

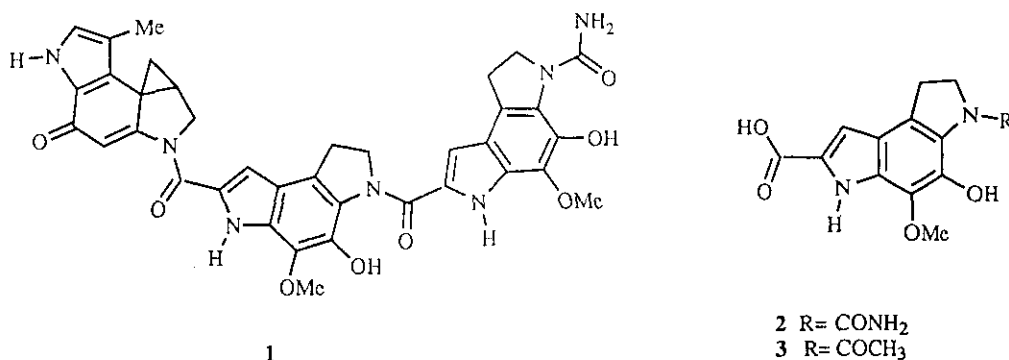
**SYNTHESIS OF METHYL 4-(2,2-DIMETHOXYETHYL)-6-HYDROXY-7-METHOXYINDOLE-2-CARBOXYLATE: A POTENTIAL INTERMEDIATE FOR THE SYNTHESIS OF THE CENTRAL AND RIGHT PARTS OF THE ANTICANCER ANTIBIOTIC CC-1065**

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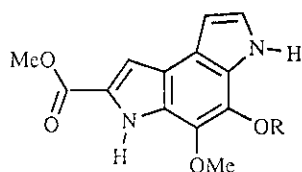
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**Abstract**- We describe an efficient synthesis of methyl 4-(2,2-dimethoxyethyl)-6-hydroxy-7-methoxyindole-2-carboxylate (**5**), a key intermediate for the synthesis of the central and right parts of the antitumor agent CC-1065 (**1**) and of the inhibitors of cyclic adenosine-3',5'-monophosphate phosphodiesterase PDE-I (**2**) and PDE-II (**3**).

CC-1065 (**1**) is an extremely potent antitumor agent that was first isolated from *Streptomyces zelensis* by workers at the Upjohn Company.<sup>1</sup> It has greater activity than adriamycin, actinomycin D, xantomycin, quinomycin C, and maytansin against L1210 leukemia cells in vitro.<sup>2</sup> Its pharmacological interest has prompted a number of synthetic studies.<sup>3</sup> There is a remarkable similarity between the central and right parts of CC-1065 and the cyclic adenosine-3',5'-monophosphate phosphodiesterase inhibitors PDE-I (**2**) and PDE-II (**3**) which were isolated from another species of *Streptomyces*.<sup>4</sup>



The central and right units of CC-1065 and the phosphodiesterase inhibitors PDE-I and PDE-II can all be synthesized from the common precursor **4**, which should be possible to obtain by nitration of methyl 4-(2,2-dimethoxyethyl)-6-hydroxy-7-methoxyindole-2-carboxylate (**5**) followed by protection of the hydroxy group and reductive cyclization.



