Total Synthesis of (+)- and (-)-Tryptoquivaline G and L by Biomimetic Double Cyclization

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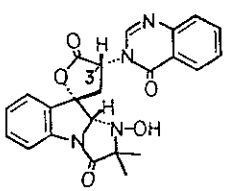
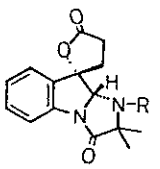
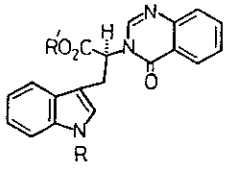
A facile biogenetic type total synthesis of (+)- and (-)-tryptoquivaline G and L by oxidaitve double cyclization of N-acyltryptohan derivative 5c was achieved. The model study was carried out by the reaction of benzyl 3-indole propionate with N-methoxycarbonyl- (2a) or N-trichloroethoxycarbonyl- (2b) methylalanine p-nitrophenyl esters (KF-18-crown-6, EtN(i-Pr)$_2$, MeCN) followed by hydrogenolysis to give the corresponding N-acylated derivatives 3a and 3b, respectively. Bromination of 3a with NBS in CH_2Cl_2-CF_3CO_2H (10 : 1) gave 4a and its cis configuration was established by x-ray analysis. The similar NBS reaction of 3b gave 4b which was converted to 4c by treatment with AcOH-Zn. The reaction of L-tryptophan benzyl ester with isatoic anhydride followed by treatment with (EtO)$_3$CH-TsOH provided 5a. Condensation of 5a with 2b (KF-18-crown-6-MeCN) gave 5b which was debenzylated to give 5c. Bromination of 5c with NBS in boiling CF_3CO_2H gave 6 and 7 which were converted to 8 and 9 (AcOH-Zn). Oxidation of 8 with m-CPBA in CH_2Cl_2 afforded (-)-tryptoquivaline L 10. Epimerization of 10 with t-BuLi-AcOH, -70°C provided (+)-tryptoquivaline G 1, whereas similar oxidation of 9 gave (-)-tryptoquivaline G 1. On the other hand, analogous series of reactions starting from D-tryptophan provided (+)-1 via 3'-epimer of 8 and (+)-tryptoquivaline L by oxidation of 3'-epimer of 9.



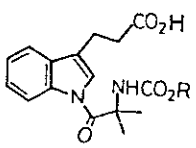
1 (+)-Tryptoquivaline G



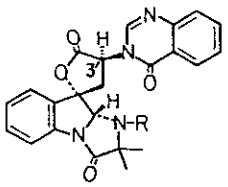
4 a, R = CO_2CH_3
b, R = $CO_2CH_2CCl_3$
c, R = H



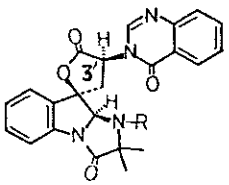
5 a, R = H, R' = Bzl
b, R = $COC(CH_3)_2NHCO_2CH_2CCl_3$, R' = Bzl
c, R = $COC(CH_3)_2NHCO_2CH_2CCl_3$, R' = H



3 a, R = CH_3
b, R = CH_2CCl_3



6, R=$CO_2CH_2CCl_3$
8, R=H
10, R=OH (-)-Tryptoquivaline L



7, R=$CO_2CH_2CCl_3$
9, R=H
1, R=OH (-)-Tryptoquivaline G