

AN ALTERNATIVE METHOD FOR SYNTHESIS OF THE CC-1065
PHARMACOPHORE, 1,2,7,7a-TETRAHYDROCYCLOPROP[1,2-*c*]INDOL-
4-ONE

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Abstract-The synthesis of the CC-1065 pharmacophore, 2-(1-methylpyrrole-2-carbonyl)-1,2,7,7a-tetrahydrocycloprop[1,2-*c*]indol-4-one (**17**), is described. The methods reported here provide an alternative route for the synthesis of compounds possessing the biologically active 1,2,7,7a-tetrahydrocycloprop[1,2-*c*]indol-4-one (CI) functionality.

CC-1065, an antibiotic isolated from *Streptomyces zelensis*,¹ is extremely potent against a variety of tumor cell lines both *in vitro* and *in vivo*.² The chemical synthesis of CC-1065 and its structural analogues as well as their mechanism(s) of antitumor activity have been extensively investigated in recent years.³ CC-1065 has been found to bind to double-stranded B-DNA within the minor groove with the sequence preference of 5'-d(A/GNTTA)-3' and 5'-d(AAAAA)-3' and to alkylate the *N*-3 position of the 3'-adenine via the activated cyclopropane moiety of the CPI left-hand unit present in the antibiotic.⁴ Despite its high potency, CC-1065 cannot be used in humans because it was found that it caused delayed death in experimental animals. In the search for compounds with improved antitumor selectivity and DNA sequence-specific binding properties, many CC-1065 analogues have been synthesized in attempts to avoid its undesirable side-effects but to maintain its cytotoxic potency against tumor cells.^{5, 3b} Amongst the analogues reported are those possessing the 1,2,7,7a-

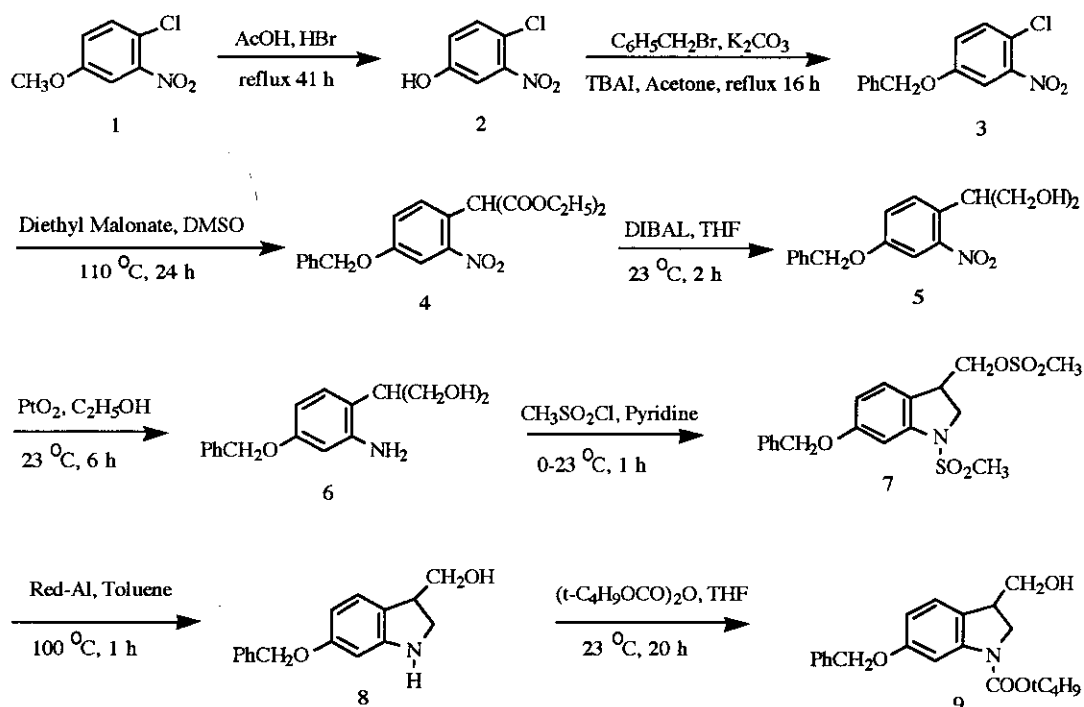
tetrahydrocycloprop[1,2-c]indol-4-one (CI) functional group.^{5g} It has been shown that the sequence-specific DNA-binding properties of these functional analogues and CC-1065 are remarkably similar suggesting that the CI unit is the minimum structural requirement for the expression of cytotoxicity (or pharmacophore) in the CC-1065 and its analogues.^{6, 5f} During the course of chemical synthesis of compounds possessing this essential biologically active CI functionality, we encountered difficulty to remove the benzyl group from 6-benzyloxy-1-*tert*-butyloxycarbonyl-3-methanesulfonyloxymethylindoline by catalytic hydrogenation using the reported method.^{5g} This prompted us to search for an alternative method to synthesize the desired product. Accordingly, we report an alternative and convenient chemical route for the synthesis of compounds possessing the biologically active CI functionality.