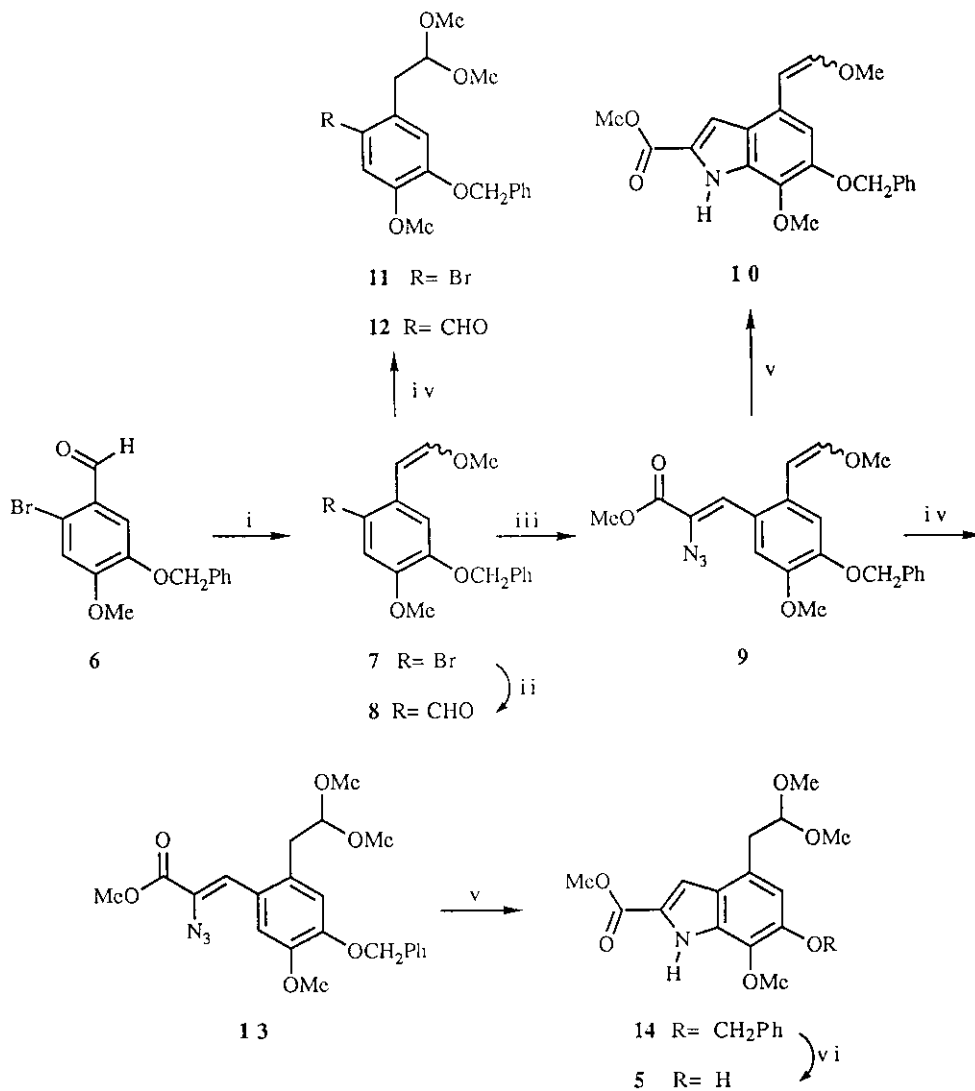
**4**

In this paper we describe the synthesis of the indole **5** from commercially available isovainillin in 34% overall yield. The key step of the synthetic plan is the formation of a pyrrole ring by vinylnitrene cyclization. This reaction is carried out by thermolysis of an azidocinnamate derivative which is readily prepared from an aromatic aldehyde.<sup>5</sup>

Wittig reaction of 5-benzyloxy-2-bromo-4-methoxybenzaldehyde (**6**) which is available from isovainillin in two steps<sup>6</sup> (79% yield) with methoxymethylenetriphenylphosphorane, gave the  $\beta$ -methoxystyrene **7**, according to <sup>1</sup>H nmr integrals, as a 2:1 mixture of the *E* and *Z* isomers; the optimum yield (99%) was obtained in tetrahydrofuran using potassium *t*-butoxide as base. Formyl-debromination<sup>7</sup> of **7** was carried out by treatment with *n*-butyllithium followed by quenching of the organolithium intermediate with *N,N*-dimethylformamide. The  $\beta$ -methoxystyrenes **7** and **8** are air sensitive, especially in solution. Compound **7**, reverting readily to **6**, must be stored under Ar.

Condensation of **8** with methyl azidoacetate<sup>8</sup> produced the unstable azidocinnamates **9** as a mixture of two isomers about the enol ether double bond, both of them having, like the other azidocinnamates synthesized in this work, the same unique but unknown stereochemistry with respect to the vinyl azide double bond. The compound **9** was immediately subjected to thermolysis in boiling xylene, yielding a complex mixture of the products whose <sup>1</sup>H nmr spectrometry suggested included just a small amount of the desired indole **10**. Nitrenes have a great tendency to add to

double bonds, and in our case the desired *NC-cyclo-CH*-imino-insertion is probably less favoured than the *epi-imino*-addition.<sup>7</sup> This result was expected in view of published precedents.<sup>5</sup>



Reagents: i:  $(C_6H_5)_3P^+CH_2OMe Cl^-$ , *t*-BuOK/ THF; ii: *n*-BuLi/ THF, then DMF; iii:  $N_3CH_2CO_2Me$ , Na/ MeOH; iv:  $SOCl_2$ / MeOH; v: xylene, reflux; vi:  $H_2$ , Pd-C, MeOH.

