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Efficient and Practical One-Pot Conversions of *N*-Tosyltetrahydroisoquinolines into Isoquinolines and of *N*-Tosyltetrahydro-β-carbolines into β-Carbolines through Tandem β-Elimination and Aromatization

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An efficient, practical, and general method for conversions of *N*-tosyltetrahydroisoquinolines (*N*-tosyl-THIQs) into isoquinolines and of *N*-tosyltetrahydro-β-carbolines (*N*-tosyl-THBCs) into β-carbolines is described. Treatment of *N*-tosyl-THIQs or *N*-tosyl-THBCs with base in dimethyl sulfoxide afforded dihydroisoquinolines or dihydro-β-carbolines as intermediates, and these were then oxidized in situ by molecular oxygen to furnish isoquinolines or β-carbolines in good to high yields. Both one-pot conversions occurred through tandem β-elimination and aromatization.

Introduction

Isoquinoline and β-carboline backbones are ubiquitous in numerous alkaloids.[1,2] Both natural and artificial isoquinolines and β-carbolines are of considerable value in medicinal chemistry and organic chemistry, having been seen to exhibit a variety of biological activities[3,4] and having also been used as versatile synthetic intermediates.[5]

Syntheses of isoquinolines and β-carbolines are very important and have therefore attracted much attention from chemists.[6,7] Because tetrahydroisoquinolines (THIQs) and tetrahydro-β-carbolines (THBCs) can readily be obtained through Pictet–Spengler reactions[8] between 2-aryl (or 2-indolyl) ethylamines and aldehydes, the aromatization of THIQs and THBCs through dehydrogenation/oxidation might therefore provide a good approach to isoquinolines and β-carbolines. Unfortunately, strong oxidants,[9] poisonous reagents,[10] and noble metal catalysts[11] are usually needed during the conversions of THIQs into isoquinolines and of THBCs into β-carbolines. We wish to report here a modified and practical method for the above conversions, in which *N*-tosyl-THIQs[12] and *N*-tosyl-THBCs were used as starting compounds instead of THIQs and THBCs.

Results and Discussion

The *N*-tosyl-THIQs **1** (Table 1) were directly obtained through *N*-sulfonyl Pictet–Spengler reactions[13] between *N*-(2-arylethyl)-*p*-toluenesulfonamides and aldehydes. The *N*-tosyl-THBCs of type **2** (Table 2, below) were obtained in a two-step fashion: Pictet–Spengler reactions between tryptamine hydrochloride or tryptophan ester hydrochloride and aldehydes[14] first gave THBCs, which were then transformed into *N*-tosyl-THBCs in excellent yields on exposure to *p*-toluenesulfonyl chloride in the presence of excess potassium carbonate powder and catalytic amounts of pyridine. With the *N*-tosyl-THIQs **1a**–**1x** and the *N*-tosyl-THBCs **2a**–**2u** to hand, we then attempted the conversions of the *N*-tosyl-THIQs into isoquinolines and of the *N*-tosyl-THBCs into β-carbolines under various sets of conditions. The results are summarized in Tables 1 and 2, below, respectively.

As can be seen in Table 1, which shows results for the treatment of the 24 *N*-tosyl-THIQs **1a**–**1x**, with different substituent patterns, with bases in dimethyl sulfoxide (DMSO), the corresponding isoquinolines **3a**–**3x** were obtained in 70–97% yields. DMSO was found to be the best solvent for the conversion of *N*-tosyl-THIQs into isoquinolines; other solvents such as acetonitrile, propanol, butanol, octanol, 1,2-dimethoxyethane, *N*,*N*-dimethylformamide, and 1,4-dioxane were also tested, but the reactions in all these solvents were much slower and gave isoquinolines only in poor or moderate yields. The patterns of the R^3 and R^4 groups had a significant impact on the reactions: in the case of R^4 = H, if R^3 was an aryl or alkyl group or a hydrogen atom, the reactions were best performed at 125 °C with NaOH as a base (Table 1, Entries 1–16), whereas if one out of R^3 and R^4 was an electron-deficient group (COOMe or COOEt), or both of them were electron-deficient groups (COOMe), the reactions could be performed at 75 °C, and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was necessary to prevent hydrolysis of ester groups (Table 1, Entries 17–24).