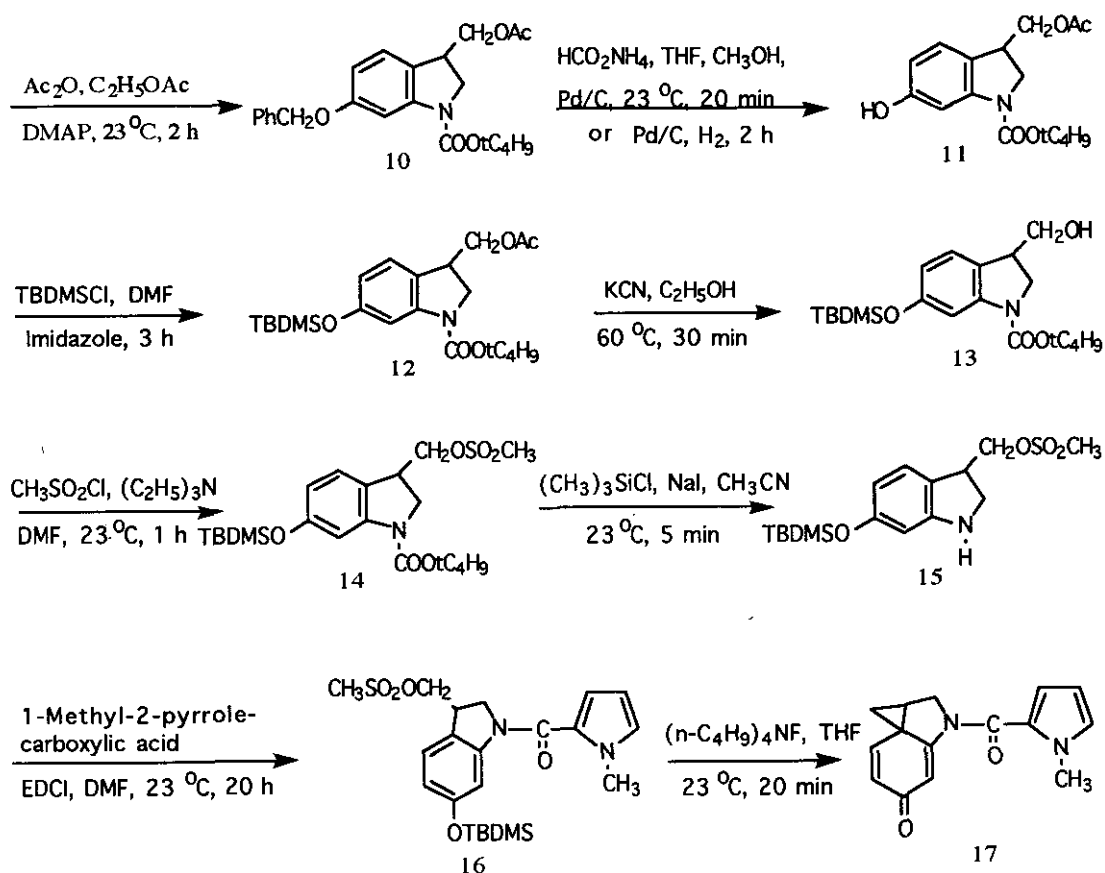
Compounds (2-7) were synthesized according the procedure by Warpehoski *et al.* (Scheme 1).⁵ⁱ The air sensitive compound (8) obtained by reductive cleavage of the methanesulfonyl group was allowed to react with di-*tert*-butyl dicarbonate to give 9.⁵ⁱ The hydroxy group of 9 was protected by reaction with acetic anhydride in the presence of 4-dimethylaminopyridine to afford 10 in high yield. The benzyl group of 10 was selectively removed either by catalytic hydrogenolysis or phase transfer hydrogenolysis using ammonium formate as hydrogen donor.^{5c} Both methods give quantitative yields. Compound (11) was converted to 12 by treating with *tert*-butyldimethylsilyl chloride in the presence of imidazole.⁷ The acetal group of the latter was selectively removed by transesterification in ethanol catalyzed by potassium cyanide.⁸ High temperature or prolonged heating also removes the *tert*-butyldimethylsilyl group. The *tert*-butoxy group is not affected under the reaction conditions. Compound (13) was allowed to react with methanesulfonyl chloride in the presence of triethylamine to afford 14. The removal of the *tert*-butoxycarbonyl group from 14 was effected by *in situ* generated trimethylsilyl iodide by mixing trimethylsilyl chloride and sodium iodide together to give the unstable 15.⁹ Without further purification the latter compound was coupled directly to the model compound 1-methyl-2-pyrrolecarboxylic acid in the presence of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide to afford 16 which proved to be quite stable to flash chromatography (SiO₂).^{5c, i} Product (16) was cyclized in the presence of *tert*-butylammonium fluoride to generated the desired final product (17) in high yield. The

