Oxidative Transformation of Indole-3-acetonitrile Derivatives into the Corresponding Indole-3-carboxylic Acids

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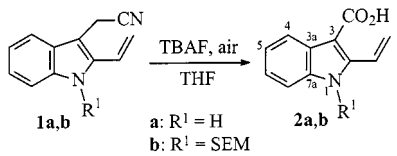
Indole-3-acetonitriles **1** were transformed into indole-3-carboxylic acids **2** and/or indole-3-carboxaldehydes **3**, when treated with tetrabutylammonium fluoride in the presence of traces of oxygen. This method constitutes a convenient preparation of indole-3-carboxylic acids **2**.

Protecting group manipulations have always represented an important section in synthetic organic chemistry. Because of our continuous interest in indole chemistry, for our work in this field we needed an efficient, non-electron-withdrawing nitrogen-protecting group that is easily removable. We first investigated the applicability of the 2-(trimethylsilyl)ethoxymethyl (SEM) group,[1] by which we protected the nitrogen of 2-vinylindole-3-yl acetonitrile (**1a**) to obtain **1b** in a nearly quantitative yield. First of all, we checked the reversibility of the reaction back to the starting unprotected indole **1a** by using tetrabutylammonium fluoride (TBAF), according to the literature procedure.[2] To our surprise, the addition of a 1 M solution of TBAF in tetrahydrofuran (THF) to **1b** directly gave indole-3-carboxylic acid **2b** without the cleavage of the SEM chain (Scheme 1). This serendipitous result gave a new direction to our investigations: since 3-cyanomethyl indoles can be readily prepared[3] through gramine chemistry from the corresponding indoles, this reaction could be considered as a carboxylation of the indole 3-position. In the literature only few indirect approaches exist for the synthesis of indole-3-carboxylic acids: Vilsmeier−Haack formylation followed by oxidation,[4] or substitution with chloroformates[5] with subsequent saponification. In order to widen the range of preparative procedures leading to indole-3-carboxylic acids, we aimed to explore the synthetic utility of the above oxidative transformation.



Scheme 1

[a] UPRES A CNRS 6013 "Isolement, Structure, Transformations et Synthèse de Produits Naturels" IFR 53 Biomolécules
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Therefore, we performed a detailed study of this reaction. It turned out that the nature of the substituent at N(1) had a dramatic role on the outcome of the reaction. When R^1 was an electron-donating group (**1b**, R^1 = SEM; **1c**, R^1 = Me; **1d**, R^1 = Bzl), the reaction was univocal and went to completion to afford the corresponding *N*-protected indolecarboxylic acids **2b**, **2c**, and **2d**, respectively. Without an *N*-protecting group (**1a**, R^1 = H), the reaction became sluggish, affording a mixture of **2a** and **3a**. When R^1 was an electron-withdrawing group (**1f**, $R^1 = CO_2Me$, **1g**, R^1 = Boc), a mixture of the urethane (**2g**, only for **1g**), the deprotected indolecarboxylic acid **2a**, and the deprotected indolecarboxaldehyde **3a** was obtained. The presence of a methoxy group on the indole ring (R^1 = Bzl, R^3 = MeO) did not notably affect the course of the reaction (Scheme 2, Table 1).

The reaction also worked when the starting material contained an ethyl group (instead of the vinyl) at position 2 of the indole moiety and was *N*-methylated (**1i**, R^1 = Me, R^2 = Et) to furnish **2i** in an excellent yield. However, for the *N*-unsubstituted derivative **1h** (R^1 = H, R^2 = Et) the same rection gave a complex reaction mixture, from which only **3h** could be isolated. In the case of indole-3-acetonitrile (**1j**, R^1 = H, R^2 = H) the rate of the reaction decreased remarkably: after 110 h only a very slight amount of the substrate was converted into aldehyde **3j** (Scheme 2, Table 1).

In order to increase the yield of indole-3-carboxylic acids **2**, we varied the excess of TBAF over the starting indole-3-acetonitriles **1**, and found that 7 to 11 equivalents of the reactant gave generally the highest yields of **2** (Table 1). It should be noted that a large excess of TBAF could be detrimental to the yield of **2** (entry 12 vs. 13). In some cases, we also observed that extractive workup prior to chromatography induced a loss of material, and better yields were obtained through direct column chromatography of the crude reaction mixture.

According to our experience, the solvent played an important role as well: the replacement of THF by CH_2Cl_2 (General Procedure D, see Experimental Section) either completely quenched the reaction (Table 1, entry 4), or seri-

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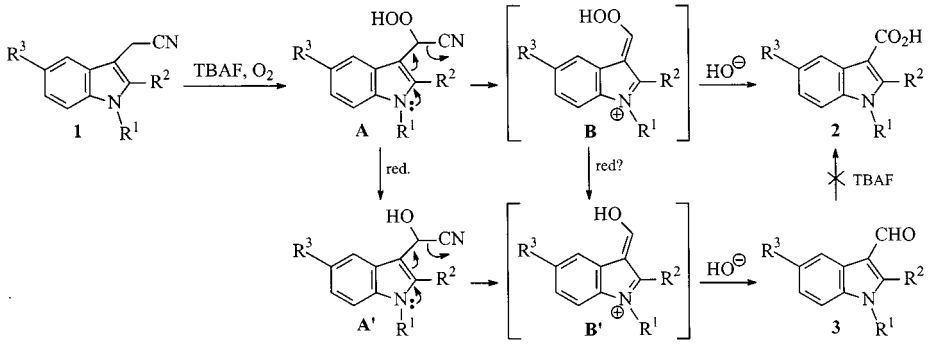


Scheme 2

Table 1. Reactions of indolylacetonitriles **1a**–**j** with tetrabutylammonium fluoride (TBAF)