We then addressed the preparation of **12**, a substrate in which side reactions in the key indole formation are less likely. Treatment of **7** with thionyl chloride in methanol effected the addition of methanol, giving the dimethyl acetal **11**. Reaction of bromide **11** with *n*-butyllithium followed by addition of *N,N*-dimethylformamide failed under a number of different experimental conditions, to give a reasonable yield of the desired aldehyde **12**. In all cases a mixture of unidentified aldehydes was obtained. Attempts to transform **8** into **12** using various acidic conditions also met with failure. Eventually, the azidocinnamate **13** could be prepared directly from the unstable vinyl azide **9** by treatment with thionyl chloride in methanol. As expected, thermolysis of **13** in boiling xylene brought about a clean closure to yield the indole **14**. The sequence of reactions from **8** to **14** must be carried out as quickly as possible since the intermediate vinyl azides **9** and **13** are very unstable. We found that the optimal overall yield (52%) from **8** to **14** was obtained when these three reactions were performed without purification of **9** and **13**.

O-Debenzylation of **14** by catalytic hydrogenation over palladium on carbon resulted in a high yield of the desired indole **5**, thus completing an efficient synthesis of the potential key intermediate for preparations of CC-1065, PDE-I and PDE-II.

## EXPERIMENTAL

Tetrahydrofuran (THF) was distilled under Ar from sodium and methanol was distilled from magnesium prior to use. Melting points are uncorrected. Infrared (ir) spectra were taken in KBr pellets on Perkin-Elmer 1420 and 180 instruments. Ultraviolet (uv) spectra were recorded using ethanol solutions on Kontron Uvikon 820 and 810 P instruments. Nuclear magnetic resonance (nmr) spectra were recorded in chloroform-*d* solutions on a Bruker WM-250 (250 MHz) instrument using tetramethylsilane as internal standard. Mass spectra (ms) were recorded on a Kratos MS-50 spectrometer, with electron impact at 70 e.v. using a DS-90 data system; high resolution data were determined using perfluorokerosene as a standard. Thin layer chromatography (tlc) was carried out on Merck GF-254 silica gel and flash chromatography on Merck 60 (230-400 mesh) silica gel.

5-Benzyloxy-2-bromo-4, $\beta$ -dimethoxystyrene (7). A suspension of 14.10 g (41.10 mmol) of triphenylmethoxymethylphosphonium chloride and 7.98 g (86.75 mmol) of freshly sublimed potassium *tert*-butoxide in 138 ml of dry THF was stirred under argon for 1 h. Aldehyde 6 (6.285 g, 19.58 mmol) was added to the ylide solution, and the mixture was stirred for 48 h at room temperature. A saturated aqueous solution of ammonium chloride was added, most of the THF was removed in a rotatory evaporator, and the residue was extracted with dichloromethane. The organic solution was dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated to a volume of c.a. 15 ml. This solution was stirred with methyl iodide (10 ml) for 1 h to eliminate triphenylphosphine. Evaporation under reduced pressure gave a crude product which was purified by flash chromatography (hexane-ethyl acetate, 3:1) on silica gel, yielding 6.805 g (99.6%) of an unseparated 2:1 mixture of the *E* and *Z* isomers of 7, mp 68-74°C; ir  $\nu_{\max}$ : 1640, 1595, 1510 cm<sup>-1</sup>; uv  $\lambda_{\max}$ : 244sh, 270, 278sh and 305 nm; <sup>1</sup>H nmr (major isomer)  $\delta$ : 7.5-7.3 (m, 5H, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 7.03 (s, 1H, ArH), 6.85 (s, 1H, ArH), 6.73 (d, J= 12.9Hz, 1H, H $\beta$ ), 5.96 (d, J= 12.9Hz, 1H, H $\alpha$ ), 5.13 (s, 2H, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.85 (s, 3H, Ar-OCH<sub>3</sub>), and 3.68 (s, 3H, -CH=CH-OCH<sub>3</sub>) ppm; <sup>1</sup>H nmr (minor isomer)  $\delta$ : 7.71 (s, 1H, ArH), 7.5-7.3 (m, 5H, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 7.02 (s, 1H, ArH), 6.11 (d, J= 7.2Hz, 1H, H $\alpha$ ), 5.47 (d, J= 7.2Hz, 1H, H $\alpha$ ), 5.15 (s, 2H, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.85 (s, 3H, Ar-OCH<sub>3</sub>), and 3.69 (s, 3H, -CH=CH-OCH<sub>3</sub>) ppm; ms: m/z (%) 350 (M<sup>+</sup>, 6), 348 (M<sup>+</sup>, 6), 259 (4), 257 (4), 231 (6), 229 (6), 150 (6), 135 (10), 91 (100), 77 (7). Exact mass calcd for C<sub>17</sub>H<sub>17</sub>O<sub>3</sub><sup>79</sup>Br: 348.0362 (M<sup>+</sup>); found (ms): 348.0374.