cyclized **17** is very unstable to chromatographic purification (SiO_2) but can be purified by sequential extraction with hexane and ethyl ether without causing decomposition.

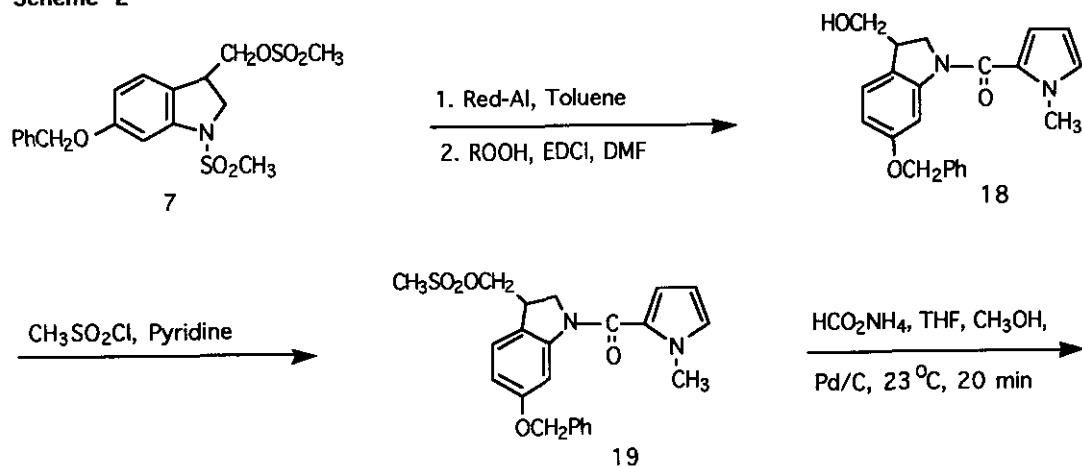
Although the synthesis of the target compound was achieved, the overall yield was not satisfactory. Therefore, another route was pursued to achieve the final goal (Scheme 2). Compound (**7**) was treated with sodium bis(2-methoxyethoxy)aluminum hydride by refluxing in toluene and then coupled with 1-methyl-2-pyrrolecarboxylic acid to produce **18** which was then treated with methanesulfonyl chloride in pyridine to afford **19**. The benzyloxy protecting group of **19** was removed by phase transfer hydrogenolysis to give **20** which was then treated with *tert*-butyldimethylsilyl chloride in the presence of imidazole to give **16**. The overall yield using this method was significantly improved and now represents a convenient route to the powerfully biologically reactive Cl moiety.

