

## SYNTHESIS OF INDOLE-FUSED 4-PYRIDONE-3-CARBOXYLIC ACIDS

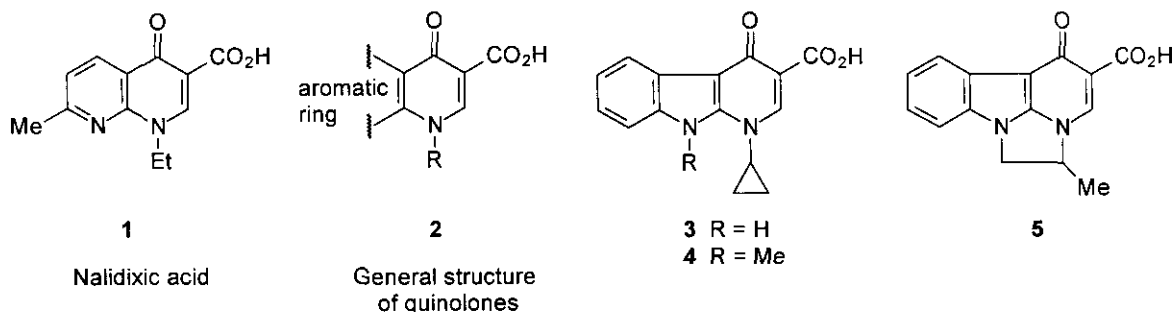
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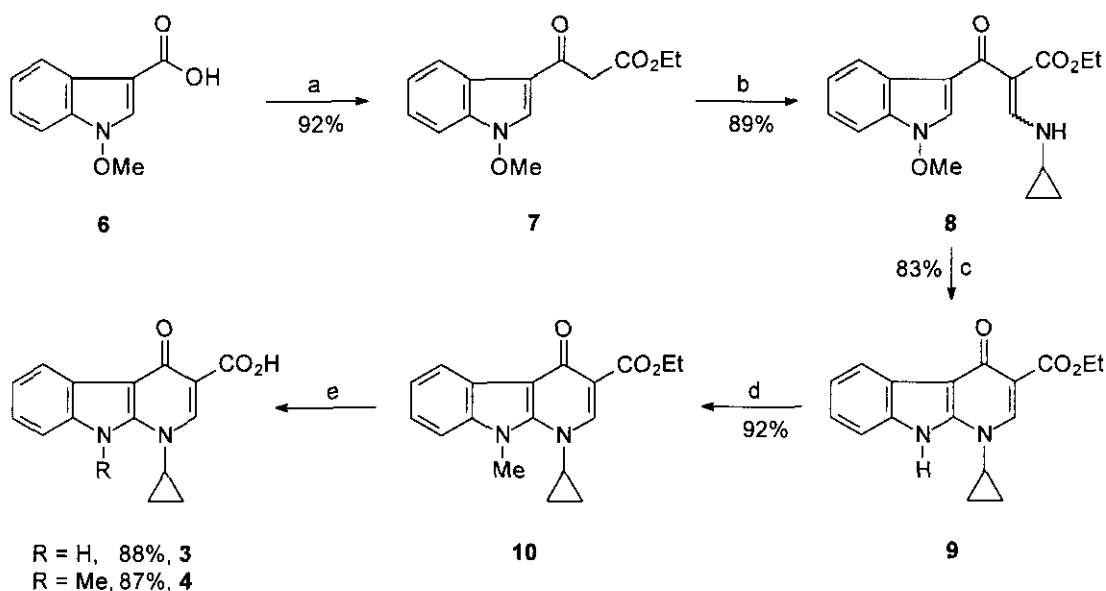
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**Abstract** - Some indole-fused tri- and tetracyclic 4-oxo-pyridine-3-carboxylic acids, quinolone-type derivatives, (3), (4), and (5) have been prepared. The synthesis is characterized by the construction of the pyridone ring through the intramolecular nucleophilic displacement cyclization at the 2-position of 3-substituted 1-methoxyindole accompanied with demethoxylation.