4-Benzyloxy-5-methoxy-2-(2-methoxyphenyl)benzaldehyde (8). A 1.92M solution of *n*-butyllithium in hexane (10.8 ml, 20.74 mmol) was added dropwise under argon to a stirred solution of 7 (6.535 g, 18.73 mmol) in dry THF (61 ml) cooled at -100°C to -90°C (inner temperature). The mixture was stirred for 0.5 h. Dry DMF (7.3 ml, 94.4 mmol) was added, and the temperature was allowed slowly to attain room temperature. A saturated aqueous solution of NH<sub>4</sub>Cl was added, most of the THF was eliminated in a rotatory evaporator, and the resulting mixture was extracted with dichloromethane. The organic solution was dried (Na<sub>2</sub>SO<sub>4</sub>), the solvent was removed, and the crude mixture was subjected to flash chromatography (hexane-ethyl acetate, 4:1) on silica gel, to give 5.185 g of an unseparated 2:1 mixture of the *E* and *Z* isomers of 8 (93% yield), mp 104-112°C; ir  $\nu_{\max}$ : 1675 (C=O), 1630, 1595, 1505 cm<sup>-1</sup>; uv  $\lambda_{\max}$ : 263, 290, and 344 nm; <sup>1</sup>H nmr (major isomer)  $\delta$ : 10.16 (s, 1H, -CHO), 7.5-7.3 (m, 6H, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub> + ArH), 6.81 (s, 1H, ArH), 6.73 (d, J= 12.8Hz, 1H, H $\beta$ ), 6.47 (d, J= 12.8Hz, 1H, H $\alpha$ ), 5.23 (s, 2H, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.93 (s, 3H,

Ar-OCH<sub>3</sub>), and 3.72 (s, 3H, -CH=CH-OCH<sub>3</sub>) ppm; <sup>1</sup>H nmr (minor isomer) δ: 10.15 (s, 1H, -CHO), 7.5-7.3 (m, 7H, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub> + 2 x ArH), 6.22 (d, J= 7.2Hz, 1H, H<sub>α</sub>), 5.93 (d, J= 7.2Hz, 1H, H<sub>α</sub>), 5.23 (s, 2H, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 3.93 (s, 3H, Ar-OCH<sub>3</sub>), and 3.70 (s, 3H, -CH=CH-OCH<sub>3</sub>) ppm; ms: m/z (%) 298 (M<sup>+</sup>, 4), 267 (2), 207 (3), 179 (3), 164 (3), 135 (3), 121 (4), 105 (4), 91 (100), 77 (9). Exact mass calcd for C<sub>18</sub>H<sub>18</sub>O<sub>4</sub>: 298.1205 (M<sup>+</sup>); found (ms): 298.1210.