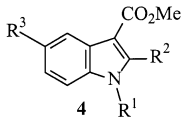
Entry	R^1	R^2	R^3	**1**	TBAF [equiv.]	Time [h]	General procedure[a]	Yield[d] [%] **2**	**3**	Other cmpds.
1	H	vinyl	H	**a**	10	110	A	21	16	
2	H	vinyl	H	**a**	10	19	B	48	13	
3	H	vinyl	H	**a**	11	149	C	63	32	
4	H	vinyl	H	**a**	10	312	D	traces	traces	
5	H	vinyl	H	**a**	5.5	24	A[b]	16	17	
6	H	vinyl	H	**a**	5.5	48	A[b]	17	32	
7	SEM	vinyl	H	**b**	17	48	A	85	0	
8	SEM	vinyl	H	**b**	11	3.2	A	92	0	
9	SEM	vinyl	H	**b**	11	22	C	81	0	
10	SEM	vinyl	H	**b**	11	52	D	35	0	
11	Me	vinyl	H	**c**	11	18	A	78	0	
12	Bzl	vinyl	H	**d**	33	14	A	39	0	
13	Bzl	vinyl	H	**d**	11	3.2	A	60	0	
14	Bzl	vinyl	MeO	**e**	11	6	A	47	0	
15	CO_2Me	vinyl	H	**f**	10.8	30	A	0	0	**2a** (9), **3a** (26)
16	Boc	vinyl	H	**g**	22.9	50	A	25	0	**2a** (24), **3a** (32)
17	H	Et	H	**h**	10.3	110	A	0	14	
18	Me	Et	H	**i**	22.5	45	A	96	0	
19	H	H	H	**j**	7.6	110	A	0	3	
20	H	H	H	**j**	7.6	110	A	0	16	
21	H	H	H	**j**	7.6	194	A[c]	0	6	**1j** (30)

[a] All reactions were carried out under N_2 atmosphere, except for entry 21, where O_2 atmosphere was used. – [b] Previously degassed TBAF solution. – [c] Under O_2 atmosphere. – [d] Isolated by column chromatography, without or with (entries 7, 11, 12, 15, 17, and 19) a previous extraction.

ously decreased the yield of **2** (entry 10). Since we thought that this difference might be attributed to the possible presence of peroxides in THF, which could be the cause of the oxidation, we first ensured the THF to be totally peroxide-free, then we degassed the solution cautiously. However, even under these conditions, the spontaneous transformation of **1b** into **2b** occurred, albeit at a considerably lower rate (entries 5 and 6). Moreover, the use of an oxygen atmosphere (entry 21), rather surprisingly, diminished the rate of the reaction as well as the yield of the products.

In certain cases, the addition of molecular sieves (4 Å) to the commercial solution of TBAF (General Procedure B, see Experimental Section) improved the yield of **2** (Table 1, entry 2 vs. 1). Since the quality of THF could also be incriminated, we prepared the reactant from commercial TBAF · 3 H_2O and freshly distilled, dry THF (General Procedure C, see Experimental Section), which gave us some success in increasing the yield of the products (entry 3 vs. 1 and 2).

Finally, most of the indole-3-carboxylic acids **2** obtained were converted into their methyl esters **4** by diazomethane, for characterization purposes.



The oxidative transformation observed is not a property of the indole nucleus: in our conditions, phenylacetonitrile was converted into benzoic acid (see Experimental Section). However, the cyano group is clearly involved in the reaction, as the methyl ester of indole-3-acetic acid (auxin) was unaffected by the treatment, with the exception of the hydrolysis of the ester function.

Thorough examination of the literature showed that the transformation of arylacetonitriles into arylcarboxylic acids was sometimes observed in variable extents during alkaline hydrolysis of the cyano group.[6] Extensive work by DiBiase

et al.[7] (*t*BuONa, O_2), Alvarez-Builla et al.[8] (P.T.C, $KMnO_4$), and Sugawara et al.[9] (anodic oxidation) showed that the process was an oxidative transformation and could be amenable to preparative yields only by the use of an oxidative source (O_2, electrolysis). Therefore, we submitted **1b** to DiBiase's conditions,[7] but it was completely destroyed within a few minutes. Clearly, our procedure is much milder and can be used in the case of indoles sensitive to oxidative conditions.

According to DiBiase et al.[7] the transformation of phenylacetonitrile into benzoic acid proceeds through an α-ketonitrile intermediate. In our experiments, however, we could never observe the formation of the corresponding α-ketonitrile species. It has also been claimed in the literature[9a] that phenylacetonitrile is first converted presumably into benzaldehyde, which would be further oxidized to give the acid. In our case, the mechanism might be similar, although according to us the aldehyde is not an intermediate in the formation of the acid. Indeed, two control experiments proved this assumption: the formyl derivatives **3a** (R^1 = H, R^2 = vinyl) and **3j** (R^1 = R^2 = H) were not at all transformed into acids **2a** and **2j**, respectively, under our conditions, even on bubbling oxygen through the solution.

In order to account for the observed differences in the results of the reactions, depending on the starting nitriles, we propose the following mechanism (Scheme 2). Oxidation of **1** by aerial oxygen in the presence of the highly basic fluoride anion[10] from TBAF would lead exclusively to hydroperoxide intermediate **A** and then elimination of cyanide anion with the assistance of indole nitrogen would afford intermediate **B**. The efficiency of the latter process depends on the electronic character (donor or acceptor) of the R^1 and R^2 substituents, the presence of an electron-donor group being more favorable for the formation of **B**. Intermediate **B** could then be further transformed, depending on R^1. When R^1 is different from H, hydroxide addition to the highly electrophilic vinylogous iminium ion **B** followed by deprotonation and hydroxide elimination would furnish carboxylic acid **2**. When, however, R^1 = H, **B** could be deprotonated, giving rise to the appearance of a less electrophilic enimine system. As we stated above, the formation of **B** from **A** is controlled by the R^1 group. When R^1 is an electron-withdrawing substituent, cyanide elimination would be less efficient; consequently, variable amounts of **A** could be reduced into **A′**, yielding aldehyde **3** via **B′** (Scheme 2).

In conclusion, due to the ready availability of the starting indole-3-acetonitriles **1**, their oxidative transformation into indole-3-carboxylic acids **2** by treatment with tetrabutylammonium fluoride in the presence of traces of oxygen represents a convenient procedure for the preparation of the latter. Moreover, this method offers a more advantageous synthetic alternative towards indole-3-carboxylic acids than the Fischer indole synthesis.[11]

Experimental Section

General Remarks: Melting points were determined on a Reichert Thermovar hot-stage apparatus and are uncorrected. − IR (film) spectra were measured with a Bomem FTIR instrument. − UV spectra were obtained with a UNICAM 8700 UV/VIS spectrophotometer in MeOH. − ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) spectra were acquired on a Bruker AC 300 spectrometer in $CDCl_3$, with TMS as internal standard. − Mass spectra were recorded with a VG Autospec apparatus. − All solvents were purified by following standard literature methods. Tetrabutylammonium fluoride (TBAF) as 1 M solution in THF and TBAF · 3 H_2O were purchased from ACROS. − Chromatography was performed on silica gel 60 (Merck) with CH_2Cl_2 and CH_2Cl_2/MeOH as eluents. Reactions were monitored on Merck TLC aluminium sheets (Kieselgel $60F_{254}$).