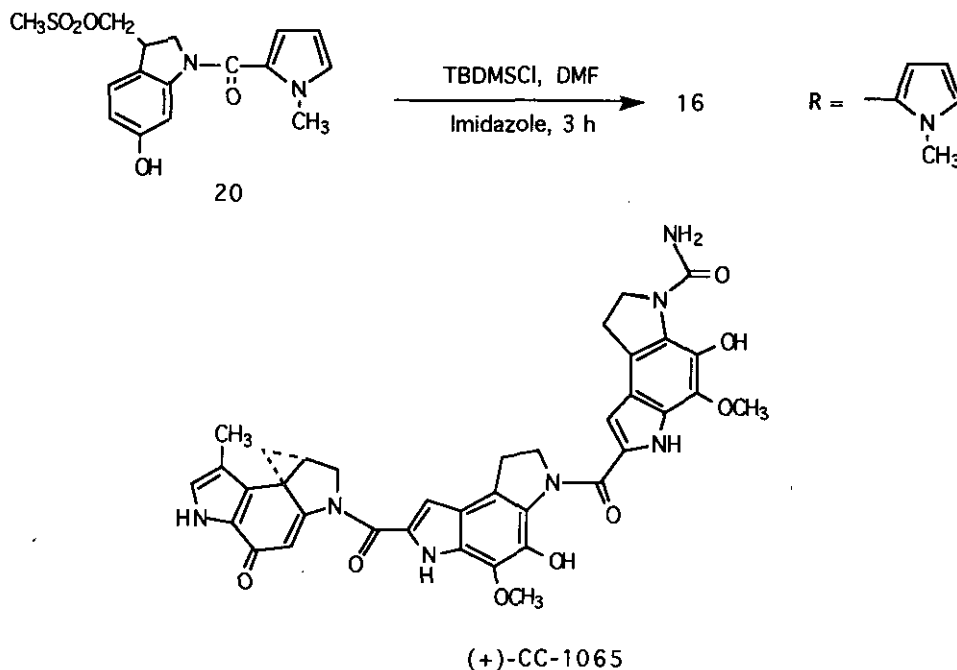
Scheme 1





Scheme 2





EXPERIMENTAL Melting points were determined using an Electrohome apparatus and are uncorrected. Nmr spectra were recorded at ambient temperature on a Bruker WH-300 spectrometer. High resolution electron impact ionization (EIHRms) mass spectra were recorded on an Associated Electrical Industries (AEI) MS-50 spectrometer. Analytical thin layer chromatography was performed on silica-coated plastic plates (silica gel 60 F-254, Merck) and visualized under uv light. Preparative separations were performed by flash chromatography on silica gel (Merck, 70-230 or 230-400 mesh). Acetone was obtained by distillation from P_2O_5 . Tetrahydrofuran was dried by distillation from sodium-benzophenone ketyl. Dimethylformamide and triethylamine were dried over molecular sieves (4A) before use. The above solvents were stored over molecular sieves (4A). All other solvents were used as received and were reagent grade where available.

4-Chloro-3-nitrophenol(2), 1-Chloro-2-nitro-4-benzyloxybenzene (3), Diethyl (4-benzyloxy-2-nitrophenyl)malonate (4), 2-(4-Benzyloxy-2-nitrophenyl)propane-1,3-diol

(5), 2-(2-Amino-4-benzyloxyphenyl)propane-1,3-diol (6), and 6-Benzyloxy-2,3-dihydro-1-(methylsulfonyl)-1*H*-indole-3-methanol, Methanesulfonate (7). The above compounds were synthesized according to the methods by Warpehoski et al.⁵ⁱ and the ¹H nmr and ms spectra were in agreement with their chemical structures.

6-Benzyloxy-1-*tert*-butyloxycarbonyl-2,3-dihydro-1*H*-indole-3-methanol, methanesulfonate (9). To 1g (2.4 mmol) of compound (7) dissolved in tetrahydrofuran (20 ml) was added toluene (50 ml) under nitrogen and 3.4 M solution of sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al) in toluene (5 ml, 17 mmol). The solution was heated to 100 °C under nitrogen for 1 h. The reaction mixture was cooled to room temperature and quenched by ice (5 g). H₂O (150 ml, saturated by nitrogen) was added and the pH of the solution was adjusted to 8 using NaHCO₃. The product was extracted by ethyl acetate (200 ml x 3, saturated by nitrogen) and the organic phase was dried over Na₂SO₄. The solvent was evaporated and the product was taken up by tetrahydrofuran (20 ml). Di-*tert*-butyl dicarbonate (5 ml, 22 mmol) was added immediately and the reaction mixture was stirred at room temperature for 20 h. The product was purified by flash chromatography eluted with ethyl acetate and hexane (1/1). Product (9) is a colorless oil (0.82 g, 95% yield). ¹H Nmr (CDCl₃, ppm): 7.69 (br s, 1 H, C7-H), 7.47-7.31 (m, 5H, C₆H₅), 7.10-7.08 (dd, 1 H, J = 8.0, 0.6 Hz, C4-H), 6.62-6.58 (dd, 1 H, J = 8.0, 2.0 Hz, C5-H), 5.08 (s, 2 H, OCH₂C₆H₅), 4.11-4.04 (dd, 1 H, J = 11.5, 10.0 Hz, NCHH), 3.93-3.87 (dd, 1 H, J = 11.5, 5.0 Hz, NCHH), 3.75-3.73 (m, 2 H, CH₂OH), 3.44 (m, 1 H, CHCH₂OH), 1.56 (s, 9 H, OC(CH₃)₃); EIHRms calcd for C₂₁H₂₅NO₄ 355.1785, found 355.1786.