(5-Benzyloxy-2-bromo-4-methoxyphenyl)acetaldehyde dimethyl acetal (11). 0.30 ml (492 mg, 4.13 mmol) of thionyl chloride were added dropwise to a stirred cold (ice-water bath) suspension of 500 mg of 7 in dry methanol (3 ml) kept in a round-bottomed flask with a CaCl<sub>2</sub> tube attached. After stirring 30 min at room temperature, the resulting solution was neutralized with a 10% aqueous solution of NaOH. Most methanol was removed in a rotatory evaporator, and the resulting mixture was extracted with dichloromethane. The organic solution was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated, and the crude mixture was subjected to flash chromatography (dichloromethane) on silica gel, to give 491 mg of 11 (90% yield), mp 47-48°C; ir ν<sub>max</sub>: 1640, 1600, 1505, 1460, 1440 cm<sup>-1</sup>; uv λ<sub>max</sub>: 232 sh, 270, 278, 294 sh and 316sh nm; <sup>1</sup>H nmr δ: 7.5-7.3 (m, 5H, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 7.01 (s, 1H, ArH), 6.84 (s, 1H, ArH), 5.13 (s, 2H, -CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 4.46 (t, 1H, J= 5.6 Hz, -CH<sub>2</sub>-CH-(OCH<sub>3</sub>)<sub>2</sub>), 3.84 (s, 3H, Ar-OCH<sub>3</sub>), 3.27 (s, 6H, -CH<sub>2</sub>-CH-(OCH<sub>3</sub>)<sub>2</sub>) and 2.91 (d, 2H, J= 5.6 Hz, -CH<sub>2</sub>-CH-(OCH<sub>3</sub>)<sub>2</sub>) ppm; ms: m/z (%) 382 (M<sup>+</sup>, 2), 380 (M<sup>+</sup>, 2), 351 (6), 350(7), 349 (6), 348 (6), 259(7), 257 (7), 231 (27), 229 (30), 209 (12), 91 (100), 75 (58). Exact mass calcd for C<sub>18</sub>H<sub>21</sub>O<sub>4</sub><sup>79</sup>Br: 380.0624 (M<sup>+</sup>); found (ms): 380.0609.

Methyl 2-azido-3-(4-benzyloxy-5-methoxy-2-(2-methoxyethenyl)-phenyl)propenoate (9). A suspension of 8 (4.877 g, 16.37 mmol) in a mixture of dry methanol (43 ml) and methyl azidoacetate (13.0 ml, 133.4 mmol) was slightly heated to obtain a clear solution. This solution was added dropwise to a cooled (salt-ice bath), stirred solution of sodium methoxide, which was freshly prepared by carefully adding sodium (3.8 g, 165 mmol) to dry methanol (69 ml). Stirring was kept for 2 h at -10°C to -15°C. The temperature was allowed to rise slowly to 4°C and the reaction mixture was left at this temperature for 48 h. A saturated aqueous solution of NH<sub>4</sub>Cl was added and the resulting mixture was extracted with dichloromethane. The organic solution was dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent evaporated, yielding 6.430 g of crude 9 which was quickly used in the following reaction without any further purification. In order to obtain optimal yields, it was necessary to avoid strong light or heating during the preparation and handling of 9. In a

separate run some crude **9** was quickly purified by flash chromatography using a small pad of tlc silica gel on a Büchner funnel, while the elution (dichloromethane-hexane, 1:1) was speeded by suction. In this way an 86% yield of an unseparated 2:1 mixture ( $^1\text{H}$  nmr integrals) of the *E* and *Z* isomers was obtained, mp 95-97°C; ir  $\nu_{\text{max}}$ : 2090, 1695 (C=O), 1635, 1500  $\text{cm}^{-1}$ ; uv  $\lambda_{\text{max}}$ : 270, 318 and 354 nm;  $^1\text{H}$  nmr (major isomer)  $\delta$ : 7.68 (s, 1H, ArH), 7.5-7.3 (m, 5H,  $-\text{CH}_2\text{C}_6\text{H}_5$ ), 7.13 (s, 1H, ArH), 6.78 (s, 1H Ar-CH=CN<sub>3</sub>COOMe), 6.58 (d,  $J=12.7\text{Hz}$ , 1H, H $\beta$ ), 5.90 (d,  $J=12.6\text{Hz}$ , 1H, H $\alpha$ ), 5.19 (s, 2H,  $-\text{CH}_2\text{C}_6\text{H}_5$ ), 3.92 (s, 3H, Ar-OCH<sub>3</sub>), 3.91 (s, 3H,  $-\text{COOCH}_3$ ) and 3.69 (s, 3H,  $-\text{CH}=\text{CH}-\text{OCH}_3$ ) ppm;  $^1\text{H}$  nmr (minor isomer)  $\delta$ : 7.64 (s, 1H, ArH), 7.5-7.3 (m, 5H,  $-\text{CH}_2\text{C}_6\text{H}_5$ ), 7.17 (s, 1H, ArH), 6.78 (s, 1H Ar-CH=CN<sub>3</sub>COOMe), 6.14 (d,  $J=7.6\text{Hz}$ , 1H, H $\beta$ ), 5.31 (d,  $J=7.6\text{Hz}$ , 1H, H $\alpha$ ), 5.24 (s, 2H,  $-\text{CH}_2\text{C}_6\text{H}_5$ ), 3.90 (s, 6H, Ar-OCH<sub>3</sub> +  $-\text{COOCH}_3$ ) and 3.67 (s, 3H,  $-\text{CH}=\text{CH}-\text{OCH}_3$ ) ppm; ms:  $m/z$  (%) 367 ( $\text{M}^+ - \text{N}_2$ , 32), 277 (19), 276 (77), 244 (29), 216 (24), 188 (18), 91 (100). Exact mass calcd for C<sub>21</sub>H<sub>21</sub>O<sub>5</sub>N: 367.1420 ( $\text{M}^+ - \text{N}_2$ ); found (ms): 367.1397.

