

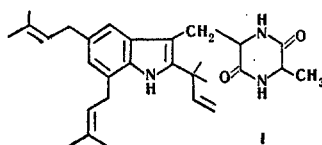
ALKYLATION OF 1-METHYLINDOLE WITH ISOPRENE HYDROCHLORIDE

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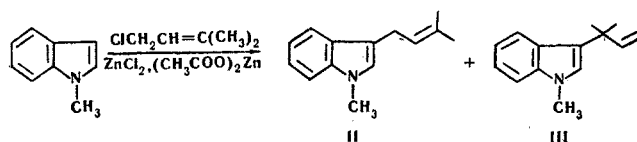
The product of the alkylation of 1-methylindole with isoprene hydrochloride in the presence of zinc chloride and zinc acetate consists of 80% 1-methyl-3-(3-methyl-2-butenyl)indole and 20% of the compound with the "inverted" prenyl radical, 1-methyl-3-(1,1-dimethyl-2-propenyl)indole.

In the biosynthesis of the saprophytic fungal metabolite echinullin (I), alkylation of the indole ring to introduce the isoprenoid residues occurs to equal extents in the benzene and pyrrole rings of the indole nucleus [1].



In model investigations on the alkylation of indolylmagnesium halides with isoprene hydrochloride, introduction of the tertiary prenyl radical was not observed [2].

We have now found that alkylation of 1-methylindole with isoprene hydrochloride, under conditions previously described for furan [3], gives, in addition to II, about 20% of III, containing an "inverted" prenyl radical.



The introduction of the tertiary radical into the ring of furan [3] and benzofuran [4] was not observed under these conditions.

The NMR spectra of II and III, after separation by gas-liquid chromatography, are given in Fig. 1. The positions of the substituents are deduced as in [5].

EXPERIMENTAL

To a solution of 10.2 g (0.07 mole) of 1-methylindole and 0.5 g of ZnCl_2 in 20 ml of absolute ether was added portionwise at 20° alternately 7.3 g (0.07 mole) of isoprene hydrochloride (an equilibrium mixture of allyl isomers), and 6.4 g (0.05 mole) of anhydrous, finely ground zinc acetate, at such a rate that an excess of zinc acetate was present in the reaction mixture. When the reaction was complete, the mixture was

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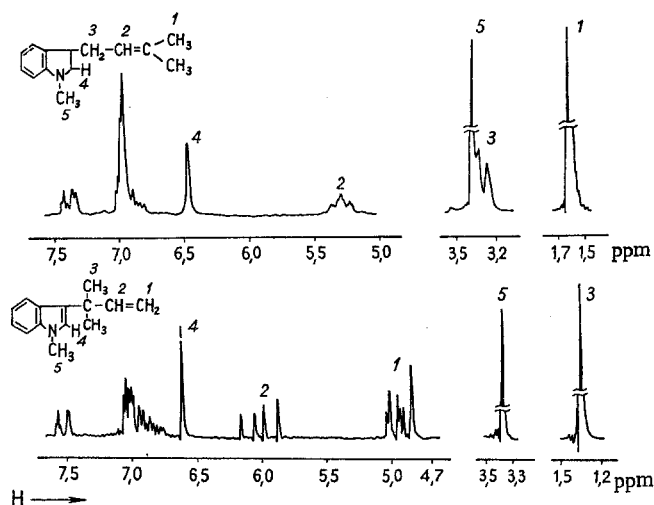


Fig. 1. NMR spectra of II and III.

stirred with 50 ml of water, and the ether layer was separated and washed with a saturated solution of NaHCO_3 . After drying over MgSO_4 , the ether was distilled off, and the residue was distilled in vacuo to give 6.9 g (58%) of a mixture of 1-methyl-3-(3-methyl-2-butenyl)indole (II) and 1-methyl-3-(1,1-dimethyl-2-propenyl)indole (III), bp 137° (2 mm), n_D^{20} 1.5767. Found: N 7.3%. $\text{C}_{14}\text{H}_{17}\text{N}$. Calculated: N 7.0%. The product did not give a picrate. The mixture was separated on a preparative gas-liquid chromatograph (PAKhV-03) at 210° . Column 2000×6 mm, packed with Reoplex-400 (polypropylene glycol adipate) on Chromosorb W, carrier gas helium, 160 ml/min.

The NMR spectra were taken on a JNM-4H-100 (100 MHz) instrument, as 20% solutions in CCl_4 , using hexamethylsiloxane as internal standard.

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