6-Benzyloxy-1-*tert*-butyloxycarbonyl-3-acetoxymethylindoline (10). To a solution of 9 (0.5 g, 1.4 mmol) and 4-dimethylaminopyridine (50 mg, 0.41 mmol) in ethyl acetate (5 ml), was added acetic anhydride (0.146 ml, 1.55 mmol). The reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated and the product was purified by flash chromatography eluting with ethyl acetate. Product (10) was obtained as a colorless oil (0.55 g, 98% yield). ¹H Nmr (CDCl₃, ppm): 7.69 (br s, 1 H, C7-H), 7.47-7.31 (m, 5H, C₆H₅), 7.10-7.08 (dd, 1 H, J = 8.0, 0.6 Hz, C4-H), 6.62-6.58 (dd, 1 H, J = 8.0, 2.0 Hz, C5-H), 5.08 (s, 2 H, OCH₂C₆H₅), 4.29-4.24 (dd, 1 H, J = 11.0, 5.0 Hz, NCHH), 4.13-4.04 (m, 2 H, NCHH,

CHHOCO), 3.71 (br s, 1 H, CHHOCO), 3.63-3.54 (m, 1 H, $\text{OCH}_2\text{CHCH}_2\text{N}$), 2.11 (s, OCOCH_3), 1.59 (s, 9 H, $\text{OC}(\text{CH}_3)_3$); EIHRms calcd for $\text{C}_{23}\text{H}_{27}\text{NO}_5$ 397.1917, found 397.1894.

6-Hydroxy-1-tert-butyloxycarbonyl-3-acetoxymethylindoline (11). Method a: To a solution of **10** (0.47 g, 1.18 mmol) in tetrahydrofuran (10 ml) and methanol (10 ml) was added 10% Pd/C (0.5 g) and ammonium formate (0.5 g) respectively. The mixture was stirred at room temperature for 20 min. The solid product was then collected and the solid was washed with methanol. The solvent was evaporated and the product was extracted from H_2O (20 ml) using ethyl acetate (20 ml x 4). The organic phase was dried over Na_2SO_4 and concentrated to 0.36 g (quantitative yield) of an colorless oil. Method b: 0.5 g (1.26 mmol) of **10** was dissolved in 20 ml of ethyl acetate and 0.1 g of 10% Pd/C was added. The mixture was subjected to hydrogenation at 40 lb/inch² for 2 h. The solid product was collected and washed with methanol. The solvent was removed by evaporation and 0.385 g of product **11** was obtained (quantitative yield). ¹H Nmr (CDCl_3 , ppm): 7.44 (br s, 1 H, C7-H), 7.04-7.01 (dd, 1 H, $J = 8.0, 0.6$ Hz, C4-H), 6.47-6.44 (dd, 1 H, $J = 8.0, 1.5$ Hz, C5-H), 4.26-4.20 (dd, 1 H, $J = 10.5, 5.5$ Hz, NCHH), 4.10-4.01 (m, 2 H, NCHH , CHHOCO), 3.79 (br s, 1 H, CHHOCO), 3.60-3.51 (m, 1 H, $\text{OCH}_2\text{CHCH}_2\text{N}$), 2.10 (s, OCOCH_3), 1.58 (s, 9 H, $\text{OC}(\text{CH}_3)_3$); EIHRms calcd for $\text{C}_{16}\text{H}_{21}\text{NO}_5$ 307.1420, found 307.1427.

