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REACTIONS OF HYDRAZONIC HALIDES WITH PYRIDINE, QUINOLINE AND ISOQUINOLINE.

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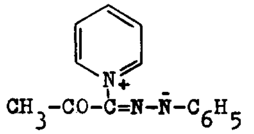
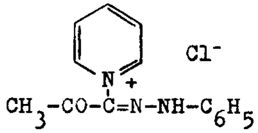
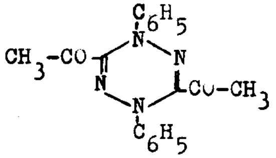
Very few examples of the reaction between hydrazonic halides and pyridine have been reported in the chemical literature. P.W.Neber and H.Wörner (1) reacted phenylhydrazonochloroacetone with pyridine: to the resulting basic compound they assigned the betainic structure (I). For the hydrocloride of (I) they proposed formula (II). Compound (I), on heating in ethanol eliminates a pyridine molecule yielding a dimer for which R.Huisgen(2) demonstrated the dihydrotetrazinic structure (III):

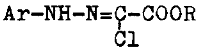

(I)


(II)


(III)

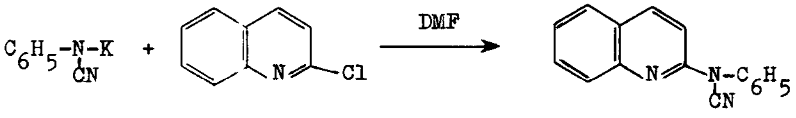
Compound (I), together with some of its analogues, has been obtained also by F.Krollpfeiffer and E.Braun (3) as a product of the reaction of acetonyl- or phenacylpyridinium salts with diazocompounds.

We have investigated the reactions of pyridine, quinoline, isoquinoline and some of their homologues with arylhydrazonochloroacetic esters:



$$\text{Ar-NH-N=}\underset{\text{Cl}}{\text{C}}\text{-COOR} \quad \text{(IV)}$$

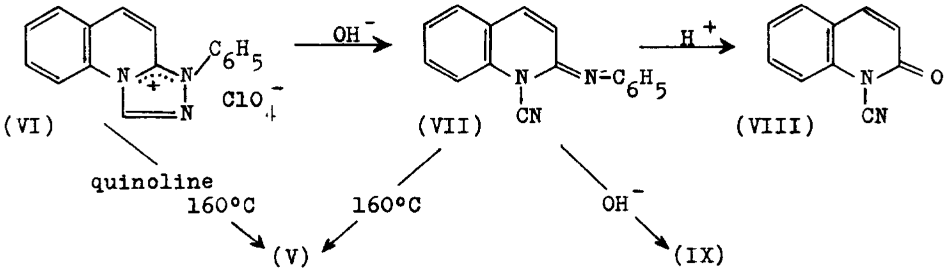
We were able to obtain the products of the kind already described by P.W. Neber and H.Worner only operating at relatively low temperatures (60-70 °C). At higher temperatures (160-180 °C) the above compounds undergo a complex trasformation process from which α-pyridyl-, 2-quinolyl- and 1-isoquinolylsubstituted arylcyanamides are eventually formed. By reacting t-butylphenylhydrazonochloroacetate (IV) (m.p. 88°C from ligroin) and quinoline at 160°C we obtained carbon dioxyde, isobutene and N-phenyl-N-(2-quinolyl)cyanamide (V) (m.p. 119°C from ligroin; IR spectrum: ν C≡N 2280 cm^{-1}, nujol). The structure of (V) was confirmed through alkaline hydrolysis to N-phenyl-2-aminoquinoline (4) and indipendent synthesis from 2-chloroquinoline and potassium phenyl-cyanamide in DMF.



(V)

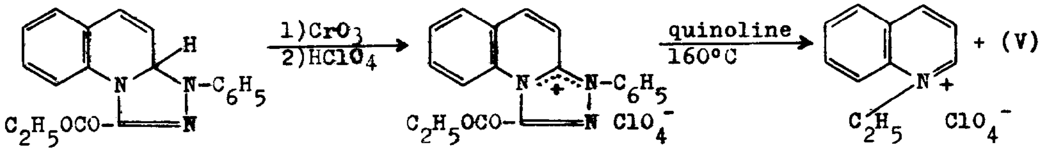
Isoquinoline, pyridine and some of their omologues presented with different arylhydrazonic halides (IV) a quite similar behaviour. For R= CH_3 or C_2H_5 the gaseous reaction products contained methyl chloride or ethyl chloride, respectively.