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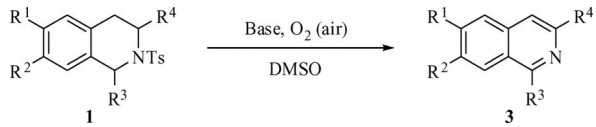
Table 1. Conversion of *N*-tosyl-THIQs into isoquinolines in DMSO under various sets of conditions.

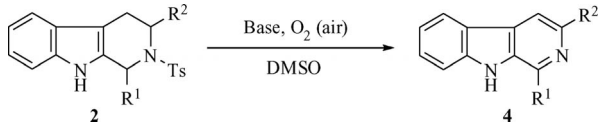


1 3

Entry	R^1	R^2	R^3	R^4	1	Base [equiv.]	*T* [°C]	*t* [h]	3	Yield [%][a]
1	H	H	Ph	H	**1a**	NaOH (3)	125	2	**3a**	92
2	H	H	4-$MeOC_6H_4$	H	**1b**	NaOH (3)	125	3	**3b**	83
3	H	H	4-ClC_6H_4	H	**1c**	NaOH (2)	125	1	**3c**	85
4	H	MeO	Ph	H	**1d**	NaOH (3)	125	2	**3d**	87
5	H	MeO	4-$MeOC_6H_4$	H	**1e**	NaOH (3)	125	2	**3e**	91
6	H	MeO	2-ClC_6H_4	H	**1f**	NaOH (2)	125	1	**3f**	86
7	MeO	MeO	Ph	H	**1g**	NaOH (3)	125	2	**3g**	92
8	MeO	MeO	3,4-$(MeO)_2C_6H_3$	H	**1h**	NaOH (3)	125	3	**3h**	82
9	MeO	MeO	3,4-$(OCH_2O)C_6H_3$	H	**1i**	NaOH (3)	125	3	**3i**	85
10	H	H	3,4-$(MeO)_2C_6H_3$	H	**1j**	NaOH (3)	125	2	**3j**	97
11	H	H	2-$EtOC_6H_4$	H	**1k**	NaOH (3)	125	3	**3k**	82
12	MeO	MeO	4-$MeOC_6H_4$	H	**1l**	NaOH (3)	125	3	**3l**	85
13	MeO	MeO	2-$EtOC_6H_4$	H	**1m**	NaOH (3)	125	3	**3m**	81
14	MeO	MeO	H	H	**1n**	NaOH (3)	125	6	**3n**	73
15	MeO	MeO	Me	H	**1o**	NaOH (3)	125	7	**3o**	72
16	MeO	MeO	*n*-hexyl	H	**1p**	NaOH (3)	125	6	**3p**	70
17	MeO	MeO	H	COOMe	**1q**	DBU[b] (3)	75	3	**3q**	83
18	MeO	MeO	Ph	COOMe	**1r**	DBU (3)	75	2	**3r**	86
19	MeO	MeO	4-$MeOC_6H_4$	COOMe	**1s**	DBU (3)	75	3	**3s**	92
20	MeO	MeO	3,4-$(MeO)_2C_6H_3$	COOMe	**1t**	DBU (3)	75	2	**3t**	91
21	H	H	COOMe	COOMe	**1u**	DBU (3)	75	1	**3u**	90
22	H	H	H	COOEt	**1v**	DBU (3)	75	5	**3v**	85
23	H	H	COOMe	H	**1w**	DBU (3)	75	2	**3w**	93
24	H	MeO	COOMe	H	**1x**	DBU (3)	75	2	**3x**	91

[a] Isolated yield. [b] 1,8-Diazabicyclo[5.4.0]undec-7-ene.

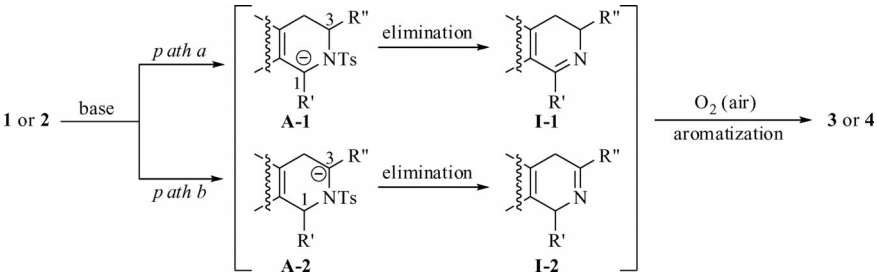
Table 2. Conversion of *N*-tosyl-THBCs into β-carbolines in DMSO under various sets of conditions.



