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AN IMPROVED SYNTHESIS OF YOHIMBINE
DIECKMANN RING CLOSURE OF UNSATURATED DIESTERS

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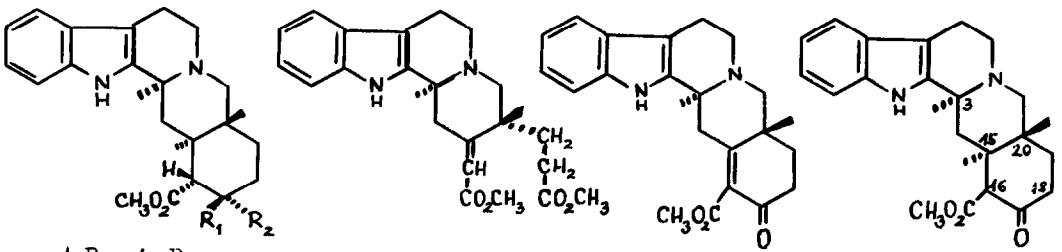
Recently we have published a stereoselective total synthesis of natural Yohimbine and β-Yohimbine/Ia,b/[1]. One of the crucial intermediates of the mentioned synthesis was the unsaturated ester II. The catalytic /Pd/ reduction of II gave two stereoisomer saturated diesters, one of them leading us after a ring closure of Dieckmann type to yohimbinone/IV/ in relatively poor /10-15%/ yield. The main product was the structure isomer of IV having the ester group in position 18.

On the assumption that the olefinic proton of II should be more acidic then the corresponding hydrogen in the saturated ester, we tried a selective Dieckmann ring closure with the unsaturated diester II.

Such type of Dieckmann ring closure is very rare in the literature and the results are contradictory[2].



	R_1	R_2	
Ia	H	OH	yohimbine
b	OH	H	β-yohimbine

II III IV

The ester II with NaH in THF at room temperature gave the aimed compound III as a crystalline material in 47% yield. /$C_{21}H_{22}N_2O_3.CH_3OH$ from methanol, mp.188-189°, after drying over P_2O_5 at 110° mp.194-195°. /IR/$CHCl_3$/ 3470/NH/, 1735/CO_2CH_3/, 1685/CO/, 1635cm^{-1}/C=C/; λ_{max}^{MeOH} /log ε/ 226nm/4.63/, 274/3.96/, 280/3.98/, 290/3.88/; NMR/$CDCl_3$/: τ 1.77 /s, 1, NH/, 2.5-2.9 /m, 4, aromatic protons/, 6.05 /s, 3, CH_3O/; MS /70 eV/ m/e /rel.intensity/: 350/100/, 349/72/, 335/33/, 317/38/, 183/70/, 182/91/, 170/40/, 169/68/; Calcd. for $C_{21}H_{22}N_2O_3$ 350.1630, Found: 350.1621/.

The ring closure is with about an order of magnitude faster than the Dieckmann reaction of the corresponding saturated diester.

It was somewhat surprising that the catalytic /Pd/ reduction of III in methanol gave predominantely /60% crystalline/ rac. yohimbinone/IV/ which belongs to the so called "normal" series with D/E trans ring-junction. No product of the "allo" series with D/E cis ring-junction could be detected.

The reduction of yohimbinone/IV/ by $NaBH_4$ in methanol gives the mixture of yohimbine and β-yohimbine /Ia,b/, however the catalytic hydrogenation /PtO_2 in methanol-acetic acid/ furnishes the yohimbine /Ia/ in high yield[3].

It is to mention that the olefinic bond in III could be equilibrated in the presence of base to the position 15-20. In this case the catalytic reduction yields also the yohimbinoneepimers of the "allo" and "epiallo" series.

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