6-tert-Butyldimethylsilyoxy-1-tert-butyloxycarbonyl-3-acetoxymethylindoline (12). *tert*-Butyldimethylsilyl chloride (212 mg, 1.41 mmol) was added to a solution of **11** (0.36 g, 1.17 mmol) and imidazole 200 mg (2.94 mmol) in dimethylformamide (1.5 ml). The reaction mixture was stirred at room temperature for 3 h. The reaction was quenched with water (20 ml) and extracted with ethyl acetate (50 ml x 3). The organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography using ethyl acetate and hexane (1/5, v/v) as an eluent. Product (**12**) is an colorless oil (0.378 g, 76% yield). ¹H Nmr (CDCl_3 , ppm): 7.30 (br s, 1 H, C7-H), 7.03-7.01 (dd, 1 H, $J = 8.0, 0.6$ Hz, C4-H), 6.46-6.42 (dd, 1 H, $J = 8.0, 2.0$ Hz, C5-H), 4.25-4.22 (dd, 1 H, $J = 10.5, 5.5$ Hz, NCHH), 4.12-4.02 (m, 2 H, NCHH , CHHOCO), 3.82 (br s, 1 H, CHHOCO), 3.60-3.51 (m, 1 H, $\text{OCH}_2\text{CHCH}_2\text{N}$), 2.10 (s,

OCOCH₃), 1.58 (s, 9 H, OC(CH₃)₃), 0.99 (s, 9 H, Si(CH₃)₃), 0.21 (s, 6 H, Si(CH₃)₂); EIHRms calcd for C₂₂H₃₅NO₅Si 421.2286, found 421.2299.

6-*tert*-Butyldimethylsilyoxy-1-*tert*-butyloxycarbonyl-3-hydroxymethylindoline (13).

Potassium cyanide (200 mg, 3.07 mmol) was added to a solution of 12 (0.378 g, 0.9 mmol) in 95% ethanol (10 ml) and the reaction mixture was heated to 60 °C. The progress of the reaction was followed by tlc (20% ethyl acetate in hexane) for every 5 min. The reaction was quenched by water (20 ml) after 30 min and extracted with ethyl acetate (20 ml x 4). The organic phase was dried over Na₂SO₄ and concentrated. The residue was purified by flash chromatography eluting with ethyl acetate and hexane (1/6, v/v). 0.254 g (75% yield) of 13 was obtained as a colorless oil and 84.2 mg of starting material was recovered. ¹H Nmr (CDCl₃, ppm): 7.40 (br s, 1 H, C7-H), 7.00-6.98 (d, 1 H, J = 8.0 Hz, C4-H), 6.41-6.37 (dd, 1 H, J = 8.0, 2.0 Hz, C5-H), 4.10-4.03 (t, 1 H, J = 10.0 Hz, NCHH), 3.91-3.85 (dd, 1 H, J = 11.5, 5.0 Hz, NCHH), 3.75-3.73 (dd, 2 H, J = 6.0, 2.0 Hz, CH₂OH), 3.46-3.37 (m, 1 H, OCH₂CHCH₂N), 1.54 (s, 9 H, OC(CH₃)₃), 0.96 (s, 9 H, Si(CH₃)₃), 0.18 (s, 6 H, Si(CH₃)₂); EIHRms calcd for C₂₀H₃₃NO₄Si 379.2179, found 379.2183.

6-*tert*-Butyldimethylsilyoxy-1-*tert*-butyloxycarbonyl-3-methanesulfonyloxymethylindoline (14).

To a solution of 13 (191 mg, 0.51 mmol) in dimethylformamide (0.5 ml) cooled to 0 °C under nitrogen was added methanesulfonyl chloride (58 µl, 0.76 mmol) and triethylamine (0.105 ml, 0.76 mmol), respectively. The reaction mixture was warmed to room temperature and stirred for 1 h. The reaction was quenched by water (10 ml) and extracted with ethyl acetate (20 ml x 4). The organic phase was dried over Na₂SO₄ and concentrated. The residue was purified by flash chromatography eluting with ethyl acetate and hexane (1/4, v/v). 172 mg (75% yield) of 14 was obtained as an oil. ¹H Nmr (CDCl₃, ppm): 7.40 (br s, 1 H, C7-H), 7.00-6.98 (dd, 1 H, J = 8.0, 0.6 Hz, C4-H), 6.41-6.37 (dd, 1 H, J = 8.0, 2.0 Hz, C5-H), 4.35-4.30 (dd, 1 H, J = 10.0, 5.0 Hz, NCHH), 4.21-4.15 (dd, 1 H, J = 10.0, 8.0 Hz, NCHH), 4.12-4.05 (m, 1 H, CHHOS), 3.92-3.86 (m, 1 H, CHHOS), 3.69-3.59 (m, 1 H, OCH₂CHCH₂N), 2.94 (s, 3 H, SO₂CH₃), 1.55 (s, 9 H, OC(CH₃)₃), 0.95 (s, 9 H, Si(CH₃)₃), 0.17 (s, 6 H, Si(CH₃)₂); EIHRms calcd for C₂₁H₃₅NO₆SSi 457.1956, found 457.1945.