General Procedures for the Preparation of Compounds 2 and 3. − General Procedure A (GPA): The commercial solution of 1 M TBAF in THF was added to indolylacetonitrile **1** at room temperature. The mixture, which immediately became brown, was stirred at room temperature under nitrogen atmosphere. The reaction was stopped when TLC monitoring showed no further conversion of the starting material **1**. Two workups of the reaction mixture were used: extraction, followed by column chromatography, or direct column chromatography. When the reaction mixture was extracted to remove the excess TBAF, it was first diluted with diethyl ether and then washed with a 10% HCl solution. To the aqueous layer was added cautiously a 5% $NaHCO_3$ solution to adjust the pH to 5−6, which was then washed several times with diethyl ether. The combined organic layers (from the two successive extractions) were dried with anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was then purified by column chromatography on silica gel (eluents: CH_2Cl_2 and CH_2Cl_2/CH_3OH). When the extraction was not applied, the crude reaction mixture was purified twice by column chromatography on silica gel (eluents: CH_2Cl_2 and CH_2Cl_2/CH_3OH).

General Procedure B (GPB): To the mixture of indolylacetonitrile **1** and molecular sieves (4 Å) was added at room temperature the commercial solution of 1 M TBAF in THF. The mixture, which immediately became dark brown, was stirred under nitrogen atmosphere at room temperature until TLC monitoring showed no further conversion of the starting material **1**. Then the crude reaction mixture was purified twice by column chromatography on silica gel (eluents: CH_2Cl_2 and CH_2Cl_2/CH_3OH).

General Procedure C (GPC): To a stirred solution of indolylacetonitrile **1** in distilled THF was added the appropriate amount of commercial solid TBAF · 3 H_2O at room temperature to form a 1 M solution of TBAF. The mixture was stirred at room temperature under nitrogen atmosphere, while it became progressively dark brown. The stirring was continued until no further conversion of the starting material **1** was observed (TLC). The crude reaction mixture was then purified twice by column chromatography on silica gel (eluents: CH_2Cl_2 and CH_2Cl_2/CH_3OH).

General Procedure D (GPD): To a stirred solution of indolylacetonitrile **1** in distilled CH_2Cl_2 was added the appropriate amount of commercial solid TBAF · 3 H_2O at room temperature to obtain a 1 M solution of TBAF. The mixture, which became progressively dark brown, was stirred at room temperature under nitrogen atmosphere until TLC monitoring showed no further conversion of the starting material **1**. Then the crude reaction mixture was purified by column chromatography on silica gel (eluents: CH_2Cl_2 and CH_2Cl_2/CH_3OH).

2-Vinylindole-3-carboxylic Acid (2a) and 2-Vinylindole-3-carboxaldehyde (3a): From **1a**, according to GPA: 5 mL (5 mmol) of 1 M TBAF solution in THF, 90 mg (0.50 mmol) of **1a**, stirred for 110 h. The crude reaction mixture was purified twice by column chroma-

tography to furnish 14 mg (16%) of **3a** as an orange solid (eluent: CH_2Cl_2) and **2a** as a brown solid (eluent: CH_2Cl_2/CH_3OH, 97:3). − M.p. of **3a**: 194−196 °C (ref.[12] m.p. 206 °C). − Yield of **2a**: 19 mg (21%). − M.p. 107−109 °C. − IR (film): $\tilde{\nu}$ = 3308 cm^{-1}, 2926, 1653 (s, CO), 1647, 1456 (s), 1211, 743. − UV: λ_{max} = 220 nm, 244, 310. − ^1H NMR ($CDCl_3$): δ = 5.52 [br d, *J* = 11.4 Hz, 1 H, CH=C*H*$_2$, (*Z*) to CH=], 5.76 [br d, *J* = 18.1 Hz, 1 H, CH=C*H*$_2$, (*E*) to CH=], 7.15−7.30 (m, 2 H, 5-H, 6-H), 7.32 (m, 1 H, 7-H), 7.70 (dd, *J* = 11.4, 18.1 Hz, 1 H, C*H*=CH$_2$), 8.25 (m, 1 H, 4-H), 8.95 (s, 1 H, NH). − ^{13}C NMR ($CDCl_3$): δ = 104.8 (C-3), 110.8 (C-7), 117.2 (CH=*C*H$_2$), 122.2, 122.3, 124.0, 126.8 (*C*H=CH$_2$), 127.0 (C-3a), 135.3 (C-7a), 142.2 (C-2), 171.0 (CO_2H). − $C_{11}H_9NO_2$. − MS (EI): *m*/*z* (%) = 187 (100) [M^+], 170 (57), 142 (100). − HRMS: calcd. 187.063329; found 187.063980. − From **1a**, according to GPB: 5 mL (5 mmol) of 1 M TBAF solution in THF, 90 mg (0.50 mmol) of **1a**, and 5 pellets of molecular sieves (4 Å), stirred for 19 h. The crude reaction mixture was purified twice by column chromatography to obtain 11 mg (13%) of **3a** (eluent: CH_2Cl_2) and 44 mg (48%) of **2a** (eluent: CH_2Cl_2/CH_3OH, 97:3). − From **1a**, according to GPC: 2.86 g (9.06 mmol) of TBAF · 3 H_2O, a solution of 150 mg (0.82 mmol) of **1a** in 9.1 mL of distilled THF, stirred for 149 h. The reaction mixture was purified twice by column chromatography to afford 45 mg (32%) of **3a** (eluent: CH_2Cl_2) and 97 mg (63%) of **2a** (eluent: CH_2Cl_2/CH_3OH, 97:3). − From **1a**, according to GPD: 1.56 g (4.94 mmol) of TBAF · 3 H_2O, a solution of 90 mg (0.49 mmol) of **1a** in 4.9 mL of distilled CH_2Cl_2, stirred for 312 h. TLC monitoring showed only some traces of **2a** and **3a**. − From **1a**, according to GPA, with previously degassed TBAF solution: A two-necked, round-bottomed flask containing 7.5 mL (7.5 mmol) of 1 M TBAF solution in THF was cooled to −15°C and evacuated for 30 sec. The flask was allowed to warm up to room temperature and was purged three times with argon. This procedure was repeated three times. The degassed TBAF solution was added to 250 mg (1.37 mmol) of **1a** under nitrogen atmosphere, and the mixture was stirred for 24 h. The crude reaction mixture was purified twice by column chromatography to yield 39 mg (17%) of **3a** (eluent: CH_2Cl_2) and 40 mg (16%) of **2a** (eluent: CH_2Cl_2/CH_3OH, 97/3). − From **1a**, according to GPA, with previously degassed TBAF solution: After the bottle containing the 1 M TBAF solution in THF had been degassed, 6 mL (6 mmol) of the solution was added to 200 mg (1.10 mmol) of **1a** under nitrogen atmosphere. After 48 h of stirring, the crude reaction mixture was purified twice by column chromatography to obtain 60 mg (32%) of **3a** (eluent: CH_2Cl_2) and 34 mg (17%) of **2a** (eluent: CH_2Cl_2/CH_3OH, 97:3). − From **1f**, according to GPA, with extraction: 5 mL (5 mmol) of 1 M TBAF solution in THF, 111 mg (0.46 mmol) of **1f**, stirred for 30 h. The crude reaction mixture was diluted with 10 mL of diethyl ether and extracted with 6 mL of 10% HCl solution. The aqueous layer was neutralized by 10 mL of 5% $NaHCO_3$ solution and washed with 3 × 9 mL of diethyl ether. After the combined organic layers had been dried, filtered, and concentrated, the crude brown oil (160 mg) was purified by column chromatography to afford 21 mg (26%) of **3a** as an orange powder (eluent: CH_2Cl_2) and 8 mg (9%) of **2a** as a brown powder (eluent: CH_2Cl_2/CH_3OH, 97:3).