Methyl 2-azido-3-(4-benzyloxy-2-(2,2-dimethoxyethyl)-5-methoxyphenyl)propenoate (13). A mixture of thionyl chloride (3 ml, 41.345 mmol) and dry methanol (40 ml) was added dropwise to a cold solution (ice-water bath) of crude **9** in dry THF (48 ml). After 5 h of stirring in a round-bottomed flask with a CaCl<sub>2</sub> tube, the mixture was neutralized with solid NaHCO<sub>3</sub> and abundant cold water was poured over it. The precipitate was filtered and dissolved in dichloromethane. This solution was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated to give crude **13**. As for **9**, strong light and heating must be avoided during the handling of **13**. In a separate run, some crude **13** was quickly purified using the same chromatographic method as for **9**. Eluting with dichloromethane afforded a 76% yield of **13**, mp 90-92°C; ir  $\nu_{\text{max}}$ : 2120, 1710 (C=O), 1610, 1590, 1510, 1410  $\text{cm}^{-1}$ ; uv  $\lambda_{\text{max}}$ : 238, 314 and 340 nm;  $^1\text{H}$  nmr  $\delta$ : 7.70 (s, 1H, ArH), 7.5-7.3 (m, 5H,  $-\text{CH}_2\text{C}_6\text{H}_5$ ), 7.17 (s, 1H, ArH), 6.79 (s, 1H Ar-CH=CN<sub>3</sub>COOMe), 5.19 (s, 2H,  $-\text{CH}_2\text{C}_6\text{H}_5$ ), 4.32 (t, 1H,  $J=5.5\text{Hz}$ ,  $-\text{CH}_2-\text{CH}-(\text{OCH}_3)_2$ ), 3.92 (s, 3H, Ar-OCH<sub>3</sub>), 3.90 (s, 3H,  $-\text{COOCH}_3$ ), 3.26 (s, 6H,  $-\text{CH}_2-\text{CH}-(\text{OCH}_3)_2$ ) and 2.88 (d, 2H,  $J=5.5\text{Hz}$ ,  $-\text{CH}_2-\text{CH}-(\text{OCH}_3)_2$ ) ppm; ms:  $m/z$  (%) 399 ( $\text{M}^+ - \text{N}_2$ , 6), 324 (9), 308 (20), 276 (7), 234 (14), 202 (9), 91 (55), 75 (100), 57 (12). Exact mass calcd for C<sub>22</sub>H<sub>25</sub>O<sub>6</sub>N: 399.1682 ( $\text{M}^+ - \text{N}_2$ ); found (ms): 399.1671.