6-*tert*-Butyldimethylsilyoxy-1-(1'-methyl-2'-pyrrolicarboxy)-3-methanesulfonyloxy-methylindoline (16). Method (a). Trimethylsilyl chloride (13.3 μ l, 0.105 mmol) was added to a mixture of **14** (40 mg, 0.0875 mmol) and sodium iodide (26 mg, 0.175 mmol) stirred under nitrogen in acetonitrile (2 ml). The reaction mixture was stirred for 40 min and quenched with sodium thiosulfate (30 mg) and methanol (1 ml). The reaction was stirred for 5 more min and then loaded onto a filter filled with SiO₂ (10 g). The product was eluted with ethyl acetate (50 ml) and the solvent was evaporated. Without further purification, the product was dissolved in dimethylformamide (2 ml) under nitrogen and 1-methyl-2-pyrrolicarboxylic acid (12 mg, 0.096 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (80 mg, 0.42 mmol) were added respectively. The reaction mixture was stirred at room temperature for 20 h. The reaction mixture was concentrated and purified by thin layer chromatography (SiO₂, 2 mm) eluting with ethyl acetate and hexane (1/3, v/v). 22.1 mg (54% yield) of product **16** was obtained. Method (b). Compound (**16**) was also synthesized using a procedure similar to that described for **12**. The yield was 75%. ¹H Nmr (CDCl₃, ppm): 7.38 (br s, 1 H, C7-H), 7.09-7.06 (d, 1 H, J = 8.0 Hz, C4-H), 6.78-6.76 (t, 1H, J = 2.0 Hz, C3'-H), 6.62-6.60 (dd, 1 H, J = 4.0, 2.0 Hz, C5'-H), 6.54-6.51 (dd, 1 H, J = 8.0, 2.0 Hz, C5-H), 6.15-6.13 (dd, 1H, J = 4.0, 2.5 Hz, C4'-H), 4.45-4.33 (m, 2 H, NCH₂), 4.25-4.17 (m, 2 H, CH₂OS), 3.87 (s, 3 H, NCH₃), 3.69-3.61 (m, 1 H, OCH₂CHCH₂N), 2.94 (s, 3 H, SO₂CH₃), 0.96 (s, 9 H, SiC(CH₃)₃), 0.18 (s, 6 H, Si(CH₃)₂); EIHRms calcd for C₂₂H₃₂N₂O₅SSi 464.1803, found 464.1816.

2-(1-Methylpyrrole-2-carbonyl)-1,2,7,7a-tetrahydrocycloprop[1,2-c]indol-4-one

(**17**). To a solution of **16** (15.8 mg, 0.034 mmol) in tetrahydrofuran (6.8 ml) was added 1 M solution of *tert*-butylammonium fluoride (0.031 ml, 31 mmol) in tetrahydrofuran and the reaction mixture was stirred at room temperature for 20 min. The solvent was removed at room temperature. The product is not stable to chromatographic purification (SiO₂). Therefore, the residue was extracted with hexane (2 ml x 2) and then with ethyl ether (2 ml x 10) sequentially. Most of the desired product had been extracted by ether. The ether was removed by blowing nitrogen into the flask affording 7 mg (81% yield) of pure **17**. ¹H Nmr (CDCl₃, ppm): 6.79-6.77 (t, 1 H, J = 2.0 Hz, C2'-H), 6.64-6.62 (dd, 1H, J = 4.0, 2.0 Hz, C5'-H), 6.57-6.54 (d, 1

H), 6.40-6.36 (dd, 1 H, $J = 10.0, 2.0$ Hz, C5-H), 6.22-6.20 (d, 1H, $J = 2.0$ Hz, C3-H), 6.09-6.07 (dd, 1 H, $J = 4.0, 2.5$ Hz, C4'-H), 4.25-4.19 (dd, 1 H, $J = 11.5, 5.0$ Hz, C1-HH), 4.04-4.00 (d, 1 H, $J = 11.5$ Hz, C1-HH), 3.84 (s, 3 H, NCH₃), 2.59-2.53 (dt, 1 H, $J = 7.7, 5.0$ Hz, C7a-H), 1.81-1.77 (dd, 1 H, $J = 7.5, 4.5$ Hz, C7-HH), 1.56-1.53 (t, 1H, $J = 5.0$ Hz, C7-HH); EIHRms calcd for C₁₅H₁₄N₂O₂ 254.1056, found 254.1049.