1-[2-(Trimethylsilyl)ethoxymethyl]-2-vinylindole-3-carboxylic Acid (2b): From **1b**, according to GPA, with extraction: 6 mL (6 mmol) of 1 M TBAF solution in THF, 110 mg (0.35 mmol) of **1b**, stirred for 48 h. The reaction mixture was diluted with 10 mL of diethyl ether and extracted with 6 mL of 10% HCl solution. The aqueous layer was neutralized by 10 mL of 5% $NaHCO_3$ solution and washed with 3 × 9 mL of diethyl ether. After the combined organic layers had been dried, filtered, and concentrated, the crude orange oil (368 mg) was purified by column chromatography to obtain **2b** as a brown oil (eluent: CH_2Cl_2/CH_3OH, 99:1). − Yield: 95 mg (85%). − IR (film): $\tilde{\nu}$ = 2951 cm^{-1}, 1661 (s, CO), 1637, 1460 (s), 1080, 835. − UV: λ_{max} = 217 nm, 238, 302. − ^1H NMR ($CDCl_3$): δ = 0.01 [s, 9 H, Si(CH_3)$_3$], 1.00 [t, *J* = 8.2 Hz, 2 H, $CH_2CH_2Si(CH_3)_3$], 3.70 (t, *J* = 8.2 Hz, 2 H, OCH_2CH_2), 5.60 (s, 2 H, NCH_2O), 5.87 [br d, *J* = 12.3 Hz, 1 H, CH=C*H*$_2$, (*Z*) to CH=], 6.05 [br d, *J* = 18.0 Hz, 1 H, CH=C*H*$_2$, (*E*) to CH=], 7.30−7.40 (m, 2 H, 5-H, 6-H), 7.50 (dd, *J* = 12.3, 18.0 Hz, 1 H, C*H*=CH$_2$), 7.55 (m, 1 H, 7-H), 8.35 (m, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = −1.4 [Si(CH_3)$_3$], 17.9 [$CH_2CH_2Si(CH_3)_3$], 66.4 (OCH_2CH_2), 73.1 (NCH_2O), 105.5 (C-3), 110.1 (C-7), 122.3, 122.7, 123.6, 123.7 (CH=*C*H$_2$), 126.5 (*C*H=CH$_2$), 126.7 (C-3a), 137.8 (C-7a), 145.1 (C-2), 170.9 (CO_2H). − $C_{17}H_{23}NO_3Si$. − MS (EI): *m*/*z* (%) = 317 (58) [M^+], 259 (38), 200 (82), 169 (100), 154 (56). − HRMS: calcd. 317.144722; found 317.145492. − From **1b**, according to GPA: 5.3 mL (5.3 mmol) of 1 M TBAF solution in THF, 153 mg (0.49 mmol) of **1b**, stirred for 3.5 h. The crude reaction mixture was purified twice by column chromatography to furnish 142 mg (92%) of **2b** (eluent: CH_2Cl_2/CH_3OH, 99:1). − From **1b**, according to GPC: 1.30 g (4.12 mmol) of TBAF · 3 H_2O, a solution of 117 mg (0.375 mmol) of **1b** in 4.1 mL of distilled THF, stirred for 22 h. The reaction mixture was purified twice by column chromatography to yield 96 mg (81%) of **2b** (eluent: CH_2Cl_2/CH_3OH, 99:1). − From **1b**, according to GPD: 1.24 g (3.95 mmol) of TBAF · 3 H_2O, a solution of 112 mg (0.36 mmol) of **1b** in 3.95 mL of distilled CH_2Cl_2. The mixture was stirred for 52 h and purified twice by column chromatography to afford 40 mg (35%) of **2b** (eluent: CH_2Cl_2/CH_3OH, 99:1).

1-Methyl-2-vinylindole-3-carboxylic Acid (**2c**): From **1c**, according to GPA, with extraction: 5 mL (5 mmol) of 1 M TBAF solution in THF, 89 mg (0.45 mmol) of **1c**, stirred for 18 h. The reaction mixture was diluted with 9 mL of diethyl ether and extracted with 4 mL of 10% HCl solution. The aqueous layer was neutralized by 9 mL of 5% $NaHCO_3$ solution and washed with 3 × 7 mL of diethyl ether. After the combined organic layers had been dried, filtered, and concentrated, the crude pink solid was purified by column chromatography to obtain **2c** as a pink crystalline powder (eluent: CH_2Cl_2/CH_3OH, 98:2). − Yield: 71 mg (78%). − M.p. 142 °C. − IR (film): $\tilde{\nu}$ = 3416 cm^{-1} (br), 1651 (s, CO), 1645, 1470, 1181, 1109. − UV: λ_{max} = 221 nm, 239, 303. − ^1H NMR ($CDCl_3$): δ = 3.88 (s, 3 H, NCH_3), 5.70 [br d, *J* = 18.0 Hz, 1 H, CH=C*H*$_2$, (*E*) to CH=], 5.96 [br d, *J* = 13.1 Hz, 1 H, CH=C*H*$_2$, (*Z*) to CH=], 7.22−7.40 (m, 3 H, 5-H, 6-H, 7-H), 7.45 (dd, *J* = 13.1, 18.0 Hz, 1 H, C*H*=CH$_2$), 8.29 (m, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 31.8 (NCH_3), 104.3 (C-3), 109.8 (C-7), 122.2, 122.4, 122.7 (CH=*C*H$_2$), 123.2, 126.7 (C-3a), 127.1 (*C*H=CH$_2$), 137.8 (C-7a), 144.6 (C-2), 170.7 (CO_2H). − $C_{12}H_{11}NO_2$. − MS (EI): *m*/*z* (%) = 201 (100) [M^+], 184 (53). − HRMS: calcd. 201.078979; found 201.078728.

