ROBINSON ANNELATION IN THE 3-INDOLINONE SERIES. SYNTHESIS OF 15-AZATETRACYCLO$[7.6.1^{1,5}0.0^{9,14}]$HEXADECA-7,9,11,13-TETRAENES

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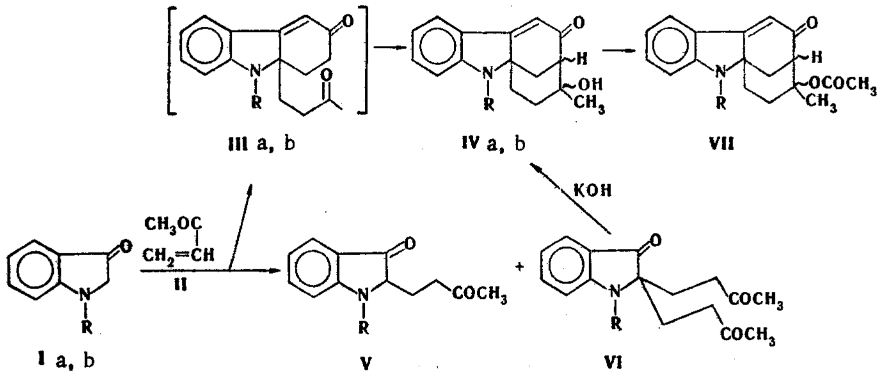
We have established that the condensation of 1-acetyl-3-indolinone (Ia) with methyl vinyl ketone (II) (in a molar ratio of 1:2.5) in an aqueous alcohol medium in the presence of bases leads to 4-methyl-4-hydroxy-6-oxo-15-azatetracyclo$[7.6.1^{1,5}0.0^{9,14}]$hexadeca-7,9,11,-13-tetraene (IVa) (in 95% yield, mp 244-246°C, M^+ 255). The best catalyst for the reaction is 5% KOH; the use of a more concentrated KOH solution or sodium ethoxide causes polymerization of ketone II. In analogy with indolinone Ia, ketone II reacts with 1-methyl-3-indolinone (Ib) in the presence of 5% KOH to give 4,15-dimethyl-4-hydroxy-6-oxo-15-azatetracyclo-$[7.6.1^{1,5}0.0^{9,14}]$hexadeca-7,9,11,13-tetraene (IVb) (in 97% yield, mp 181-186°C).

Under the influence of a catalytic amount of triethylamine, Ia and II undergo a Michael reaction, in the course of which a monoadduct and a diadduct (V and VI in 57 and 24% yields, respectively) are formed.



Ia IVa, V, VI, VII R=$COCH_3$; Ib, IVb R=CH_3

When IVa is heated with acetic anhydride and potassium acetate, it is converted to diacetyl derivative VII, with mp 195-196°C and M^+ 349, in 73% yield.

The IR spectrum (in mineral oil) of IVa contains absorption bands at 1605 and 1630 cm^{-1} (C=CHCO) and at 3250 and 3290-3350 cm^{-1} (NH and OH). In addition to the absorption bands at 1610 and 1630 cm^{-1}, the IR spectrum of diacetate VII contains absorption bands of $NCOCH_3$ and $OCOCH_3$ groups at 1680 and 1740 cm^{-1}, respectively, but absorption bands of NH and OH groups are absent. In addition to absorption bands in the short-wave region of the spectrum [λ_{max} (log ε): 206 (4.17), 250 (4.28), and 298 nm (4.06)], the UV spectrum (in alcohol) of IVa contains absorption bands in the long-range region [λ_{max} (log ε): 435 nm (3.88)], and IVb has a similar UV spectrum. The signals of the protons of the CH_3, OH, and C=CH groups in the PMR spectrum (in d_5-pyridine) of IVa show up in the form of singlets at 1.56, 6.09, and 6.43 ppm, respectively. A narrow unresolved multiplet of a methylidyne proton with a width of ∿8 Hz at half the height of the signal is isolated in the multiplet of the protons of the two cyclohexane rings.

We assumed that the key compound in the synthesis of IVa is diadduct VI, which is initially converted to IIIa in the course of the Robinson annelation; as a result of intramolecular aldol condensation, IIIa is converted to the desired IVa. It was found that diadduct VI is converted quantitatively to IVa under the influence of KOH in alcohol.

The results of elementary analysis were in agreement with the calculated values.

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