# Synthesis of Clitocine, a New Insecticidal Nucleoside from the Mushroom *Clitocybe inversa*

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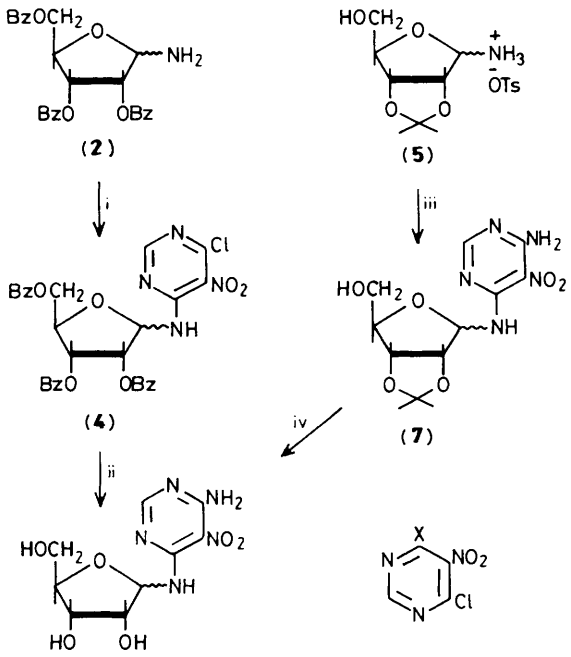
Clitocine, a new insecticidal nucleoside from the mushroom *Clitocybe inversa*, was synthesized.

Clitocine (**1b**), isolated by Kubo *et al.*[1] from the mushroom *Clitocybe inversa*, shows strong insect growth inhibitory activity against the pink bollworm, *Pectinophora gossipiella*. This interesting biological activity together with an interesting biogenetic relationship with adenosine prompted us to synthesize clitocine. We now report a two-step synthesis of clitocine from readily available starting materials.

Condensation of 2,3,5-tribenzoylribofuranosylamine[2] (**2**) with 4,6-dichloro-5-nitropyrimidine[3] (**3**) in the presence of triethylamine gave a mixture of α- and β-anomers (**4**) (7 : 1) in




**Scheme 1.** *Reagents and conditions:* i, (**3**), $Et_3N$, DMF, room temp.; ii, $NH_3$, MeOH, 0 °C; iii, (**6**), $Et_3N$, DMF, room temp.; iv, $CF_3CO_2H$–$H_2O$ (9 : 1), room temp., 6 min.

19% yield. Treatment of (**4**) with ammonia-saturated methanol at room temperature gave clitocine in 72% yield. The physical properties (t.l.c., h.p.l.c., and n.m.r.) were identical with those of natural clitocine. However, the inefficiency and lack of reproducibility of the condensation step [probably due to the instability of (**3**) with base and the possibility of O → N migration of the 2-*O*-benzoyl group of (**2**)] led us to pursue a second approach.

Treatment of the toluenesulphonate[2] (**5**) and 4-chloro-5-nitro-6-aminopyrimidine[4] (**6**) with triethylamine in dimethylformamide (DMF) at room temperature gave (**7**) in 66% yield as a mixture of anomers (α:β 1:2.8). The β-isomer (m.p. 167—169 °C) could be separated by preparative layer chromatography (silica gel, $CHCl_3$–MeOH, 95:5). Since the *N*-glycosidic linkage was cleaved more easily than the isopropylidene group, carefully selective conditions were needed to remove the protecting group. After numerous unsuccessful attempts, we found that treatment of the β-isomer of (**7**) with aqueous trifluoroacetic acid (90%) at room temperature for 6 min gave clitocine in 43% yield after separation by column chromatography ($ODSC_{18}$; MeOH–$H_2O$, 8:2). The physical properties (m.p., h.p.l.c., i.r., n.m.r., and mass spectra) were identical in all respects with those of natural clitocine. Hydrolysis of the mixture of isomers of (**7**) gave a 1 : 2 mixture of (**1a**) and (**1b**).

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