1-Benzyl-2-vinylindole-3-carboxylic Acid (**2d**): From **1d**, according to GPA, with extraction: 5 mL (5 mmol) of 1 M TBAF solution in THF, 41 mg (0.15 mmol) of **1d**, stirred for 14 h. The mixture was diluted with 4 mL of diethyl ether and extracted with 2 mL of 10% HCl solution. The aqueous layer was neutralized by 4 mL of 5% $NaHCO_3$ solution and washed with 3 × 3 mL of diethyl ether. After the combined organic layers had been dried, filtered, and concentrated, the crude yellow-green oil was purified by column chromatography to yield **2d** as a beige powder (eluent: CH_2Cl_2/CH_3OH, 99:1). − Yield: 16 mg (39%). − M.p. 184 °C. − IR (film): $\tilde{\nu}$ = from 3081 to 3030 cm^{-1} (br), 2946, 1657 (s, CO), 1465, 1453 (s), 737. − UV: λ_{max} = 215 nm, 242, 305, 325. − ^1H NMR ($CDCl_3$): δ = 5.50 (s, 2H, NCH_2Ph), 5.55 [dd, *J* = 0.8, 18.2 Hz, 1 H, CH=C*H*$_2$, (*E*) to CH=], 5.69 (dd, *J* = 0.8, 12.1 Hz, 1 H, CH=

C*H*$_2$, (*Z*) to CH=], 7.05 (dd, *J* = 1.6, 6.3 Hz, 2 H$_{Bzl}$), 7.15−7.30 (m, 6 H, 5-H, 6-H, 7-H, 3 H$_{Bzl}$), 7.42 (dd, *J* = 12.1, 18.2 Hz, 1 H, C*H*=CH$_2$), 8.37 (dd, *J* = 1.0, 6.5 Hz, 1 H, 4-H). − ^{13}C NMR (CDCl$_3$): δ = 48.0 (NCH$_2$Ph), 104.9 (C-3), 109.9 (C-7), 122.3, 122.4 (CH=C*H*$_2$), 122.6, 123.5, 125.6, 126.7 (*C*H=CH$_2$), 126.9 (C-3a), 127.5, 129.0, 136.7, 137.5, 144.7 (C-2), 170.9 (CO$_2$H). − $C_{18}H_{15}NO_2$. − MS (EI): *m*/*z* (%) = 277 (100) [M$^+$]. − HRMS: calcd. 277.110279; found 277.110321. − From **1d**, according to GPA: 7.15 mL (7.15 mmol) of 1 M TBAF solution in THF, 177 mg (0.65 mmol) of **1d**, stirred for 3.2 h. The crude reaction mixture was purified twice by column chromatography to obtain 108 mg (60%) of **2d** (eluent: CH$_2$Cl$_2$/CH$_3$OH, 99:1).

1-Benzyl-5-methoxy-2-vinylindole-3-carboxylic Acid (**2e**): From **1e**, according to GPA: 5.75 mL (5.75 mmol) of 1 M TBAF solution in THF, 158 mg (0.52 mmol) of **1e**, stirred for 6 h. The crude reaction mixture was purified twice by column chromatography to furnish **2e** as a beige powder (eluent: CH$_2$Cl$_2$/CH$_3$OH, 97:3). − Yield: 75 mg (47%). − M.p. 172 °C. − IR (film): $\tilde{\nu}$ = 3082 cm^{-1} (br), 2944, 1653 (s, CO), 1617, 1483 (s), 1451 (s), 1437, 1154. − UV (film): λ_{max} = 215 nm, 248, 307, 325. − ^{1}H NMR (CDCl$_3$): δ = 3.80 (s, 3 H, OCH$_3$), 5.58 [br d, *J* = 16.3 Hz, 1 H, CH=C*H*$_2$, (*E*) to CH=], 5.60 (s, 2 H, NCH$_2$Ph), 5.63 (br d, *J* = 12.1 Hz, 1 H, CH=C*H*$_2$, (*Z*) to CH=], 6.87 (dd, *J* = 2.4, 8.9 Hz, 1 H, 6-H), 7.00 (m, 2 H$_{Bzl}$), 7.25−7.40 (m, 5 H, 4-H, C*H*=CH$_2$, 3 H$_{Bzl}$), 7.60 (d, *J* = 2.4 Hz, 1 H, 7-H). − ^{13}C NMR (CDCl$_3$): δ = 47.6 (NCH$_2$Ph), 55.8 (OCH$_3$), 101.5 (C-3), 104.0 (C-7), 112.0, 113.4, 121.8 (CH=*C*H$_2$), 126.2, 127.0, 127.6 (*C*H=CH$_2$), 127.7 (C-3a), 129.1, 132.7, 137.9, 143.0 (C-2), 155.8 (C-5), 166.4 (CO$_2$H). − $C_{19}H_{17}NO_3$. − MS (EI): *m*/*z* (%) = 307 (100) [M$^+$], 292 (19). − HRMS: calcd. 307.120844; found 307.123962.

1-(*tert*-Butoxycarbonyl)-2-vinylindole-3-carboxylic Acid (**2g**): From **1g**, according to GPA: 2 mL (2 mmol) of 1 M TBAF solution in THF, 37 mg (0.13 mmol) of **1g**, stirred for 50 h. The crude reaction mixture was purified twice by column chromatography to furnish 7.2 mg (32%) of **3a** (eluent: CH$_2$Cl$_2$) and 15.3 mg of the mixture of **2a** and **2g** (eluent: CH$_2$Cl$_2$/CH$_3$OH, 97:3). The relative proportion of **2a** and **2g** was determined by ^{1}H NMR spectroscopy. − NMR yield of **2a**: 24%. − NMR yield of **2g**: 25%. − Spectral analyses were realized by deduction; ^{1}H NMR (CDCl$_3$) of **2g**: δ = 1.6 [s, 9 H, C(CH$_3$)$_3$], 5.55 [dd, *J* = 1.5, 17,8 Hz, CH=C*H*$_2$, (*E*) to CH=], 5.59 [dd, *J* = 1.5, 11.7 Hz, CH=C*H*$_2$, (*Z*) to CH=], 7.10 (dd, *J* = 11.7, 17.8 Hz, 1 H, C*H*=CH$_2$), 7.10−7.45 (m, 3 H, 4-H, 5-H, 6-H), 7.98 (br d, *J* = 7.3 Hz, 1 H, 7-H).