The quinolones, a member of biologically active heterocyclic compounds, have become one of the most promising group of antibacterial drugs in the chemotherapeutic arsenal<sup>1</sup> since the introduction of nalidixic acid (1)<sup>2</sup> in the treatment of urinary tract infections. Many analogues including 6-fluoroquinolones like norfloxacin,<sup>3</sup> amifloxacin,<sup>4</sup> ciprofloxacin,<sup>5</sup> ofloxacin,<sup>6</sup> and tosufloxacin,<sup>7</sup> which involve peripheral and nuclear modifications of 1,8-naphthyridine structure have been developed with potent broad



spectrum activity and good oral efficacy.<sup>8</sup> Several methods are available for the construction of quinolone skeleton; Gould-Jacobs reaction using a condensate derived from an appropriate aromatic amine and diethyl ethoxymethylenemalonate,<sup>9</sup> cyclization of an benzoylaminoacrylate derivative using a suitable base,<sup>5,10</sup> and etc.<sup>11</sup> As shown in the structure (2), a 1-substituted 1,4-dihydro-4-oxopyridine-3-carboxylic acid with an annelated aromatic or heteroaromatic ring<sup>1a,12</sup> such as benzene, pyridine, thiophene, pyrrole, or imidazole derivatives fused at the 5, 6-position is the basic structure of this class of antibacterial agents. However, to our knowledge, the indole-fused analogues of the general formula (2) have never been prepared. As part of our ongoing research to find potent antibacterial agents and useful synthetic methods of heterocyclic compounds, we synthesized fused tri- and tetracyclic 4-pyridone-3-carboxylic acids, quinolone-type derivatives (3), (4), and (5) having an indole moiety as an annelated heteroaromatic ring which were viewed as analogues of 1, respectively. The present investigation was focused on the development of indole-fused 4-pyridone-3-carboxylic acid compounds. Scheme 1 shows the synthesis of tricyclic derivatives (3) and (4).

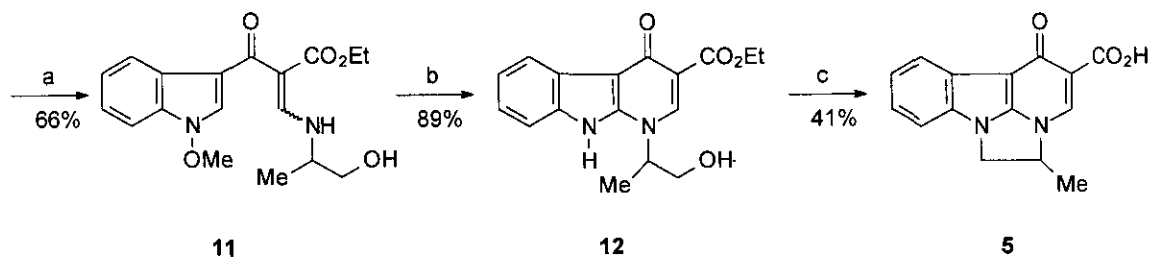


#### Reagents and conditions

<sup>a</sup> (1)  $(\text{COCl})_2$  (2)  $\text{EtO}_2\text{CCH}_2\text{CO}_2\text{H}/n\text{-BuLi}$  (3)  $\text{H}^+$  <sup>b</sup> (1)  $\text{CH}(\text{OEt})_2/\text{Ac}_2\text{O}$  (2)  $\text{C}_3\text{H}_5\text{NH}_2$  <sup>c</sup>  $\text{NaH}$   
<sup>d</sup>  $\text{MeI}/\text{K}_2\text{CO}_3$  <sup>e</sup>  $\text{NaOH}$

Scheme 1

Reaction of 1-methoxy-1*H*-3-indolecarboxylic acid (**6**)<sup>13</sup> with oxalyl chloride afforded the corresponding acid chloride, which, without purification, reacted with dilithio dianion of monoethyl malonate<sup>14</sup> to give the ethyl 3-(1-methoxy-1*H*-3-indolyl)-3-oxopropanoate (**7**) in good yield. Treatment of **7** with triethyl orthoformate by refluxing in acetic anhydride gave the enol ether intermediate, which reacted *in situ* with cyclopropylamine to give the ethyl propenoate derivative (**8**). The compound (**8**) was an approximately 1:1 mixture of (*Z*)- and (*E*)-geometrical isomers based on the integration of characteristic <sup>1</sup>H NMR signals. Synthesis of the pyridine nucleus bearing an indole moiety (**9**) from the compound (**8**) was accomplished in good yield with sodium hydride in DMF at room temperature by using the procedure described by Somei *et al.*<sup>15</sup> Treatment of **9** with methyl iodide and potassium carbonate gave the corresponding *N*-methyl derivative (**10**) in a high yield, which was hydrolyzed with aqueous sodium hydroxide to give the *N*-methyl acid derivative (**4**) in 87% yield. In the same method, the acid derivative (**3**) was prepared from the precursor ester (**9**) in 88% yield.



