REACTION OF 2-SUBSTITUTED 6-METHYL-4H-1,3-OXAZIN-4-ONE DERIVATIVES WITH ENAMINE[1]

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Reaction of 1-(1-cyclopenten-1-yl)pyrrolidine (IIa) with 6-methyl-2-phenyl-4H-1,3-oxazin-4-one (Ia), 2-ethoxy-2,6-dimethyl-3,4-dihydro-2H-1,3-oxazin-4-one (Ib), and 2-benzyl-2-ethoxy-6-methyl-3,4-dihydro-2H-1,3-oxazin-4-one (Ic) gave rise to 4-acetyl-3-hydroxy-1-phenyl-6,7-dihydro-5H-2-pyrindine (IIIa), 4-acetyl-3-hydroxy-1-methyl-6,7-dihydro-5H-2-pyrindine (IIIb), and 4-acetyl-1-benzyl-3-hydroxy-6,7-dihydro-5H-2-pyrindine (IIIc), respectively.

Similar reaction of 1-(1-cyclohexen-1-yl)pyrrolidine (IIb) with Ia afforded 4-acetyl-3-hydroxy-1-phenyl-5,6,7,8-tetrahydroisoquinoline (IV).

The present communication describes a novel reaction of enamine with the 1,3-oxazin-4-one derivative such as 6-methyl-2-phenyl-4H-1,3-oxazin-4-one (Ia), prepared from the reaction of diketene with ethyl benzimidate,[2] to give the ring-transformed product.

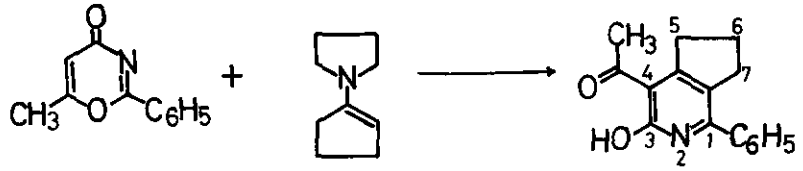
When 6-methyl-2-phenyl-4H-1,3-oxazin-4-one (Ia) was allowed to react with an equimolar amount of 1-(1-cyclopenten-1-yl)pyrrolidine (IIa) in absolute EtOH under reflux, a crystalline substance was obtained. Purification by recrystallization from AcOH afforded yellow prisms of mp 273-276° (decomp.), $C_{16}H_{15}O_2N$ (IIIa), in 65% yield. The ir spectrum (KBr) of IIIa showed absorption bands at 1645 and 1622 cm^{-1}. The nmr spectrum (CF_3CO_2H, ppm) revealed signals at 2.30-2.53 (2H, m), for the C_6-methylene, 3.22 (2H, t, J=8 cps), and 3.65 (2H, t, J=8 cps) for the C_7 and C_5 methylenes, 2.92 (3H, s) and 7.67 (5H, s) for acetyl methyl and benzene ring protons, respectively. These data are well consistent with the structure of IIIa as 4-acetyl-3-hydroxy-1-phenyl-6,7-dihydro-5H-2-pyrindine.

Similarly, 2-ethoxy-2,6-dimethyl-3,4-dihydro-2H-1,3-oxazin-4-one (Ib, R=methyl)[3] was allowed to react with IIa to give colorless prisms (EtOH) of mp 214-216° (decomp.), $C_{11}H_{13}O_2N$ (IIIb), in 33% yield. The structure was established as 4-acetyl-3-hydroxy-1-methyl-6,7-dihydro-5H-2-pyrindine (IIIb, R=methyl) from the following spectral data: ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 1650, 1635. nmr ($CDCl_3$) ppm: 1.18-2.12 (2H, m, C_6-CH_2), 2.32 (3H, s, C_1-CH_3), 2.68 (3H, s, $COCH_3$), 2.65 (2H, t, J=8 cps, C_7-CH_2), 3.15 (2H, t, J=8 cps, C_5-CH_2), 13.15-13.60 (1H, br, OH).