2-Ethylindole-3-carboxaldehyde (**3h**): From **1h**, according to GPA, with extraction: 5 mL (5 mmol) of 1 M TBAF solution in THF, 89 mg (0.48 mmol) of **1h**, stirred for 110 h. The mixture was diluted with 9 mL of diethyl ether and extracted with 4 mL of 10% HCl solution. The aqueous layer was neutralized by 9 mL of 5% NaHCO$_3$ solution and washed with 3 × 7 mL of diethyl ether. After the combined organic layers had been dried, filtered, and concentrated, the crude orange oil (164 mg) was purified by column chromatography to afford **3h** as a brown powder (eluent: CH$_2$Cl$_2$/CH$_3$OH, 96:4). − Yield: 12 mg (14%). − M.p. 148 °C (ref.[13] m.p. 167−171 °C).

2-Ethyl-1-methylindole-3-carboxylic Acid (**2i**): From **1i**, according to GPA: 2.5 mL (2.5 mmol) of 1 M TBAF solution in THF, 22 mg (0.11 mmol) of **1i**, stirred for 45 h. The crude reaction mixture was purified twice by column chromatography to obtain **2i** as a beige crystalline powder (eluent: CH$_2$Cl$_2$/CH$_3$OH, 99:1). − Yield: 22 mg (96%). − M.p. 190 °C. − IR (film): $\tilde{\nu}$ = 3428 cm^{-1} (br), 1642 (s, CO), 1468. − UV (film): λ_{max} = 218 nm, 229, 249, 284, 290. − ^{1}H NMR (CDCl$_3$): δ = 1.34 (t, *J* = 8.1 Hz, 3 H, CH$_2$C*H*$_3$), 3.31 (q, *J* = 8.1 Hz, 2 H, C*H*$_2$CH$_3$), 3.78 (s, 3 H, NCH$_3$), 7.22−7.45 (m, 3 H, 5-H, 6-H, 7-H), 8.28 (m, 1 H, 4-H), 9.55 (br s, 1 H, CO$_2$H). − ^{13}C NMR (CDCl$_3$): δ = 13.5 (CH$_2$*C*H$_3$), 19.0 (*C*H$_2$CH$_3$), 29.5 (NCH$_3$), 102.4 (C-3), 109.2 (C-7), 121.8, 122.0, 122.2, 127.1 (C-3a), 136.7 (C-7a), 152.0 (C-2), 171.3 (CO$_2$H). − $C_{12}H_{13}NO_2$. − MS (EI): *m*/*z* (%) = 203 (90) [M$^+$], 188 (100). − HRMS: calcd. 203.094629; found 203.093956.

Indole-3-carboxaldehyde (**3j**): From **1j**, according to GPA, with extraction: 5 mL (5 mmol) of 1 M TBAF solution in THF, 103 mg (0.66 mmol) of **1j**, stirred for 110 h. The mixture was diluted with 10 mL of diethyl ether and extracted with 6 mL of 10% HCl solution. The aqueous layer was neutralized by 10 mL of 5% NaHCO$_3$ solution and washed with 3 × 9 mL of diethyl ether. After the combined organic layers had been dried, filtered, and concentrated, the crude orange oil (616 mg) was purified by column chromatography to afford 3 mg (3%) of **3j** as a yellow powder (eluent: CH$_2$Cl$_2$/CH$_3$OH, 98:2). − From **1j**, according to GPA: 5 mL (5 mmol) of 1M TBAF solution in THF, 100 mg (0.64 mmol) of **1j**, stirred for 110 h. The crude reaction mixture was purified twice by column chromatography to obtain 15 mg (16%) of **3j** (eluent: CH$_2$Cl$_2$/CH$_3$OH, 98:2). − From **1j**, according to GPA, under oxygen atmosphere: 5 mL (5 mmol) of 1 M TBAF solution in THF, 103 mg (0.64 mmol) of **1j**, stirred for 194 h under oxygen atmosphere. The crude reaction mixture was purified twice by column chromatography to furnish 31 mg (30%) of **1j** (eluent: CH$_2$Cl$_2$) and 6 mg (6%) of **3j** (eluent: CH$_2$Cl$_2$/CH$_3$OH, 98:2).

Oxidation of Phenylacetonitrile to Benzoic Acid by TBAF: According to GPA, with extraction: 5 mL (5 mmol) of 1 M TBAF solution in THF, 130 mg (1.11 mmol) of phenylacetonitrile, stirred for 120 h. The crude reaction mixture was diluted with 10 mL of diethyl ether and extracted with 6 mL of 10% HCl solution. The aqueous layer was neutralized by 10 mL of 5% NaHCO$_3$ solution and washed with 3 × 9 mL of diethyl ether. After the combined organic layers had been dried, filtered, and concentrated, the crude yellow solid (232 mg) was purified by column chromatography to afford 51 mg (38%) of benzoic acid as a pale yellow powder (eluent: CH$_2$Cl$_2$/CH$_3$OH, 99:1).

Control Experiments for the Oxidation of Indole-3-carboxaldehydes 3a,i into Indole-3-carboxylic Acids 2a,i. − Oxidation of 3a According to GPA: 1.5 mL (1.5 mmol) of 1 M TBAF solution in THF, 21 mg (0.12 mmol) of **3a**, stirred for 95 h. TLC monitoring showed no conversion of the starting material **3a** into the corresponding carboxylic acid **2a**. − **Oxidation of 3i According to GPA**: 4 mL (4 mmol) of 1 M TBAF solution in THF, 74 mg (0.51 mmol) of **3i**, stirred for 120 h. TLC monitoring showed no conversion of the starting material **3i** into the corresponding carboxylic acid **2i**.

General Procedure for the Methylation of Indole-3-carboxylic Acids 2 by Diazomethane (GP): To a stirred solution of indole-3-carboxylic acid **2** in CH$_2$Cl$_2$ was added the ethereal solution of CH$_2$N$_2$ at 0 °C. The mixture was stirred at room temperature under N$_2$ atmosphere, until TLC monitoring showed no further conversion of the starting material **2**. Then the crude reaction mixture was purified by column chromatography (eluent: CH$_2$Cl$_2$) to give esters **4**.