6-Benzoyloxy-3-hydroxymethyl-1-(N-methyl-2-pyrrolicarboxy)indoline (18). 18 was synthesized using the same methods described for 8 and 16. The yield was 48%. ¹H Nmr (CDCl₃, ppm): 7.68 (br s, 1 H, C7-H), 7.43-7.28 (m, 5H, C₆H₅), 7.12-7.10 (d, 1 H, $J = 8.0$ Hz, C4-H), 6.76-6.75 (t, 1H, $J = 2.0$ Hz, C3'-H), 6.68-6.62 (m, 2H, C5'-H, C5-H), 6.15-6.12 (dd, 1H, $J = 4.0, 2.5$ Hz, C4'-H), 5.05 (s, 2H, C₆H₅CH₂), 4.43-4.36 (dd, 1H, $J=11.0, 9.0$ Hz, NCHH), 4.27-4.21 (dd, 1H, $J=11.0, 5.0$ Hz, NCHH), 3.86 (s, 3 H, NCH₃), 3.78 -3.67 (m, 2H, CH₂OH), 3.47-3.38 (m, 1 H, OCH₂CHCH₂N), EIHRms calcd for C₂₂H₂₂N₂O₃ 362.1632, found 362.1632.

6-Benzoyloxy-1-(N-methyl-2-pyrrolicarboxy)-3-methanesulfonyloxymethylindoline (19). 19 was synthesized using the same method described for 14. The yield was 49%. ¹H Nmr (CDCl₃, ppm): 7.68 (d, $J=2.0$ Hz, 1H, C7-H), 7.44-7.31 (m, 5H, C₆H₅), 7.17-7.13 (d, 1 H, $J = 8.0$ Hz, C4-H), 6.79-6.78 (t, 1H, $J = 2.0$ Hz, C3'-H), 6.70-6.67 (dd, $J=8.0, 2.0$ Hz, C5-H), 6.64-6.62 (dd, 1H, $J = 5.0, 1.5$ Hz, C5'-H), 6.17-6.15 (dd, 1H, $J = 4.0, 2.5$ Hz, C4'-H), 5.05 (s, 2H, C₆H₅CH₂), 4.48-4.33 (m, 2H, SO₂CH₂), 4.27-4.17 (m, 2H, NCH₂), 3.87 (s, 3 H, NCH₃), 3.70 -3.64 (m, 1 H, OCH₂CHCH₂N), 2.95 (s, 3H, SO₂CH₃), EIHRms calcd for C₂₃H₂₄N₂O₅S 440.1407, found 440.1398.

6-Hydroxy-1-(N-methyl-2-pyrrolicarboxy)-3-methanesulfonyloxymethylindoline (20). The benzyl group was removed by phase-transfer hydrogenation as described for 11. The yield was quantitative. ¹H Nmr (CDCl₃, ppm): 7.70 (d, 1H, $J=2.0$ Hz, C7-H), 7.12-6.99 (d, 1 H, $J = 8.0$ Hz, C4-H), 6.81-6.79 (t, 1H, $J = 2.0$ Hz, C3'-H), 6.64-6.62 (dd, $J=5.0, 1.5$ Hz, C5'-H), 6.59-6.56 (dd, 1H, $J = 8.0, 2.0$ Hz, C5-H), 6.34 (br s, 1H, OH), 6.18-6.15 (dd, 1H, $J = 4.0, 2.5$ Hz, C4'-H), 4.48-4.32 (m, 2H, SO₂CH₂), 4.27-4.16

3.87 (s, 3 H, NCH₃), 3.69 -3.63 (m, 1 H, OCH₂CHCH₂N), 2.94 (s, 3H, SO₂CH₃), EIHRms calcd for C₁₆H₁₈N₂O₅ 350.0937, found 350.10937.

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