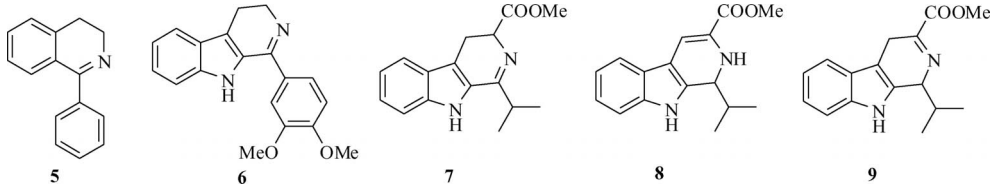
2 4

Entry	R^1	R^2	2	Base [equiv.]	*T* [°C]	*t* [h]	4	Yield [%][a]
1	3,4-$(MeO)_2C_6H_3$	H	**2a**	NaOH (3)	125	5	**4a**	89
2	3,4-$(OCH_2O)C_6H_3$	H	**2b**	NaOH (3)	125	4	**4b**	86
3	4-$MeOC_6H_4$	H	**2c**	NaOH (3)	125	5	**4c**	96
4	4-$EtOC_6H_4$	H	**2d**	NaOH (3)	125	3	**4d**	90
5	2-$MeOC_6H_4$	H	**2e**	NaOH (3)	125	4	**4e**	95
6	2-$EtOC_6H_4$	H	**2f**	NaOH (3)	125	5	**4f**	93
7	Ph	H	**2g**	NaOH (3)	125	4	**4g**	95
8	*i*Pr	H	**2h**	NaOH (3)	125	5	**4h**	85
9	Et	H	**2i**	NaOH (3)	125	5	**4i**	83
10	Me	H	**2j**	NaOH (3)	125	5	**4j**	82
11	3,4-$(MeO)_2C_6H_3$	COOEt	**2k**	DBU[b] (3)	20	4	**4k**	91
12	3,4-$(MeO)_2C_6H_3$	COOMe	**2l**	DBU (3)	20	4	**4l**	85
13	3,4-$(OCH_2O)C_6H_3$	COOEt	**2m**	DBU (3)	20	5	**4m**	86
14	3,4-$(OCH_2O)C_6H_3$	COOMe	**2n**	DBU (3)	20	5	**4n**	92
15	4-$MeOC_6H_4$	COOEt	**2o**	DBU (3)	20	4	**4o**	87
16	4-$MeOC_6H_4$	COOMe	**2p**	DBU (3)	20	4	**4p**	94
17	Ph	COOMe	**2q**	DBU (3)	20	3	**4q**	89
18	2-ClC_6H_4	COOMe	**2r**	DBU (3)	20	3	**4r**	88
19	*i*Pr	COOMe	**2s**	DBU (3)	20	4	**4s**	83
20	Et	COOEt	**2t**	DBU (3)	20	5	**4t**	85
21	Me	COOMe	**2u**	DBU (3)	20	6	**4u**	82

[a] Isolated yield. [b] 1,8-Diazabicyclo[5.4.0]undec-7-ene.



Scheme 1. A plausible mechanism for the two one-pot conversions.



Scheme 2. Some dihydroisoquinoline and dihydro-β-carboline intermediates.

As can be seen in Table 2, which shows results for the treatment of the 21 *N*-tosyl-THBC derivatives **2a**–**2u** with bases in DMSO, the corresponding β-carbolines **4a**–**4u** were obtained in 82–96% yields. DMSO was also found to be the best solvent for the conversion of *N*-tosyl-THBCs into β-carbolines. The reaction conditions depended on the electronic nature of the R^2 group: if R^2 was a hydrogen atom the reactions were best performed at 125 °C with NaOH as a base (Table 2, Entries 1–10), whereas if R^2 was an electron-deficient group (COOMe or COOEt) the reactions could take place smoothly at room temperature with DBU as a base (Table 2, Entries 11–21). Other weak bases such as pyridine, 4-(dimethylamino)pyridine, potassium carbonate, and sodium carbonate were also tried, but only DBU gave β-carbolines in good to high yields.