By reacting 3 moles of quinoline with 1 mole of t-butyl or ethyl phenylhydrazonochloroacetate at 70°C for 12 hours and by adding to the reaction product perchloric acid the perchlorate (VI) was obtained (m.p. 264°C from acetic acid). (VI) was converted in high yields to (V) at 160°C in presence of quinoline. The structure of (VI) was confirmed through its transformation in (VII) (m.p. 149°C from ethanol; IR spectrum: ν C≡N 2280 cm^{-1}, ν C=N 1665 cm^{-1}, nujol) by treatment with diluted NaOH. Heating to 160°C converts (VII) to (V). From (VII) we were also able to obtain 2-phenylaminoquinoline (IX) or N-cyano-2-quinolone (VIII) with alkalies or acids, respectively. Alkaline cleavage of (VIII) (m.p. 136°C from ethanol; IR spectrum: ν C≡N 2280 cm^{-1}, ν C=O 1705 cm^{-1}, nujol) yields 2-quinolone (5):



Quite similarly to (VI) behaved the corresponding salts which were obtained from pyridine and isoquinoline.

High yields of a basic compound to which the triazolinic structure (X) (m.p. 123°C from ethanol) was assigned has been obtained by reacting quinoline with (IV) (Ar = C_6H_5 , R = C_2H_5) in presence of 1 mole of triethylamine at 20°C for 24 hours. (X) has been oxydated with CrO_3 in acetic acid. Through addition of $HClO_4$ to the reaction mixture it was isolated the quinolino-triazolium perchlorate (XI) (m.p. 185°C from acetic acid; IR spectrum: ν C=O 1740 cm^{-1}). By heating (XI) with quinoline at 160°C (V) and N-ethylquinolinium perchlorate (XII) (m.p. 104°C from ethanol) were obtained in satisfactory yields:



(X) (XI) (XII)

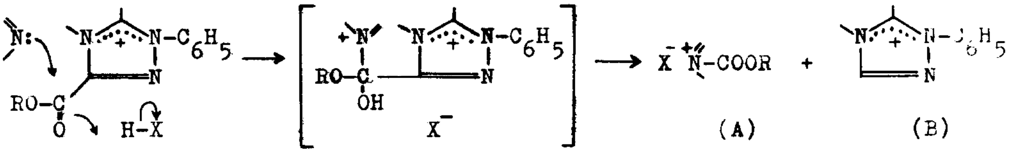
Isoquinoline reacted similarly.

The above facts can be rationalized by formulating formation of the arylcyanamides as taking place through the following steps.

(a) Reaction of hydrazonic halides (IV) with the heterocyclic bases affording the triazolinic compounds (X and analogues). (°)

(b) Dehydrogenation, brought about by an unknown chemical species, to the triazolium salts (XI and analogues).

(c) Elimination of the carboxyalkyl chain from the triazolium salts; this elimination is accomplished by the base according the following mechanism:



From the adduct (A) isobutene is produced when R = t-C_4H_9 and an alkyl chloride is formed when R = CH_3 or C_2H_5. The literature reports (7,8) that t-alkyl chlo-

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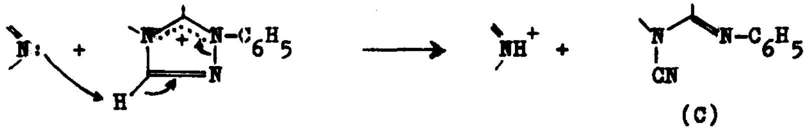
(°) We have assigned to this compound a cyclic structure quite similar to the structure of the triazolines obtained by R.Huisgen through the reaction of hydrazonic halides with azomethine bases (6). Howewer an open structure of type (I) cannot be ruled out.

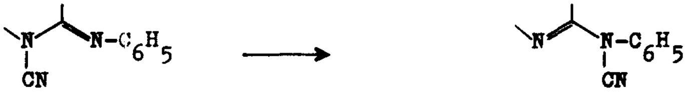
roformates are cleaved by pyridine to olefines. In the same conditions primary alkyl chloroformates yield alkyl chlorides.

(d) Deprotonation of the triazolium salt (B) followed by ring cleavage by a second molecule of heterocyclic base at an elevated temperature:



(C)

(e) Thermal isomerisation of the cyanocompound (C) to the hexocyclic cyanoderivative:



The formation of N-ethylquinolinium perchlorate in the reaction of (XI) with quinoline is well explained by the hypothesis that the intermediate (A) ($X = ClO_4^-$ and $R = C_2H_5$) is more easily attacked by another quinoline molecule than by ClO_4^-, the nucleophylic character of the latter beeing negligible.

All the products described in this work gave satisfactory analytical values.

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