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TRANSFORMATION OF A PLANCHER PYRROLENINE IN AN AZIRIDINO-PYRROLINE

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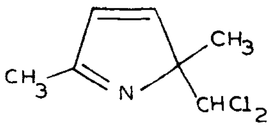
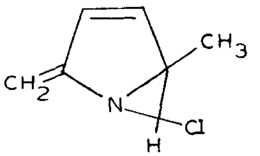
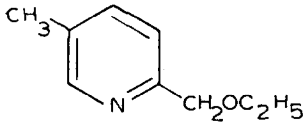
Recently, Johnson et Al. refer in a short communication (1) that Plancher's base (I), when treated with sodium ethoxyde, gives through the hypothetical intermediate (II) the 2-ethoxy=methyl-5-methyl-pyridine (III)



(I)



(II)



(III)

Since we also were working in the same field [1], we refer here briefly that, studying the same reaction, we were able to isolate in addition to pyridine (III) - of which the previous Authors did not give any properties - an aziridino-pyrroline

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[1] In a previous paper (R.Nicoletti and M.L.Forcellese, Ann.Chim., (Rome) in press), regarding the action of dichlorocarbene on some pyrrolic derivatives, we reported that Plancher's base (I) treated with alkali does not give the 2,5-dimethyl-3-chloro=pyridine (Cf. G.Plancher and U.Ponti - Atti Accad.Lincei 18 (II) 469 (1909)) but a pyridine different in nature.

type compound, closely related to the hypothetical intermediate (II).

The compound (I) reacts slowly at reflux with an excess of ethanolic sodium ethoxyde (11% weight/vol.); after 30 hours, thin layer analysis shows that in the reaction mixture two main substances are present. A careful chromatographic separation on purified silica gel enabled us to obtain two pure compounds (A,B).

The more polar of them (substance A) was recognized to be (III), on the basis of spectroscopic evidence [2] (see Table I) and by comparison with an authentic specimen. The latter was obtained from 2-chloromethyl-5-methyl-pyridine (2) by the action of sodium ethoxyde in ethanol. It is an oil (b.p. 83-84°/5 mm; picrate m.p. 111-112,5°).

TABLE I

Spectroscopic data of the 2-ethoxy-methyl-5-methyl-pyridine (III)

U.V.Spectrum:	λ_{max} 267 mμ (ε = 3100; solvent ethanol)			
I.R.Spectrum:	Max. at 6.24 ; 6,36 ; 8.26 ; 8.99 ; 11.11 ; 11.67 ; 12.09 ; 13.75 μ (liquid film)			
NMR Spectrum	δ	Multiplicity	Proton number	Assignements
	1.22	3 (J = 7 c/s)	3	$-O-CH_2-\underline{CH}_3$
	2.28	-	3	β-py-$\underline{CH}_3$
	3.53	4 (J = 7 c/s)	2	$-O\underline{CH}_2-CH_3$
	4.50	-	2	α-py - $\underline{CH}_2$-O
	7.32	multiplet	2	$C^{H}_{\beta} - C^{H}_{\gamma}$
	8.27	-	1	C_{α}-H

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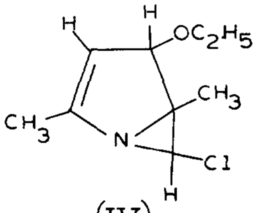
[2] NMR Spectra were determined on a Varian A 60 Instrument: solvent CCl_4, TMS as internal reference.

The less polar of them (substance B) was also an oil (b.p. 100°/5 mm) and its elemental analysis indicated molecular formula $C_9H_{13}NOCl$. Since the NMR spectrum (vide infra) also showed the presence of an ethoxyl group, apparently in the reaction a chlorine atom has been replaced by such a group. However, spectroscopic properties indicated that base (I) and compound B differ substantially.

Ultra-violet spectrum presents a maximum at 213 $m\mu$ ($\mathcal{E}$ = 5700; solvent n-hexane) (λ_{max} of (I) : 232 $m\mu$). This fact shows the loss of the conjugated system: such an absorption may be accounted for by the presence of a double bond, probably carrying a substituent with a strong batochromic effect (such as $-N{<}^{R}_{R}$).

The presence of only one double bond was consistent with the presence of only one band (at 5.05) in infra-red in the region 6 - 6.6 μ (compound (I) presents two bands at 6.18 and 6.51μ).

On the basis of these considerations and the molecular formula, it was reasonable to assume that another ring has been formed in the reaction. Thus, we supposed that structure (IV) had to be assigned to compound (B).