A plausible mechanism for both one-pot conversions is shown in Scheme 1. The *N*-tosyl-THIQs **1** or *N*-tosyl-THBCs **2** would first react with a base to form the anions **A-1** or **A-2**, and these would then immediately undergo β-elimination[15] to afford the dihydro intermediates **I-1** or **I-2**. The dihydro intermediates **I-1** or **I-2** would then be oxidized in situ by molecular oxygen in air to furnish the final product isoquinolines **3** or β-carbolines **4**.[16] The reaction pathways would be governed by the acidities of the protons on C-1 and C-3: if the proton on C-1 was more acidic, path *a* would be followed, whereas if the proton on C-3 was more acidic, path *b* would be followed.

In order to verify this possible mechanism, we tried to isolate some intermediates (see also Scheme 2) of both one-pot conversions. When we stopped the conversion of compound **1a** into compound **3a** at a mid-point, we were able to isolate the 3,4-dihydroisoquinoline **5**. Similarly, the 3,4-dihydro-β-carboline **6** could be isolated during the conversion of compound **2a** into **4a**. However, when the conversion of compound **2s** into **4s** was stopped at the mid-point, the two intermediate compounds **7** and **8**, but little compound **9**, could be isolated. It was quite possible that compound **9** was unstable and rapidly changed into the more stable compound **8** through tautomerization.

Oxygen in air was necessary for the both of the above one-pot conversions: when the reactions were performed under argon the β-elimination took place smoothly, but the aromatization was sluggish. When compound **1a** was treated under argon with NaOH (3 equiv.) at 125 °C in DMSO for 2 h, for example, compounds **3a** and **5** were obtained in 9% and 83% yields, respectively.

Conclusions

In conclusion, a mild, practical, and highly efficient method for one-pot conversions of *N*-tosyl-THIQ derivatives into isoquinolines and of *N*-tosyl-THBCs into β-carbolines is described. Some advantages such as mild reaction conditions, good to high yields, ease of manipulation, cheapness of all reagents, and the use of air as a clean oxidant, as well as the wide scope of these reactions, might allow this method to be very useful, especially for large-scale preparations. Because the *N*-tosyl-THIQ and *N*-tosyl-THBC starting compounds are readily available from Pictet–Spengler reactions, the method described here should provide a good, practical, and general approach to 1-substituted or 1,3-disubstituted isoquinolines and β-carbolines.

Experimental Section

General Method: ^{1}H NMR and ^{13}C NMR spectra were acquired with a Bruker AM 500 instrument, chemical shifts are given on the δ scale as parts per million (ppm) with tetramethylsilane (TMS) as the internal standard. IR spectra were recorded with a Nicolet Magna IR-550 instrument. Mass spectra were recorded with a HP5989A instrument. Column chromatography was performed on silica gel (Qingdao Ocean Chemical Corp.). All chemicals were analytically pure.

Typical Procedure for the Preparation of the *N*-Tosyl-THIQ Derivatives 1

1-Phenyl-2-tosyl-1,2,3,4-tetrahydroisoquinoline (1a): Boron trifluoride–diethyl ether (10.64 g, 74.97 mmol) was added to a solution of *N*-(2-phenylethyl)-*p*-toluenesulfonamide (13.77 g, 50.01 mmol) and benzaldehyde (5.35 g, 50.41 mmol) in toluene (150 mL). The solution was then heated and stirred under N_2 at 60 °C for 8 h. After the solution had cooled down to room temperature, water (150 mL) was added. Two layers were separated, and the aqueous solution was extracted twice with toluene (2 × 50 mL). The extracts were combined and dried with anhydrous $MgSO_4$, and the solvent was removed by distillation under vacuum to give a crude solid that was recrystallized from ethanol/water (90:10) to afford compound **1a** (14.91 g, 41.02 mmol) as white crystals in 82% yield, m.p. 164–165 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, CH_3 in Ts), 2.53–2.57 (m, 1 H, 4-H), 2.62–2.69 (m, 1 H, 4-H), 3.73–3.77 (m, 2 H, 3-H), 6.22 (s, 1 H, 1-H), 6.97–6.98 (m, 2 H, Ar-H), 7.06 (d, J = 8.0 Hz, 2 H, 3,5-H in Ts), 7.09–7.13 (m, 2 H, Ar-H), 7.17–7.18 (m, 2 H, Ar-H), 7.21–7.25 (m, 3 H, Ar-H), 7.53 (d, J = 8.0 Hz, 2 H, 2,6-H in Ts) ppm. IR (KBr): $\tilde{\nu}$ = 2950, 1600, 1450, 1330, 1160, 1090, 820, 700, 670, 630 cm^{-1}. MS (EI): m/z (%) = 363 (46) $[M]^+$, 286 (100), 208 (41), 179 (13), 155 (12), 130 (6), 105 (3), 91 (22), 77 (3).

