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FISHER INDOLE SYNTHESIS
THE SYNTHESIS OF 1-ACETYL-6:7-DIHYDRO-2:3-BENZINDOLO(2':3'-4:5)AZEPINE

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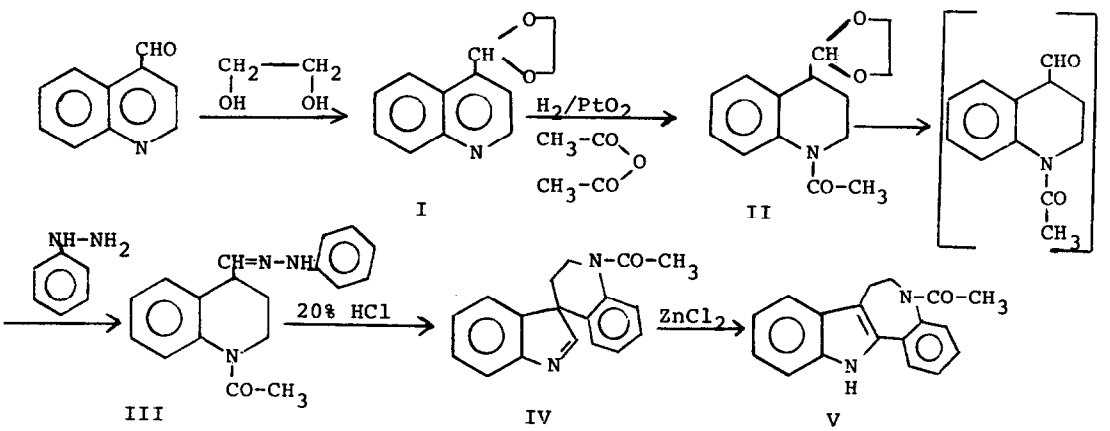
Literature examples of preparations of the indolobenzazepines are limited[1,2,3]. During the search for a more generally applicable method for forming the indolobenzazepine system (V), it became apparent that the well established Plancher rearrangement[4,5,6] (IV → V) could be modified to form the desired fused indole polycyclic system, simply by employing a spiroindolenine as the reactant. The mechanism of the reaction involves initial protonation of the basic indolenine nitrogen atom, followed by Wagner-Merrwein type rearrangement and loss of a proton to yield the wanted indolobenzazepine system.



To make possible selective reduction of the pyridine portion of the quinoline ring without affecting the aldehyde group, the dioxolane derivative (I) of quinoline-4-aldehyde[7] was prepared by azeotropic distillation with ethylene glycol in the presence of p-toluenesulfonic acid in benzene. A viscous liquid at 156-7°/2mm was obtained (65%), ($C_{12}H_{11}NO_2$). IR($CHCl_3$): 2.67μ (-C=N-) and

9.05μ (-C-O-C-), but no carbonyl bond. Direct acylation and catalytic hydrogenation of I with acetic anhydride/acetic acid and H_2/PtO_2 at ~60° under 60lb/in^2 pressure yielded compound II at 142-4°/0.2mm, (71%), ($C_{14}H_{17}NO_3$). IR($CHCl_3$): 6.15μ (amide) and 9.00μ (-C-O-C-). Hydrolysis of the dioxolane (II) with 5% HCl yielded the aldehyde, which was immediately converted to the phenylhydrazone (III) in the usual manner[8]. mp 183-5°, (67%), ($C_{18}H_{19}N_3O$). The Fisher cyclization of III was found to proceed smoothly in 20% HCl/MeOH at room temperature for 3 days. After the methanol was removed, the residue was treated with 10% NH_4OH. The precipitate was collected and crystallized from chloroform-ether. mp 263-5°, (74%), ($C_{18}H_{16}N_2O$). The structure of IV was verified by UV(MeOH): 208mμ (log ε 4.40) and 255mμ (log ε 3.97). IR(KBr): 2.60μ (-C=N-), 6.15μ (amide), which were compared with IR and UV spectra of 3,3-dimethylindolenine[9] and cyclohexanespiroindolenine[6]. Picrate: mp 179-81°. The Plancher rearrangement occurred readily with $ZnCl_2$ at 170°/N_2 from IV producing 1-acetyl-6:7-dihydro-2:3-benzindolo(2′:3′-4:5)azepine (V), which was purified on a neutral AlO_3 column by elution with benzene, mp 201-3°, (56%), ($C_{18}H_{16}N_2O$). Picrate: mp 157-8°. UV(MeOH): 225mμ (log ε 4.15) and 282mμ (log ε 3.72); the typical indole absorptions, IR(KBr): 2.88μ (-NH) and 6.15μ (amide) were compared with absorptions of 2,3-dimethylindole[9], cycloheptenoindole[6], and 6:7-dihydro-1-methyl-2:3-benzindolo(2′:3′-4:5)azepine[1].

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