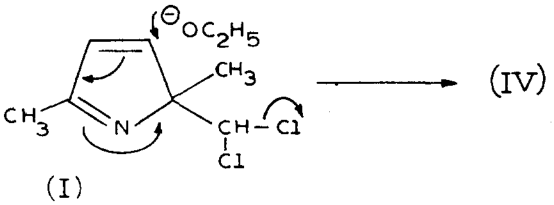


(IV)

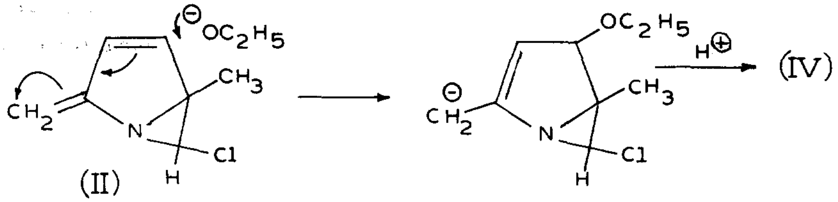
In very good agreement, NMR spectrum presents the peaks due to ethoxyl (triplet centered at 1.18 δ ; quadruplet at 3.45 δ ; J = 7 c/s), to a methyl fixed on a tertiary carbon atom (sharp peak at 1.45 δ) and to a methyl attached to a carbo[illegible] which carries a double band (unresolved multiplet at δ = 1.90 ; see note [3]). In addition, three other signals are present (due each to a hydrogen atom). At the lower field two unsharp peaks [3] are attributable the first to an olefinic proton (δ = 5.13) and the second one (δ = 4.55) to an allylic proton fixed on carbon which carries an oxygen atom; the third signal (sharp) is due to an uncoupled proton (δ = 3.30).

It seems likely that the compound (IV) arises from a nucleophilic attack of ethoxyde anion on the base (I) directly, and/or on intermediate diene (II)

a)



b)



The chemical behaviour of (IV) towards acids is very interesting and significant.

By the action of the concentrated hydrochloric acid at 60°, (IV) is mainly transformed back into the base (I): in the

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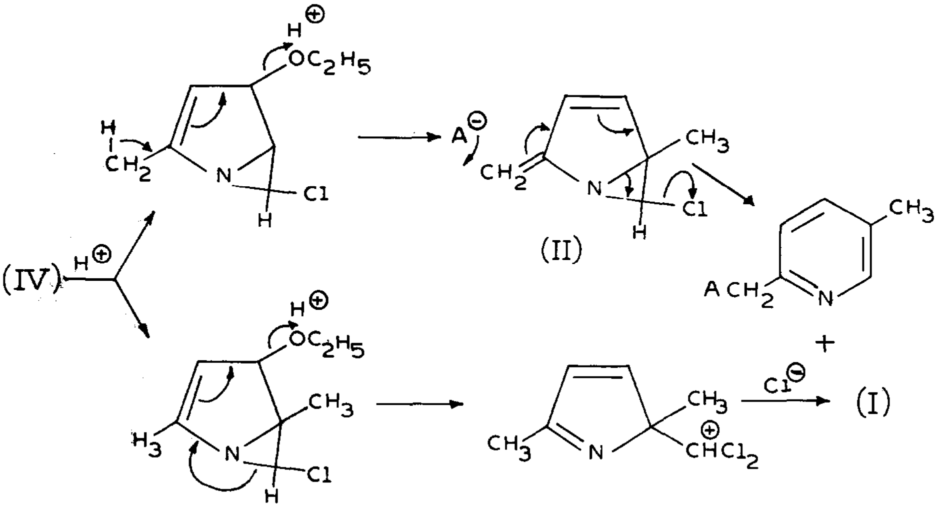
[3] The complex couplings amoung two hydrogen atoms and one methyl are easily understandable in terms of spin-spin coupling between allylic and omoallylic positions (Cf. inter alia J.T.Pinhey Tetrahedron Letters, 275 (1963) and references cited therein).

mixture of this reaction a small quantity of another substances is also present. The last, on the basis of NMR measurements and gas chromatographic analysis was recognized to be 2-chloromethyl-5-methyl-pyridine (V).

Likewise, the action of acetic acid at 60° on (IV) gives a mixture, in which compound (I) and 2-acethoxymethyl-5-methyl-pyridine (VI) are present roughly in the same quantity (both identified by gas chromatographic analysis and NMR spectrum of the mixture).

The capability of compound (IV) to give simultaneously base (I) and pyridic derivatives, by treatement with acids, may be easily justified only with the presence in the molecule of an 1-aza-[3.1.0] bicyclo-hexane type skeleton (3). These transformations may be rationalized as follows:



(V) : A = Cl

(VI) : A = CH_3COO

In the case of the reaction in acetic acid the chloride anion necessary to the formation of base (I) becomes available in the last stage of the scheme of the formation of (V).

The isolation of (IV) and its chemical behaviour support, therefore, the mechanism proposed by the British Authors, who postulate the intermediate (II) as key product in the pyrrolenine (I) ⟶ pyridine (III) transformation. Also in a similar reaction, in the ring enlargement of 1-ethyl-2-chloromethyl-pyrrolidine (4), an aziridine-type bicyclic compound was presumed to be the intermediate; in that case no experimental fact supported this hypothesis.

REFERENCES

(1) R.L.Johnson, C.W.Rees, C.E.Smithen, Proc.Chem.Soc. 217, (1964)

(2) Y.Arata and K.Achiwa, Yakugasky Zasshi, 79, 108 (1959); Chem.Abstr., 53, 10211 (1959)

(3) The compound (IV) is also the second example of compound having an 1-aza 3.1.0 bicyclo hexane skeleton [Cf.Chem. Abstr., 55, 8439 (1961) (Patent)].

(4) R.C.Fuson and C.L.Zirkle, Journ.Am.Chem.Soc., 70, 2760 (1948)