Typical Procedure for the Preparation of the *N*-Tosyl-THBC Derivatives 2

1-(3,4-Dimethoxyphenyl)-2-tosyl-1,2,3,4-tetrahydro-9*H*-pyrido[3,4-*b*]indole (2a): 3,4-Dimethoxybenzaldehyde (1.83 g, 11.01 mmol) was added to a solution of tryptamine hydrochloride (1.97 g, 10.02 mmol) in absolute ethanol (30 mL), and the mixture was then heated at reflux for 20 h under nitrogen. After the reaction was complete, the solution was then concentrated under reduced pressure. The residue was partitioned between ethyl acetate (50 mL) and an aqueous solution of potassium carbonate (10% w/v, 25 mL) and the organic phase was separated and washed twice with brine (2 × 10 mL). After having been dried with anhydrous $MgSO_4$, the organic solution was concentrated under vacuum to give 1-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-β-carboline as a crude solid, which was used for the next step without purification. A solution of the above crude solid and pyridine (0.24 g, 3.03 mmol) in dichloromethane (60 mL) was cooled to 0 °C with an ice-bath, powdered K_2CO_3 (4.15 g, 30.03 mmol) was added, and *p*-toluenesulfonyl chloride (2.01 g, 10.54 mmol) was then added in portions over 20 min. After the addition was complete, the ice-bath was removed, and the mixture was stirred at room temperature for 2 h. Water (25 mL) was added, and the mixture was transferred into a separating funnel. The organic phase was separated, and washed successively with aqueous HCl solution (2 N, 15 mL), water (10 mL), and brine (10 mL). After the organic solution had been dried with anhydrous $MgSO_4$, the solvent was removed under vacuum to give a crude solid that was rinsed with a mixed solvent of ethyl acetate and hexane (1:3) to afford compound **2a** (4.27 g, 9.23 mmol) as an off-white solid in 92% yield over two steps, m.p. 186–187 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.26 (s, 3 H, CH_3 in Ts), 2.48–2.67 (m, 2 H, 3-H), 3.23–3.34 (m, 1 H, 4-H), 3.71 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.98 (dd, J_1 = 14.4, J_2 = 5.3 Hz, 1 H, 4-H), 6.21 (s, 1 H, 1-H), 6.56 (d, J = 8.3 Hz, 1 H, Ar 6′-H), 6.64 (d, J = 8.3 Hz, 1 H, Ar 5′-H), 6.94 (s, 1 H, Ar 2′-H), 7.05 (d, J = 8.0 Hz, 2 H, 3,5-H in Ts), 7.07 (dd, J_1 = 7.7, J_2 = 7.6 Hz, 1 H, 6-H), 7.15 (dd, J_1 = 7.6, J_2 = 7.8 Hz, 1 H, 7-H), 7.28 (d, J = 7.8 Hz, 1 H, 8-H), 7.38 (d, J = 7.7 Hz, 1 H, 5-H), 7.54 (d, J = 8.0 Hz, 2 H, 2,6-H in Ts), 8.23 (s, 1 H, indole NH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.94, 148.91, 143.2, 138.0, 136.1, 131.9, 130.4, 129.3, 126.7, 126.5, 122.1, 120.8, 119.3, 118.2, 111.8, 111.0, 110.4, 109.5, 55.80 (OCH_3), 55.73 (OCH_3), 55.66 (C-1), 39.4 (C-3), 21.3 (C-4), 20.1 (CH_3 in Ts) ppm. IR (KBr): $\tilde{\nu}$ = 3373 (N–H), 2933, 1597, 1516, 1464, 1329, 1267, 1155, 1137, 1026, 980, 748, 671 cm^{-1}. MS (EI): m/z (%) = 462 (12) $[M]^+$, 306 (100), 275 (9), 248 (18), 217 (3), 204 (4), 170 (3), 144 (16). $C_{26}H_{26}N_2O_4S$ (462.56): calcd. C 67.51, H 5.67, N 6.06; found C 67.68, H 5.46, N 6.12.