#### Reagents and conditions

<sup>a</sup> (1) CH(OEt)<sub>3</sub>/Ac<sub>2</sub>O (2) MeCH(NH<sub>2</sub>)CH<sub>2</sub>OH <sup>b</sup> NaH <sup>c</sup> (1) PPh<sub>3</sub>/CCl<sub>4</sub>/Et<sub>3</sub>N (2) NaOH

#### Scheme 2

By analogy with the synthesis of tricyclic compounds (**3**) and (**4**), the tetracyclic acid derivative (**5**) was prepared as shown in **Scheme 2**. The requisite compound (**12**) was also prepared in moderate yield from **7** using 2-amino-1-propanol and then cyclization of **11** by the same procedure as that for the synthesis of **9** from **8**. Finally, the tetracyclic acid product (**5**) was obtained in moderate yield by the treatment of **12** with triphenylphosphine and carbon tetrachloride in boiling acetonitrile under anhydrous

conditions,<sup>16</sup> followed by the hydrolysis of the resulting ester. The pharmacology of these compounds (3), (4), and (5) and the synthesis of substituted indole-fused analogues are presently under study.

## EXPERIMENTAL

<sup>1</sup>H NMR (300 MHz) spectra were obtained on a Varian Gemini 300 spectrometer and chemical shifts are noted as  $\delta$  (ppm) units relative to tetramethylsilane as an internal standard. Melting points (mp) were determined on a Thomas-Hoover capillary or Electrochemical melting point apparatus and are uncorrected. IR spectra were obtained on a Perkin Elmer 16F PC FT-IR and frequencies are given in reciprocal centimeters ( $\text{cm}^{-1}$ ). Electron-impact mass spectra (EIMS) were recorded in the form of  $m/z$  (intensity relative to base = 100) on a Hewlett Packard GC-MSD (5890II-5972) system. High resolution mass spectra (HRMS) were determined on a VG70-VSEQ mass spectrometer. Elementary analyses were obtained on a FISON S EA 1108. All chromatographic isolations were accomplished by flash chromatography using silica gel (Merck 9385, 230~400 mesh). The new solid compounds were recrystallized from a 1:1 mixture of methanol and methylene chloride. All reactions were monitored by TLC on glass plates coated with a 0.25 mm layer of silica gel (Merck 60-F254). All solvents were dried according to the general procedures and stored under a nitrogen atmosphere.

### 1-Methoxy-1*H*-3-indolecarbonyl chloride

To a stirred solution of 1-methoxy-1*H*-3-indolecarboxylic acid (6) (1.50 g, 7.85 mmol) and DMF (one drop) in  $\text{CH}_2\text{Cl}_2$  (50 mL) was slowly added oxalyl chloride (1.03 mL, 11.8 mmol) at rt. The reaction mixture was stirred at the same temperature for 3 h and concentrated under reduced pressure to afford yellow residue, 1-methoxy-1*H*-3-indolecarbonyl chloride (1.63 g, 99%), which was used directly without further purification.

### Ethyl 3-(1-methoxy-1*H*-3-indolyl)-3-oxopropanoate (7)

To a stirred solution of monoethyl malonate (670 mg, 5 mmol) and biquinoline (1 mg) in