Methyl 6-benzyloxy-4-(2,2-dimethoxyethyl)-7-methoxyindole-2-carboxylate (14). To dry boiling xylene (100 ml) under argon in a round-bottomed flask provided with a condenser, a hot solution of crude **13** in dry xylene (65 ml) was quickly added using a syringe. After refluxing for 1 h, the

xylene was evaporated and the brown tar obtained was subjected to flash chromatography ( $\text{CH}_2\text{Cl}_2$ -hexane, 1:1) on silica gel to obtain 3.425 g of **14** in 52% overall yield from **8**, mp 109°C; ir  $\nu_{\text{max}}$ : 1690 (C=O), 1625, 1515, 1360  $\text{cm}^{-1}$ ; uv  $\lambda_{\text{max}}$ : 236 and 310 nm;  $^1\text{H}$  nmr  $\delta$ : 8.93 (br s, 1H, NH), 7.5-7.3 (m, 5H,  $-\text{CH}_2\text{C}_6\text{H}_5$ ), 7.23 (d, 1H,  $J = 2.2$  Hz,  $\text{H}_3$ ), 6.83 (s, 1H,  $\text{H}_5$ ), 5.18 (s, 2H,  $-\text{CH}_2\text{C}_6\text{H}_5$ ), 4.61 (t, 1H,  $J = 5.6$  Hz,  $-\text{CH}_2\text{-CH-(OCH}_3)_2$ ), 4.01 (s, 3H, Ar-OCH<sub>3</sub>), 3.93 (s, 3H,  $-\text{COOCH}_3$ ), 3.31 (s, 6H,  $-\text{CH}_2\text{-CH-(OCH}_3)_2$ ) and 3.09 (d, 2H,  $J = 5.6$  Hz,  $-\text{CH}_2\text{-CH-(OCH}_3)_2$ ) ppm; ms:  $m/z$  (%) 399 ( $\text{M}^+$ , 10), 368 (6), 308 (37), 248 (6), 234 (30), 216 (11), 202 (24), 173 (7), 144 (6), 91 (60), 75 (100). Exact mass calcd for  $\text{C}_{22}\text{H}_{25}\text{O}_6\text{N}$ : 399.1682 ( $\text{M}^+$ ); found (ms): 399.1676.

Methyl 4-(2,2-dimethoxyethyl)-6-hydroxy-7-methoxyindole-2-carboxylate (5). A solution of **14** (692 mg, 1.734 mmol) in dry methanol (10 ml) was stirred with Raney nickel (200 mg) for 30 min (this caution must be taken to avoid Pd-C catalyst poisoning). The suspended solid was filtered out and washed with dry methanol (20 ml). 10% Pd-C (70 mg) was then added to the combined methanolic solutions, and the mixture was stirred for 5 h under hydrogen. The Pd-C was filtered out and the filtrate was concentrated. Flash chromatography ( $\text{CH}_2\text{Cl}_2$ ) on silica gel of the crude concentrate gave 478 mg of indole **5** (89% yield), mp 131-132°C; ir  $\nu_{\text{max}}$ : 3330 ( $-\text{OH}$ ), 1695 (C=O), 1625, 1525, 1445  $\text{cm}^{-1}$ ; uv  $\lambda_{\text{max}}$ : 249 and 311 nm;  $^1\text{H}$  nmr  $\delta$ : 9.16 (br s, 1H, NH), 7.24 (d, 1H,  $J = 2.2$  Hz,  $\text{H}_3$ ), 6.75 (s, 1H,  $\text{H}_5$ ), 5.9 (br s, 1H,  $-\text{OH}$ ), 4.68 (t, 1H,  $J = 5.6$  Hz,  $-\text{CH}_2\text{-CH-(OCH}_3)_2$ ), 3.95 (s, 3H, Ar-OCH<sub>3</sub>), 3.94 (s, 3H,  $-\text{COOCH}_3$ ), 3.35 (s, 6H,  $-\text{CH}_2\text{-CH-(OCH}_3)_2$ ) and 3.09 (d, 2H,  $J = 5.6$  Hz,  $-\text{CH}_2\text{-CH-(OCH}_3)_2$ ) ppm; ms:  $m/z$  (%) 309 ( $\text{M}^+$ , 7), 278 (5), 246 (3), 234 (4), 202 (11), 174 (2), 159 (4), 146 (2), 103 (3), 89 (2), 75 (100). Exact mass calcd for  $\text{C}_{15}\text{H}_{19}\text{O}_6\text{N}$ : 309.1212 ( $\text{M}^+$ ); found (ms): 309.1223.

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