Typical Procedure for the Conversion of the *N*-Tosyl-THIQ Derivatives 1 into Isoquinolines 3 with NaOH as Base

1-Phenylisoquinoline (3a): An aqueous solution of sodium hydroxide (30% w/w, 1.60 g, 12.00 mmol) was added to a solution of compound **1a** (1.46 g, 4.02 mmol) in DMSO (12 mL). The mixture was heated to around 125 °C, and then stirred at this temperature for 2 h. The reaction was monitored by TLC. After the reaction was complete, the mixture was allowed to cool to room temperature and diluted with water (60 mL). The aqueous solution was then extracted twice with ethyl acetate (2 × 40 mL). The extracts were combined and dried with anhydrous $MgSO_4$. Evaporation of the solvent gave a crude oil which was purified by flash chromatography (eluent: EtOAc/hexane 1:5) to furnish compound **3a** (0.76 g, 3.70 mmol) as a white solid in 92% yield, m.p. 93–94 °C (ref.[17] 93–94 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.58 (m, 4 H, Ar-H), 7.65 (d, J = 5.7 Hz, 1 H, 4-H), 7.67–7.73 (m, 3 H, Ar-H), 7.89 (d, J = 8.2 Hz, 1 H, 5-H), 8.11 (d, J = 8.5 Hz, 1 H, 8-H), 8.62 (d, J = 5.7 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 120.40, 127.17, 127.46, 127.65, 128.01, 128.84, 129.06, 130.42, 130.45, 137.31, 140.11, 142.73, 161.20 ppm. IR (KBr): $\tilde{\nu}$ = 3055, 1619, 1583, 1554, 1441, 1383, 1354, 825, 769, 701 cm^{-1}. MS (EI): m/z (%) = 205 (75) $[M]^+$, 204 (100), 176 (12), 151 (4), 102 (7), 88 (3), 77 (1), 75 (2).

Typical Procedure for the Conversion of the *N*-Tosyl-THIQ Derivatives 1 into Isoquinolines 3 with DBU as Base

Methyl 6,7-Dimethoxyisoquinoline-3-carboxylate (3q): DBU (1.84 g, 12.09 mmol) was added to a solution of compound **1q** (1.62 g, 4.00 mmol) in DMSO (12 mL). The solution was warmed to around 75 °C and was then stirred at this temperature for 3 h. The reaction was monitored by TLC. After the reaction was complete, the mixture was allowed to cool to room temperature and diluted with water (60 mL). The aqueous solution was then extracted twice with ethyl acetate (2 × 40 mL). The extracts were combined and dried with anhydrous $MgSO_4$. Evaporation of the solvent gave a crude oil that was purified by flash chromatography (eluent: EtOAc/hexane 1:4) to furnish compound **3q** (0.82 g, 3.32 mmol) as a white solid in 83% yield, m.p. 210–211 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.05 (s, 3 H, OCH_3), 4.06 (s, 3 H, OCH_3), 4.07 (s, 3 H, OCH_3), 7.20 (s, 1 H, 5-H), 7.28 (s, 1 H, 8-H), 8.46 (s, 1 H, 1-H), 9.12 (s, 1 H, 4-H) ppm. IR (KBr): $\tilde{\nu}$ = 3014, 1710, 1616, 1514, 1437, 1287, 1255, 1156, 1005, 852, 604 cm^{-1}. HRMS: calcd. for $C_{13}H_{13}NO_4$: 247.0845; found 247.0841.

Typical Procedure for the Conversion of the *N*-Tosyl-THBCs 2 into the β-Carbolines 4 with NaOH as Base

Preparation of 1-(3,4-Dimethoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (4a): An aqueous solution of sodium hydroxide (30% w/w, 1.60 g, 12.00 mmol) was added to a solution of compound **2a** (1.84 g, 3.98 mmol) in DMSO (12 mL). The mixture was heated to around 125 °C and was then stirred at this temperature for 5 h. The reaction was monitored by TLC. After the reaction was complete, the mixture was allowed to cool to room temperature and diluted with water (60 mL). The precipitate was collected by suction and washed several times with water. The crude product was then purified by flash chromatography (eluent: EtOAc/dichloromethane 1:4) to fur-