dry THF (15 mL) at  $-70^{\circ}\text{C}$  was slowly added a solution of 1.6 M *n*-BuLi in hexane (5.6 mL) until a pink color remained at  $-5^{\circ}\text{C}$  under nitrogen atmosphere. To the cooled reaction mixture at  $-70^{\circ}\text{C}$  was slowly added a solution of 1-methoxy-1*H*-3-indolecarbonyl chloride (530 mg, 2.5 mmol) in THF (50 mL). Upon addition, the dry ice bath was removed and the reaction mixture was allowed to warm up to rt. The reaction mixture was acidified with 1 N hydrochloric acid (5 mL) and extracted with ethyl acetate (50 mL). The ethyl acetate fraction was washed with saturated aqueous sodium bicarbonate solution and then water. The organic layer was dried over  $\text{MgSO}_4$  and evaporated to dryness under reduced pressure. The residue was purified by column chromatography on silica gel using benzene/EtOAc (20/1) mixture as an eluent to yield **7** as a pale yellow oil (670 mg, 92 %):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  = 1.27 (t, 3H,  $J=7.1$  Hz), 3.85 (s, 2H), 4.18 (s, 3H), 4.21 (q, 2H,  $J=7.1$  Hz), 7.31~7.36 (m, 2H), 7.45~7.47 (m, 1H), 7.99 (s, 1H), 8.36~8.39 (m, 1H); IR (KBr)  $\nu$  = 1370, 1514, 1654, 1740, 2982  $\text{cm}^{-1}$ ; EIMS  $m/z(\%)$  = 261 (58,  $\text{M}^+$ ), 174 (100), 159 (53), 143 (33); HRMS (EI)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{15}\text{NO}_4(\text{M}^+)$ : 261.1001; found: 261.1001.

### Ethyl 3-cyclopropylamino-2-[(1-methoxy-1*H*-3-indolyl)carbonyl]-2-propenoate (**8**)

A mixture of ethyl 3-(1-methoxy-1*H*-3-indolyl)-3-oxopropanoate (**7**) (160 mg, 0.62 mmol), triethyl orthoformate (0.15 mL, 2.48 mmol) and acetic anhydride (0.16 mL, 5.6 mmol) was heated at  $145^{\circ}\text{C}$  for 5 h with removal of ethyl acetate formed during the reaction. The solution was evaporated under reduced pressure to mobile oil, which was dissolved in ethanol (2 mL) and ether (0.5 mL). To this solution was added cyclopropylamine (46 mg, 0.82 mmol) dissolved in ethanol (1 mL) at  $0^{\circ}\text{C}$ . After the addition, the mixture was stirred for 2 h at rt and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using *n*-hexane/EtOAc (7/1) mixture as an eluent to yield **8** as a pale yellow oil (179 mg, 89 %):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  = 0.75~0.85 (m, 4H), 0.99 and 1.06 (each t, 3H,  $J=7.1$  Hz) 2.87~2.89 (m, 1H), 4.03~4.09 (m, 2H), 4.12 (s,  $3\times 0.5\text{H}$ ), 4.14 (s,  $3\times 0.5\text{H}$ ), 7.21~7.29 (m, 1H), 7.41~7.43 (m, 1H), 7.73~7.76 (m, 1H), 8.05~8.13 (m, 1H), 8.94~8.99 (m,  $1\times 0.5\text{H}$ ), 10.19~10.23 (m,  $1\times 0.5\text{H}$ ); IR (KBr)  $\nu$  = 1094, 1512, 1632, 1704, 2982  $\text{cm}^{-1}$ ; EIMS  $m/z(\%)$  =

328 (40,  $M^+$ ), 251 (100), 174 (22); HRMS (EI)  $m/z$  calcd for  $C_{18}H_{20}N_2O_4(M^+)$ : 328.1423; found: 328.1424.