Methyl 2-Vinylindole-3-carboxylate (**4a**): According to GP, 0.5 mL of ethereal CH$_2$N$_2$ solution, 44 mg (0.235 mmol) of **2a** in 4 mL of CH$_2$Cl$_2$, stirred for 10 min. The crude brown oil (52 mg) was purified by column chromatography to obtain 6 mg (13%) of **4a** as a white crystalline powder. − M.p. 136 °C. − IR (film): $\tilde{\nu}$ = 3322 cm^{-1} (br), 2955, 2928, 1669 (s, CO), 1651, 1454 (s), 1204, 1082. − UV: λ_{max} = 221 nm, 242, 312. − ^{1}H NMR (CDCl$_3$): δ = 3.95 (s, 3 H, OCH$_3$), 5.51 [br d, *J* = 11.4 Hz, 1 H, CH=C*H*$_2$, (*Z*) to

CH=], 5.78 [br d, J = 18.1 Hz, 1 H, CH=CH_2, (*E*) to CH=], 7.18−7.29 (m, 2 H, 5-H, 6-H), 7.34 (m, 1 H, 7-H), 7.69 (dd, J = 11.4, 18.1 Hz, 1 H, CH=CH_2), 8.15 (m, 1 H, 4-H), 8.89 (s, 1 H, NH). − ^{13}C NMR ($CDCl_3$): δ = 51.1 (OCH_3), 105.6 (C-3), 110.8 (C-7), 116.7 (CH=CH_2), 121.9, 122.1, 123.9, 126.9 (*C*H=CH_2), 127.2 (C-3a), 135.3 (C-7a), 144.2 (C-2), 166.1 (CO_2CH_3). − $C_{12}H_{11}NO_2$. − MS (EI): *m*/*z* (%) = 201 (75) [M^+], 186 (5), 170 (100), 115 (34). − HRMS: calcd. 201.078979; found 201.078964.

Methyl 1-[2-(Trimethylsilyl)ethoxymethyl]-2-vinylindole-3-carboxylate (**4b**): According to GP, 2.5 mL of ethereal CH_2N_2 solution, 47 mg (0.15 mmol) of **2b** in 5 mL of CH_2Cl_2, stirred for 1 h. The crude orange oil (85 mg) was purified by column chromatography to afford 27 mg (55%) of **4b** as a pale yellow oil. − IR (film): $\tilde{\nu}$ = 2951 cm^{-1}, 1698 (s, CO), 1460, 1439, 1150 (s), 1080 (s), 835. − UV: λ_{max} = 217 nm, 240, 305. − ^{1}H NMR ($CDCl_3$): δ = −0.05 [s, 9 H, Si(CH_3)$_3$], 0.90 [t, J = 7.5 Hz, 2 H, CH_2CH_2Si(CH_3)$_3$], 3.59 (t, J = 7.5 Hz, 2 H, OC$H_2$$CH_2$), 3.90 (s, 3 H, OCH_3), 5.50 (s, 2 H, NCH_2O), 5.75 [dd, J = 0.6, 11.9 Hz, 1 H, CH=CH_2, (*Z*) to CH=], 5.95 [dd, J = 0.6, 18.2 Hz, 1 H, CH=CH_2, (*E*) to CH=], 7.19−7.30 (m, 2 H, 5-H, 6-H), 7.39 (dd, J = 11.9, 18.2 Hz, 1 H, CH=CH_2), 7.45 (m, 1 H, 7-H), 8.15 (m, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = −1.45 [Si(CH_3)$_3$], 17.9 [CH_2*C*H_2Si(CH_3)$_3$], 51.0 (OCH_3), 66.2 (O*C*$H_2$$CH_2$), 73.0 ($NCH_2O$), 106.2 (C-3), 110.1 (C-7), 122.0, 122.4, 123.2 (CH=CH_2), 123.5, 126.3 (C-3a), 126.5 (*C*H=CH_2), 137.7 (C-7a), 144.0 (C-2), 165.8 (CO_2CH_3). − $C_{18}H_{25}NO_3Si$ − MS (EI): *m*/*z* (%) = 331 (46) [M^+], 214 (66), 169 (100), 154 (73). − HRMS: calcd. 331.160372; found 331.159754.

Methyl 1-Methyl-2-vinylindole-3-carboxylate (**4c**): According to GP, 0.5 mL of ethereal CH_2N_2 solution, 13 mg (0.06 mmol) of **2c** in 4 mL of CH_2Cl_2, stirred for 10 min. The crude orange oil (15 mg) was purified by column chromatography to obtain 13 mg (93%) of **4c** as a white-yellow crystalline powder. − M.p. 79 °C. − IR (film): $\tilde{\nu}$ = 2922 cm^{-1}, 1694 (s, CO), 1165, 1101 (s). − UV: λ_{max} = 220 nm, 243, 307. − ^{1}H NMR ($CDCl_3$): δ = 3.85 (s, 3 H), 3.94 (s, 3 H), 5.67 [dd, J = 0.6, 18.2 Hz, 1 H, CH=CH_2, (*E*) to CH=], 5.81 [dd, J = 0.6, 12.6 Hz, 1 H, CH=CH_2, (*Z*) to CH=], 7.21−7.38 (m, 3 H, 5-H, 6-H, 7-H), 7.40 (dd, J = 12.6, 18.2 Hz, 1 H, CH=CH_2), 8.17 (m, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 31.7 (NCH_3), 50.9 (OCH_3), 105.0 (C-3), 109.7 (C-7), 122.0, 122.1, 122.4 (CH=CH_2), 123.1, 126.2 (C-3a), 127.1 (*C*H=CH_2), 137.6 (C-7a), 143.6 (C-2), 166.0 (CO_2CH_3). − $C_{13}H_{13}NO_2$. − MS (EI): *m*/*z* (%) = 215 (82) [M^+], 200 (7), 184 (100). − HRMS: calcd. 215.094629; found 215.093876.

