TOTAL SYNTHESIS OF TRYPTOQUIVALINES

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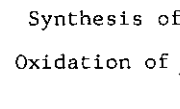
We report a short synthesis of (+) and (-)-tryptoquivaline G, 1b and (-) and (+)-tryptoquivaline L, 1c by oxidative double cyclization. We also report the first total synthesis of (+)-tryptoquivaline, 1a which is a tremorgic mycotoxin.

1. Synthesis of tryptoquivaline G AND L

Oxidation of 2 with NBS in TFA gave 3 and



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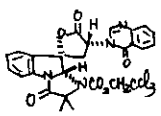

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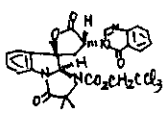

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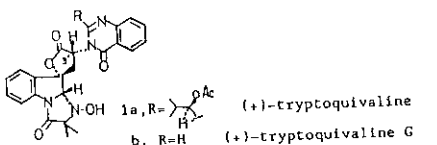
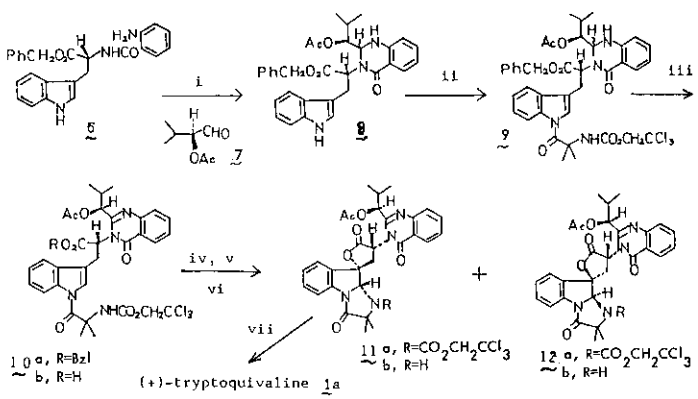


4 which were deprotected followed by m-CPBA oxidation to give (+)-1b, (+)-1c, respectively. Analogous reactions starting from L-tryptophan gave (-)-1c and (-)1b.

2. Synthesis of tryptoquivaline 1a

The condensation of (s)-α-acetoxyisovaleraldehyde 7 with 6 gave 8. Acylation of 8 with 5 followed by DDQ oxidation and debenzylation gave 10b. The reaction of 10b with NIS provided 11a which was treated with Zn-AcOH followed by m-CPBA to give tryptoquivaline 1a, mp 214-217°C, $[\alpha]_D$ +160° (c 0.10, $CHCl_3$) which was identical with the specimen obtained from Aspergillus fumigatus.



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i, 7, molecular sieves 4A, TsOH, CH_2Cl_2, r.t.; ii, $CCl_3CH_2O_2CNHCMe_2CO_2C_6H_4$-p-$NO_2$, 5, KF,MeCN, 18-crown-6, EtN(i-Pr)$_2$, 35°C, 4 h; iii, DDQ, $CHCl_3$, 30°C, 3 h; iv, H_2, Pd/C; v, N-iodosuccinimide(3 equiv), CF_3CO_2H, 50° C ; vi, Zn, AcOH; vii, m-$ClC_6H_4CO_3H$.