### Ethyl 1-cyclopropyl-4-oxo-4,9-dihydro-1*H*-pyrido[2,3-*b*]indole-3-carboxylate (9)

To a stirred solution of ethyl 3-cyclopropylamino-2-[(1-methoxy-1*H*-3-indolyl)-carbonyl]-2-propenoate (8) (275 mg, 0.84 mmol) in dry DMF (1 mL) under ice cooling was slowly added a 60% sodium hydride in oil suspension (37 mg, 0.92 mmol). The reaction mixture was warmed up to rt and further stirred for 2 h under nitrogen atmosphere. After the reaction mixture was cooled in the ice bath, ice cooled water (2 mL) was added and the formed precipitate was filtered. The residual solid was washed successively with water, ethanol, and ether and then dried under reduced pressure to yield 9 as a white solid (210 mg, 83 %): mp 273~274°C;  $^1H$  NMR (DMSO- $d_6$ )  $\delta$  = 1.18~1.22 (m, 4H), 1.28 (t, 3H,  $J=7.1$  Hz), 3.64~3.69 (m, 1H), 4.22 (q, 2H,  $J=7.1$  Hz), 7.18~7.23 (m, 1H), 7.28~7.33 (m, 1H), 7.55 (d, 1H,  $J=8.1$  Hz), 8.14 (s, 1H), 8.18 (d, 1H,  $J=8.1$  Hz), 12.1 (s, 1H); IR (KBr)  $\nu$  = 1252, 1566, 1630, 1716, 2986, 3522  $cm^{-1}$ ; Anal. Calcd for  $C_{17}H_{16}N_2O_3 \cdot H_2O$ : C, 64.94; H, 5.78; N, 8.92. Found: C, 64.90; H, 5.89; N, 8.76. EIMS  $m/z(\%)$  = 296 (80,  $M^+$ ), 250 (100), 221 (68), 193 (78); HRMS (EI)  $m/z$  calcd for  $C_{17}H_{16}N_2O_3(M^+)$ : 296.1161; found: 296.1164.

### 1-Cyclopropyl-4-oxo-4,9-dihydro-1*H*-pyrido[2,3-*b*]indole-3-carboxylic acid (3)

A suspended solution of ethyl 1-cyclopropyl-4-oxo-4,9-dihydro-1*H*-pyrido[2,3-*b*]indole-3-carboxylate (9) (62 mg, 0.21 mmol) in 1 N sodium hydroxide (5 mL) was heated to 110°C for 2 h with stirring. The reaction mixture was cooled to 0°C and acidified with 2 N hydrochloric acid to pH 4. The resulting precipitate was collected by filtration and washed with water, dried under vacuum to yield 3 as a white solid (50 mg, 88 %): mp 343~345°C;  $^1H$  NMR (DMSO- $d_6$ )  $\delta$  = 1.21~1.33 (m, 4H), 3.83~3.92 (m, 1H), 7.33 (m, 1H), 7.46 (m, 1H), 7.66 (d, 1H,  $J=8.0$  Hz), 8.20 (d, 1H,  $J=8.0$  Hz), 8.46 (s, 1H); IR (KBr)  $\nu$  = 1264, 1458, 1560, 1616, 3226  $cm^{-1}$ ; Anal. Calcd for  $C_{15}H_{12}N_2O_3 \cdot 1/3H_2O$ : C, 65.68; H, 4.41; N, 10.21. Found: C, 65.78; H, 4.50; N, 10.47. EIMS  $m/z(\%)$  = 268 (5,  $M^+$ ), 224 (100), 195 (14), 155 (30); HRMS (EI)  $m/z$  calcd for  $C_{15}H_{12}N_2O_3(M^+)$ : 268.0848; found: 268.0844.

**Ethyl 1-cyclopropyl-9-methyl-4-oxo-4,9-dihydro-1H-pyrido[2,3-b]indole-3-carboxylate (10)**

To a stirred solution of ethyl 1-cyclopropyl-4-oxo-4,9-dihydro-1H-pyrido[2,3-b]indole-3-carboxylate (**9**) (50 mg, 0.17 mmol) in dry DMF (1 mL) at rt was added a potassium carbonate (58 mg, 0.42 mmol), and then the reaction mixture was stirred for 30 min. To this mixture was slowly added iodomethane (238 mg, 1.67 mmol) and the mixture was stirred for 3 h at the same temperature. Ice cooled water (2 mL) was added to the reaction mixture to afford a white precipitate, which was filtered and then washed with water and ether to afford **10** as a white solid (48 mg, 92 %): mp 291~292°C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>)  $\delta$  = 1.25~1.37 (m, 7H), 4.14~4.29 (m, 3H), 4.18 (s, 3H), 7.27 (m, 1H), 7.38 (m, 1H), 7.63 (d, 1H, *J*=8.0 Hz), 8.16 (s, 1H), 8.30 (d, 1H, *J*=8.0 Hz); IR (KBr)  $\nu$  = 1242, 1524, 1622, 1720, 2994 cm<sup>-1</sup>; *Anal.* Calcd for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub> • H<sub>2</sub>O: C, 65.83; H, 6.14; N, 8.53. Found: C, 66.10; H, 5.94; N, 8.52. EIMS *m/z*(%) = 310 (4, M<sup>+</sup>), 296 (65), 238 (100), 224 (37), 168 (31); HRMS (EI) *m/z* calcd for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>(M<sup>+</sup>): 310.1317; found: 310.1315.

