_{24}H_{25}N_3O{\cdot}0.7H_2O$: C, 75.05; H, 6.51; N, 10.94. Found: C, 74.99; H, 6.66; N, 10.67.

Metalation Using Methyllithium. General Procedure. To a flame-dried, septum-capped, and nitrogen-flushed round-bottom flask was added β-carbolinecarboxamide **5**, dissolved in anhydrous THF. A continuous flow of nitrogen was maintained over the stirred mixture which was cooled externally with a dry ice–acetone bath. When an internal temperature of −78 °C was attained (20 min), a 1.6 M solution of methyllithium in diethyl ether (5 molar equiv) was added by syringe over a period of 10 min. The reaction mixture developed a pale blue color 5–10 min after complete addition of methyllithium. The solution was stirred for 2 h at −78 °C, and the cooling bath was then replaced by an ice–water bath. After 20 min, during which time the solution had become dark blue, the electrophile (5 molar equiv) was added dropwise over a period of 7–10 min, and the reaction mixture was stirred at 20 °C until the blue color had completely disappeared (10 min–4 h). The solution was then cooled to 0 °C, and distilled water was slowly added such that the internal temperature of the reaction mixture never exceeded 5 °C. The solution was concentrated to half volume under reduced pressure, excess chloroform was added, and the mixture was washed with water (2×), the organic phase was dried (Na_2SO_4), and the solvents were removed *in vacuo* (20 Torr/20 °C). The residue was purified as described below for each electrophile.

Electrophiles. (a) Anisaldehyde. Compound **10** (91%) was obtained by crystallization of the crude reaction product from ethyl acetate–heptane, mp 169–170 °C (ethyl acetate–heptane): IR (KBr) 1615, 1641, 2937, 3369 cm^{-1}; FAB(+ve)MS *m/z* 452; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.76 (3H, s), 4.02 (3H, s), 4.60 (2H, d, J = 6.0 Hz), 6.79 (2H, d, J = 8.0 Hz), 7.15 (1H, d merged with a m), 7.23 (7H, m), 7.61 (3H, t merged with a d, J = 8.0 Hz), 8.02 (1H, d, J = 10.0 Hz, exchangeable with D_2O), 8.18 (1H, d, J = 8.0 Hz), 8.75 (2H, bm merged with s, m exchangeable with D_2O). Anal. Calcd for $C_{28}H_{25}N_3O_3{\cdot}0.5H_2O$: C, 73.04; H, 5.43; N, 9.13. Found: C, 72.86; H, 5.58; N, 8.90.

Cyclization of Compound 10. A solution of the alcohol **10** (50 mg) in a 5% solution of sulfuric acid in acetonitrile (10 mL) was stirred overnight at room temperature. The reaction mixture was then extracted with ethyl acetate (3 × 10 mL), and the combined organic extracts were washed successively with saturated aqueous sodium hydrogen carbonate and water. The organic phase was dried over sodium sulfate, the solvents were removed *in vacuo*, and the residue was crystallized from ethyl acetate–heptane to give lactone **11** (33 mg, 88%), mp 233 °C (ethyl acetate–heptane): IR (KBr) 1771 cm^{-1}; EIMS *m/z* 344; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.78 (3H, s), 4.10 (3H, s), 6.87 (2H, d), 7.23 (4H, m), 7.59 (2H, d merged with t, J = 8.0 Hz), 8.72 (1H, s), 9.16 (1H, s). Anal. Calcd for $C_{21}H_{16}N_2O_3{\cdot}O.4H_2O$: C, 71.75; H, 4.65; N, 7.97. Found: C, 71.79; H, 4.94; N, 8.08.

(b) Benzophenone. The crude reaction mixture was purified by column chromatography on silica gel at atmospheric pressure using ethyl acetate–heptane (2:3) as developer to give lactone **13** in 65% yield after crystallization from methanol, mp > 310 °C: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 4.12 (3H, s), 7.09–7.35 (6H, m), 7.49 (5H, m), 7.55 (3H, m), 9.19 (1H, s); IR (KBr) 1763, 1645 cm^{-1}; EIMS *m/z* 390 (M^+). Anal. Calcd for $C_{26}H_{18}N_2O_2{\cdot}0.2\,H_2O$: 79.26; H, 4.67; N, 7.11. Found: C, 79.03; H, 4.80; N, 7.05.

(c) *N,N*-Dimethylformamide. Lactam **15** was obtained by crystallization of the crude reaction product from methanol (93% yield), mp 255–256 °C: ^{1}H NMR (DMSO-d_6, 250 MHz) δ 4.09 (3H, s), 4.52 (1H, d, J = 15 Hz), 5.03 (1H, d), 6.18 (1H, d, J = 9.5 Hz), 7.06 (1H, d, exchangeable with D_2O), 7.28-7.41 (6H, m), 7.70 (1H, dt, J = 7.0 and 1.0 Hz), 7.81 (1H, d, J = 8.0 Hz), 8.30 (1H, d), 9.20 (1H, s); ^{13}C NMR (DMSO-d_6, 300 MHz) δ 29.7, 42.4, 78.2, 110.4, 118. 7, 120.3, 122.4, 124.4, 127.1, 127.8, 128.5, 128.8, 132.6, 134.1, 137.7, 137.9, 139.0, 141.9, 165.9; IR (KBr) 3271, 1705, 1629, 1499 cm^{-1}; EIMS *m/z* 343 (M^+). Anal. Calcd for $C_{21}H_{17}N_3O_2{\cdot}0.5H_2O$: C, 73.47; H, 4.96; N, 12.24. Found: C, 73.27; H, 4.94; N, 12.21.

(d) Propyl Iodide. The crude reaction product, in which starting material **5** was the only contaminant, was purified by preparative-scale HPLC using a Novapak 6 μM C-18 reversed-phase column (25 × 100 mm) and methanol–water (85:15) as developer at a flow rate of 7 mL/min to give compound **16** in 68% yield, mp 151–152 °C: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.23 (3H, t, J = 5.0 Hz), 1.91 (2H, m), 3.85 (2H, dd, J = 8.0 Hz and 5.0 Hz), 3.97 (3H, s), 4.71 (2H, d, J = 6.0 Hz), 7.29–7.44 (6H, m), 7.51 (1H, d, J = 8.0 Hz), 8.27 (1H, d), 8.63 (2H, s merged with D_2O exchangeable m of NH); IR (film) 1624, 1666 cm^{-1}; HREIMS 357.1862 (calcd for $C_{23}H_{23}N_3O$ 357.1841).

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