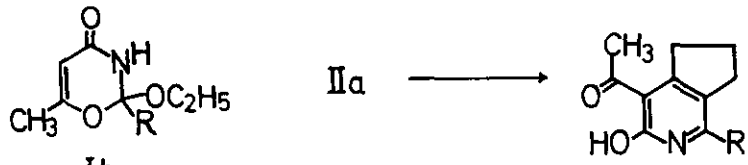
Reaction of 2-benzyl-2-ethoxy-6-methyl-3,4-dihydro-2H-1,3-oxazin-4-one (Ic, R=benzyl)[2] with IIa under the same condition afforded a 10% yield of 4-acetyl-1-benzyl-3-hydroxy-6,7-dihydro-5H-2-pyrindine, $C_{17}H_{17}O_2N$ (IIIc, R=benzyl), as colorless prisms (EtOH) of mp 209-211° (decomp.) [ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660, 1640; nmr ($CDCl_3$)

ppm: 1.70-2.40 (2H, m, C_6-CH_2), 2.50-3.00 (2H, m, C_7-CH_2), 2,64 (3H, s, $COCH_3$), 3.15 (2H, t, J=8 cps, C_5-CH_2), 3.92 (2H, s, CH_2), 7.28 (5H, s, C_6H_5) 12.90-13.70 (1H, br, OH)].

Although similar treatment of 1-(1-cyclohexen-1-yl)pyrrolidine (IIb) with Ib and Ic gave resinous products, the reaction of IIb with Ia afforded a 17% yield of colorless needles (EtOH) of mp 235° (decomp.), $C_{17}H_{17}O_2N$ (IV), whose structure was characterized as 4-acetyl-3-hydroxy-1-phenyl-5,6,7,8-tetrahydroisoquinoline on the basis of the following spectral data: ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680, 1630; nmr ($CDCl_3$) ppm: 1.30-1.90 (4H, m, C_6 and C_7-CH_2), 2.32 (3H, s, $COCH_3$), 2.30-2.60 (2H, m, C_8-CH_2), 2.60-2.90 (2H, m, C_5-CH_2), 7.40 (5H, s, C_6H_5), 11.90-12.80 (1H, br, OH).



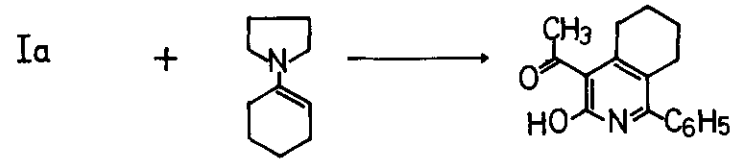
Ia IIa IIIa



Ib,c

b : R=CH_3
c : R=$CH_2C_6H_5$

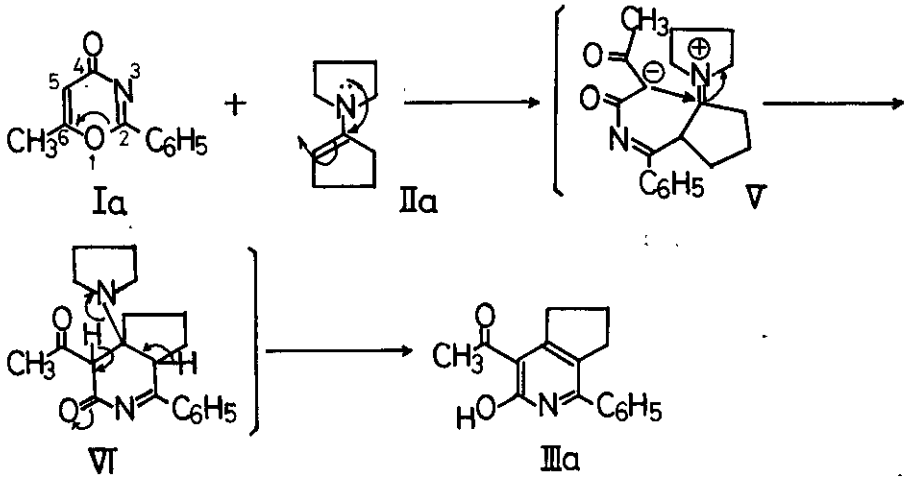
IIa IIIb,c



Ia IIb IV

A likely mechanism of the formation of III and IV can be eluci-

dated as follows. For instance, the nucleophilic addition of the enamine carbon to the C_2-carbon of the oxazine with concomitant opening of the ring gives rise to the N-acetoacetyl intermediate (V), which recyclizes to VI. Elimination of pyrrolidine followed by prototropy affords the pyridine derivative (IIIa).



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