**1-Cyclopropyl-9-methyl-4-oxo-4,9-dihydro-1H-pyrido[2,3-b]indole-3-carboxylic acid (4)**

The compound (**4**) was prepared in 87 % yield (17 mg) as a white solid from **10** (20 mg) by using the procedure described for the conversion of **9** to **3**: mp 285~286°C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>)  $\delta$  = 1.32~1.43 (m, 4H), 4.32 (s, 3H), 7.38 (m, 1H), 7.52 (m, 1H), 7.77 (d, 1H, *J*=8.0 Hz), 8.28 (d, 1H, *J*=8.0 Hz), 8.47 (s, 1H); IR (KBr)  $\nu$  = 1262, 1464, 1530, 1624, 1690, 3536 cm<sup>-1</sup>; *Anal.* Calcd for C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub>: C, 68.12; H, 5.00; N, 9.93. Found: C, 68.10; H, 5.04; N, 9.85. HRMS (EI) *m/z* calcd for C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub>(M<sup>+</sup>): 282.1004; found: 282.1004.

**Ethyl 3-[(2-hydroxy-1-methylethyl)amino]-2-[(1-methoxy-1H-3-indolyl)carbonyl]-2-propenoate (11)**

A mixture containing ethyl 3-(1-methoxy-1H-3-indolyl)-3-oxopropanoate (**7**) (20.3 mg, 0.78 mmol), triethyl orthoformate (0.5 mL, 3.8 mmol) and acetic anhydride (0.7 mL, 7.4 mmol) was heated to 145°C for 5 h, during which period the resulting ethyl acetate was removed. The solution was concentrated under reduced pressure to give a mobile oil, which was dissolved in ethanol (1 mL) and ether (0.5 mL). To this solution was added

2-amino-1-propanol (160 mg, 2.1 mmol) dissolved in ethanol (1 mL) and the reaction mixture was stirred for 2 h. The solvent was evaporated under reduced pressure to afford a residue, which was chromatographed on silica gel using  $\text{CHCl}_3/\text{MeOH}$  (25/1) mixture as an eluent to yield **11** as a pale yellow oil (440 mg, 66 %):  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  = 0.98 and 1.03 (each t, 3H,  $J=7.1$  Hz), 1.23 and 1.26 (each d, 3H,  $J=6.0$  Hz), 2.94~3.17 (m, 1H), 3.42~3.60 (m, 2H), 3.60~3.72 (m, 1H), 4.05 (q, 2H,  $J=7.1$  Hz), 4.10 (s, 3H), 7.17~7.30 (m, 1H), 7.40~7.44 (m, 1H), 7.75~7.81 (m, 1H), 8.02~8.11 (m, 1H), 8.95~8.99 and 10.19~10.23 (each m, 1H); IR (KBr)  $\nu$  = 1226, 1510, 1618, 1656, 2937, 3422  $\text{cm}^{-1}$ ; EIMS  $m/z$  (%) = 346 (90,  $\text{M}^+$ ), 296 (100), 211 (60), 174 (60), 144 (37); HRMS (EI)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_5(\text{M}^+)$ : 346.1529; found: 346.1529.