Methyl 1-Benzyl-2-vinylindole-3-carboxylate (**4d**): According to GP, 2.5 mL of ethereal CH_2N_2 solution, 21 mg (0.075 mmol) of **2d** in 2.5 mL of CH_2Cl_2, stirred for 25 min. The crude reaction mixture was purified by column chromatography to afford 7 mg (32%) of **4d** as a pale yellow crystalline powder. − M.p. 90−92 °C. − IR (film): $\tilde{\nu}$ = 2947 cm^{-1}, 1698 (s, CO), 1439, 1144, 1117. − UV: λ_{max} = 215 nm, 243, 307, 325. − ^{1}H NMR ($CDCl_3$): δ = 3.97 (s, 3 H, OCH_3), 5.52 [br d, J = 18.4 Hz, 1 H, CH=CH_2, (*E*) to CH=], 5.53 (s, 2 H, NCH_2Ph), 5.65 [br d, J = 12.1 Hz, 1 H, CH=CH_2, (*Z*) to CH=], 7.05 (dd, J = 1.1, 6.5 Hz, 2 H_{Bzl}), 7.15−7.30 (m, 6 H, 4-H, 5-H, 7-H, 3 H_{Bzl}), 7.39 (dd, J = 12.1, 18.4 Hz, 1 H, CH=CH_2), 8.20 (dd, J = 0.8, 8.2 Hz, 1 H, 6-H). − ^{13}C NMR ($CDCl_3$): δ = 47.9 (NCH_2Ph), 51.0 (OCH_3), 105.6 (C-3), 110.4 (C-7), 122.0, 122.1 (CH=CH_2), 122.3, 123.4, 125.6, 126.4 (C-3a), 126.7 (*C*H=CH_2), 127.5, 129.0, 136.9, 137.4, 143.6 (C-2), 165.9 (CO_2CH_3). − $C_{19}H_{17}NO_2$. − MS (EI): *m*/*z* (%) = 291 (100) [M^+], 276 (24). − HRMS: calcd. 291.125929; found 291.127266.

Methyl 1-Benzyl-5-methoxy-2-vinylindole-3-carboxylate (**4e**): According to GP, 1 mL of ethereal CH_2N_2 solution, 26 mg (0.09 mmol) of **2e** in 3 mL of CH_2Cl_2, stirred for 40 min. The crude brown solid was purified by column chromatography to obtain 12 mg (43%) of **4e** as a light brown amorphous solid. − IR (film): $\tilde{\nu}$ = 2922 cm^{-1} (br), 1694 (s, CO), 1480, 1437 (s), 1201 (s), 1148, 1119. − UV: λ_{max} = 216 nm, 247, 310. − ^{1}H NMR ($CDCl_3$): δ = 3.90 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 5.47 (s, 2 H, NCH_2Ph), 5.48 [dd, J = 1.0, 18.2 Hz, 1 H, CH=CH_2), (*E*) to CH=], 5.62 [dd, J = 1.0, 12.1 Hz, 1 H, CH=CH_2, (*Z*) to CH=], 6.86 (dd, J = 2.5, 8.9 Hz, 1 H, 6-H), 6.99−7.08 (m, 2 H_{Bzl}), 7.24−7.29 (m, 4 H, 7-H, 3 H_{Bzl}), 7.33 (dd, J = 12.1, 18.2 Hz, 1 H, CH=CH_2), 7.69 (d, J = 2.5 Hz, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 48.0 (NCH_2Ph), 50.9 (CO_2CH_3), 55.7 (OCH_3), 103.6, 105.2 (C-3), 111.2, 113.6, 121.7 (CH=CH_2), 125.6, 126.9 (*C*H=CH_2), 127.4 (C-3a), 127.5, 128.9, 129.0, 132.5, 136.9, 143.6 (C-2), 166.0 (CO_2CH_3). − $C_{20}H_{19}NO_3$. − MS (EI): *m*/*z* (%) = 321 (100) [M^+], 306 (17), 291 (62). − HRMS: calcd. 321.136494; found 321.134995.

Methyl 1-(*tert*-Butoxycarbonyl)-2-vinylindole-3-carboxylate (**4g**): According to GP, 0.1 mL of ethereal CH_2N_2 solution, 3 mg of the mixture of **2a** and **2g** in 2 mL of CH_2Cl_2, stirred for 30 min. The crude reaction mixture was purified by column chromatography to afford 3 mg of a mixture of **4a** and **4g** as a pale brown oil. The relative proportion of **4a** and **4g** was determined by ^{1}H NMR. − NMR yield of **4a**: 52%. − NMR yield of **4g**: 48%. − ^{1}H NMR of **4g** ($CDCl_3$): δ = 1.65 [s, 9 H, C(CH_3)$_3$], 3.95 (s, 3 H, OCH_3), 5.57 [br d, J = 17.8 Hz, CH=CH_2, (*E*) to CH=], 5.64 [br d, J = 11.7 Hz, CH=CH_2, (*Z*) to CH=], 7.15 (dd, J = 11.7, 17.8 Hz, 1 H, CH=CH_2), 7.21−7.40 (m, 3 H, 4-H, 5-H, 6-H), 8.15 (br d, J = 7.3 Hz, 1 H, 7-H).

Methyl 2-Ethyl-1-methylindole-3-carboxylate (**4i**): According to GP, 0.8 mL of CH_2N_2, 29 mg (0.14 mmol) of **2i** in 15 mL of CH_2Cl_2, stirred for 10 min. The crude orange oil (31 mg) was purified by column chromatography to obtain 20 mg (64%) of **4i** as a pale yellow crystalline powder. − M.p. 72−74 °C. − IR (film): $\tilde{\nu}$ = 2946 cm^{-1}, 1694 (s, CO), 1537, 1472, 1213, 1105. − UV (film): λ_{max} = 216 nm, 231, 252, 286, 290. − ^{1}H NMR ($CDCl_3$): δ = 1.25 (t, J = 8 Hz, 3 H, CH_2CH_3), 3.25 (q, J = 8 Hz, 2 H, C$H_2$$CH_3$), 3.70 (s, 3 H, NCH_3), 3.95 (s, 3 H, OCH_3), 7.19−7.28 (m, 2 H, 5-H, 6-H), 7.30 (m, 1 H, 7-H), 8.13 (m, 1 H, 4-H). − ^{13}C NMR ($CDCl_3$): δ = 13.5 (CH_2CH_3), 18.9 (CH_2CH_3), 29.4 (NCH_3), 50.7 (OCH_3), 102.9 (C-3), 109.2 (C-7), 121.5, 121.7, 122.1, 126.5 (C-3a), 136.5 (C-7a), 150.9 (C-2), 166.3 (CO_2CH_3). − $C_{13}H_{15}NO_2$. − MS (EI): *m*/*z* (%) = 217 (100) [M^+], 202 (53), 186 (70). − HRMS: calcd. 217.110279; found 217.110302.

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