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Chiral Methyl 7,8,9-Trichloro-6,7,8,9-tetrahydro-5-oxopyrido-[2,3-a]indolizine-10-carboxylates (OPIC)

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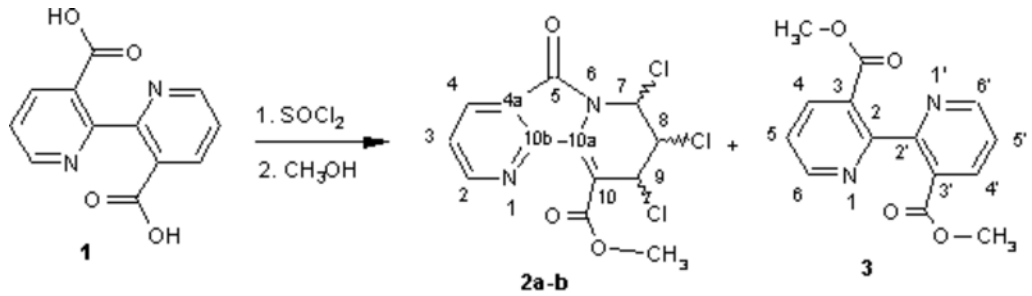
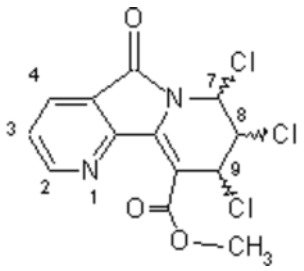


The 3,3'-dihydoxycarbonyl-2,2'-bipyridine acid **1** used for the preparation of diastereoisomeric compounds **2a-b** has been obtained by described method of Blau [1].

Procedure A: To 10 mL of clean thionyl chloride (new bottle without further distillation), were added 600 mg (2.5 mmol) of 3,3'-dihydroxycarbonyl-2,2'-bipyridine **1** and the mixture was refluxed for 5 h. Then the excess of $SOCl_2$ was removed under vacuum to leave an unstable yellow residue [1]. 20 mL of toluene and then 1 mL of MeOH were added and the solution was heated at reflux for 3 h. 40 mL of chloroform were added and the organic phase was washed with a cooled solution of sodium hydrogen carbonate (2.5%), and then dried on sodium sulfate. The crude product was chromatographed on silica column. Only compound **3** was obtained as product of reaction (55-60%); the rest is the unreacted stating material **1**.

Procedure B: When we used an old bottle of $SOCl_2$, in the same conditions (procedure A), three white solids were successively obtained: a mixture of petroleum ether/dichloromethane 10/90 eluted first compound **2a** (310 mg, 31 %), and then in the ratio 5/95 derivative **2b** (70 mg, 7%) was recovered; and finally with ether/acetone 40/60, the diester **3** (450 mg, 52%) was eluted, which has been described elsewhere [2].



Compound 2a: methyl (7*S*,8*R*,9*S*)-7,8,9-trichloro-5-oxo-5,7,8,9-tetrahydropyrido-[2,3-*a*] indolizine-

10-carboxylate (*Labelling used for NMR assignments*)

m.p. = 121-122 °C; Analysis Calc. (Found) for $C_{13}H_9N_2O_3Cl_3$: C 44.94 (44.98), H 2.59 (2.63), N 8.06 (7.99)**;** Mass spectrum : m/z = 347.0 (Calc. for $C_{13}H_9N_2O_3Cl_3$: 346.60); IR (KBr) n cm^{-1}: 1744 (C=O, s), 1717 (C=O, s), 1601,1581 (C=C, w), 1434 (C=N, m), 1297 (C-O, w); ^{1}H NMR (250.14 MHz; $CDCl_3$) d ppm: 8.9 (dd, H_2, $^3J_{H2-H3}$ = 4.9 Hz, $^4J_{H2-H4}$ = 1.6 Hz), 8.2 (dd, 1 H, H_4,$^3J_{H4-H3}$ = 7.8 Hz,$^4J_{H4-H2}$ = 1.6 Hz), 7.53 (dd, 1 H, H_3, $^3J_{H3-H4}$ = 7.8 Hz, $^3J_{H3-H2}$ = 4.9 Hz), 6.49 (dd, 1 H, H_7, $^3J_{H7-H8}$ = 1.33 Hz, $^4J_{H7-H9}$ = 2.1 Hz), 5.35 (t, 1 H, H_8, $^3J_{H8-H7}$ = 1.33 Hz, $^3J_{H8-H9}$ = 1.33 Hz), 5.03 (dd, 1 H, H_9, $^3J_{H9-H8}$ = 1.33 Hz,$^4J_{H7-H9}$ = 2.1 Hz), 4.0 (s, 3 H, CH_3).

Compound 2b: methyl (7*R*,8*R*,9*S*)-7,8,9-trichloro-5-oxo-5,7,8,9-tetrahydropyrido-[2,3-*a*]-indolizine-10-carboxylate

Mass spectrum : m/z = 347.0 (Calc. for $C_{13}H_9N_2O_3Cl_3$: 346.60); ^{1}H NMR (200.131 MHz; $CDCl_3$) d ppm: 8.86 (dd, 1 H, H_2, $^3J_{H2-H3}$ = 4.9 Hz, $^4J_{H2-H4}$ = 1.6 Hz), 8.14 (dd, 1 H, H_4, $^3J_{H4-H3}$ = 7.8 Hz, $^4J_{H4-H2}$ = 1.6 Hz), 7.48 (dd, 1 H, H_3, $^3J_{H3-H4}$ = 7.8 Hz, $^3J_{H3-H2}$ = 4.9 Hz), 6.47 (d,1 H, H_8, $^3J_{H8-H9}$ = 3 Hz), 5.26 (d, 1 H, H_{10}, $^3J_{H10-H9}$ = 9.8 Hz), 4.52 (dd, 1 H, H_9, $^3J_{H9-H8}$ = 3.05 Hz, $^3J_{H9-H10}$ = 9.75 Hz), 3.96 (s, 3H, CH_3).

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References and Notes

1. Blau, F. *Ber. Dtsch. Chem. Ges.* **1888**, *21*, 1077.

2. Ben-Hadda, T.; Sam, N.; Le Bozec, H.; Dixneuf, P. H. *Inorg. Chem. Com*, **1999**, *2*, 460.

Sample Availability: Available from the authors