**Ethyl 1-(2-hydroxy-1-methylethyl)-4-oxo-4,9-dihydro-1H-pyrido[2,3-b]indole-3-carboxylate (12)**

The compound (**12**) was prepared in 89 % yield as a white solid (400 mg) from ethyl 3-[(2-hydroxy-1-methylethyl)amino]-2-[(1-methoxy-1H-3-indolyl)carbonyl]-2-propenoate (**11**) (500 mg, 1.45 mmol) and a 60% sodium hydride in oil suspension (87 mg, 2.17 mmol) by following the procedure given above for the conversion of **8** to **9**: mp 290~292°C;  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  = 1.29 (t, 3H,  $J=7.2$  Hz), 1.51 (d, 3H,  $J=6.8$  Hz), 3.75~3.80 (m, 2H), 4.23 (q, 2H,  $J=7.2$  Hz), 4.72~4.83 (m, 1H), 7.23 (m, 1H), 7.30 (m, 1H), 7.51 (d, 1H,  $J=7.5$  Hz), 8.26 (d, 1H,  $J=7.5$  Hz), 8.31 (s, 1H); IR (KBr)  $\nu$  = 1052, 1204, 1630, 1720, 3056  $\text{cm}^{-1}$ ; Anal. Calcd for  $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_4$ : C, 64.94; H, 5.78; N, 8.92. Found: C, 64.50; H, 5.79; N, 8.87. EIMS  $m/z$ (%) = 314 (10,  $\text{M}^+$ ), 284 (10), 256 (20), 210 (100), 154 (20), 127 (18); HRMS (EI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_4(\text{M}^+)$ : 314.1267; found: 314.1267.

**2-Methyl-5-oxo-1,2-dihydro-5H-2a,9b-diazacyclopenta[j,k]fluorene-4-carboxylic acid (5)**

To a boiling mixture of ethyl 1-(2-hydroxy-1-methylethyl)-4-oxo-4,9-dihydro-1H-pyrido[2,3-b]indole-3-carboxylate (**12**) (400 mg, 1.3 mmol), triphenylphosphine (1.04 g, 4 mmol) and triethylamine (400 mg, 4 mmol) in dry acetonitrile (10 mL) under nitrogen atmosphere was added carbon tetrachloride (2 mL, 19.5 mmol) and heated for 30 min with stirring. After the reaction mixture was cooled to 0°C, to this was added dilute



hydrochloric acid (1 mL), chloroform (5 mL) and then washed with water. The organic fraction was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure to afford a residue. The residue was purified by column chromatography on silica gel using  $\text{CHCl}_3/\text{MeOH}$  (10/1) mixture as an eluent to yield a yellow oil, tetracyclic ethyl ester (180 mg, 47 %):  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  = 1.35 (t, 3H,  $J=7.2$  Hz), 1.72 (d, 3H,  $J=6.6$  Hz), 4.27 (q, 2H,  $J=7.2$  Hz), 4.26~4.32 (m, 1H), 4.83~4.89 (m, 1H), 5.41~5.53 (m, 1H), 7.23 (m, 1H), 7.31 (m, 1H), 7.51 (d, 1H,  $J=7.5$  Hz), 7.96 (d, 1H,  $J=7.5$  Hz), 8.56 (s, 1H); IR (KBr)  $\nu$  = 1182, 1448, 1590, 1720, 2920  $\text{cm}^{-1}$ ; *Anal.* Calcd for  $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_3$ : C, 64.94; H, 5.78; N, 8.92. Found: C, 64.60; H, 5.62; N, 8.92. EIMS  $m/z(\%)$  = 296 (20,  $\text{M}^+$ ), 281 (10), 267 (30), 251 (50), 223 (100). This ester (200 mg, 6.75 mmol) was converted into corresponding tetracyclic acid (5) as a white solid (170 mg, 87 %) by using the procedure described for the conversion of 9 to 3: mp 284~286°C;  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  = 1.78 (d, 1H,  $J=6.5$  Hz), 4.33 (dd, 1H,  $J=6.3, 9.2$  Hz), 4.91~4.99 (m, 1H), 5.57~5.68 (m, 1H), 7.33 (m, 1H), 7.46 (m, 1H), 7.62 (d, 1H,  $J=7.8$  Hz), 8.01 (d, 1H,  $J=7.8$  Hz), 8.93 (s, 1H); IR (KBr)  $\nu$  = 1446, 1596, 1712, 2924, 3525  $\text{cm}^{-1}$ ; *Anal.* Calcd for  $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_3$ : C, 67.16; H, 4.51; N, 10.45. Found: C, 67.38; H, 4.60; N, 10.50. EIMS  $m/z(\%)$  = 268 (40,  $\text{M}^+$ ), 251 (100), 183 (10), 155 (30).

## ACKNOWLEDGEMENTS

This work was fully supported by the Korea Institute of Science and Technology.

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