nish compound **4a** (1.08 g, 3.55 mmol) as white solid in 89% yield, m.p. 106–107 °C (ref.[18] 104–105 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.98 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 7.06 (d, J = 8.1 Hz, 1 H, Ar 6′-H), 7.32 (dd, J_1 = 7.8, J_2 = 6.9 Hz, 1 H, 6-H), 7.48–7.59 (m, 4 H, 7-H, 8-H, Ar 2′-H and 5′-H), 7.93 (d, J = 5.3 Hz, 1 H, 4-H), 8.17 (d, J = 7.8 Hz, 1 H, 5-H), 8.55 (d, J = 5.3 Hz, 1 H, 3-H), 8.59 (s, 1 H, indole NH) ppm. IR (KBr): $\tilde{\nu}$ = 3363 (N–H), 2935, 1626, 1516, 1457, 1409, 1319, 1260, 1235, 1144, 1025, 747 cm^{-1}. MS (EI): *m*/*z* (%) = 304 (100) $[M]^+$, 289 (20), 273 (19), 258 (22), 245 (11), 217 (9), 230 (6), 152 (3), 133 (3), 115 (2).

Typical Procedure for the Conversion of the *N*-Tosyl-THBCs 2 into the β-Carbolines 4 with DBU as Base

Preparation of Ethyl 1-(3,4-Dimethoxyphenyl)-9*H*-pyrido[3,4-*b*]-indole-3-carboxylate (4k): DBU (1.37 g, 9.00 mmol) was added to a solution of compound **2k** (1.59 g, 2.97 mmol) in DMSO (12 mL). The solution was then stirred at room temperature for 4 h. The reaction was monitored by TLC. After the reaction was complete, the mixture was diluted with water (60 mL). The precipitate was collected by suction and washed several times with water. The crude product was then purified by flash chromatography (eluent: EtOAc/chloroform 1:4) to furnish compound **4k** (1.02 g, 2.71 mmol) as a white solid in 91% yield, m.p. 140–141 °C. ^{1}H NMR (500 MHz, $[D_6]$DMSO): δ = 1.38 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 3.88 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.40 (q, J = 7.1 Hz, 2 H, OCH_2CH_3), 7.20 (d, J = 8.6 Hz, 1 H, Ar 5′-H), 7.31 (dd, J_1 = 7.4, J_2 = 7.7 Hz, 1 H, 6-H), 7.50–7.62 (m, 3 H, 7-H, Ar 2′-H and 6′-H), 7.69 (d, J = 8.2 Hz, 1 H, 8-H), 8.40 (d, J = 7.7 Hz, 1 H, 5-H), 8.86 (s, 1 H, 4-H), 11.88 (s, 1 H, indole NH) ppm. ^{13}C NMR (125 MHz, $[D_6]$DMSO): δ = 165.6 (*C*OOEt), 149.7, 148.8, 142.3, 141.5, 136.8, 134.5, 130.3, 128.9, 128.5, 121.9, 121.3, 120.3, 116.1, 112.8, 112.1, 111.8, 60.6 (OCH_2CH_3), 55.7 (OCH_3), 55.5 (OCH_3), 14.4 (OCH_2CH_3) ppm. IR (KBr): $\tilde{\nu}$ = 3423 (N–H), 2937, 1709 (C=O), 1626, 1516, 1371, 1348, 1257, 1143, 1025, 746 cm^{-1}. MS (EI): *m*/*z* (%) = 376 (37) $[M]^+$, 304 (100), 289 (11), 273 (16), 259 (7), 243 (9), 229 (12), 216 (9), 188 (3), 137 (2). $C_{22}H_{20}N_2O_4$ (376.41): calcd. C 70.20, H 5.36, N 7.44; found C 70.14, H 5.22, N 7.52.

Supporting Information (see also the footnote on the first page of this article): Characterization data for compounds **3b**–**3p**, **3r**–**3x**, **4b**–**4j**, **4l**–**4u**, and **5**–**8**. ^{1}H NMR spectra of compounds **3a**–**3x**, **4a**–**4u**, and **5**–**8**. ^{13}C NMR spectra of compounds **3a**, **3g**, **3h**, **3i**, **3j**, **3o**, **3s**, **3t**, **3w**, **3x**, **4b**, **4d**, **4e**, **4f**, **4k**, **4m**, **4o**, **4p**, **4q**, **4s** and **7**.

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