A Unique Pyrimidine Ring Contraction leading to Pyrroles

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ZINC-DUST DEHALOGENATIONS of pyrimidines are well known. These reactions are usually carried out in neutral, basic, or mildly acidic conditions.[1] Here is described the dehalogenation of certain 4-chloropyrimidines using zinc and aqueous acetic acid, leading to certain pyrroles otherwise difficult to prepare.

Treatment of the pyrimidine (Ia) with zinc and 50% aqueous acetic acid at 95° for 1 hr. gave, after dilution with water, benzene extraction, and purification by chromatography, the pyrrole isomers (IIa and IIIa) in the ratio of about 1:5. It was difficult to separate these isomers completely, and crystalline material was not obtained. When the reaction was stopped after 5 min. the dehalogenated pyrimidine (Ib) was obtained. Further treatment of (Ib) with zinc and acetic acid gave the pyrroles (IIa and IIIa). The pyrroles rapidly turned pink in solution or on t.l.c. plates.

The dichloropyrimidine (Ic) reacted with zinc and acetic acid to give, after 3 hr., the pyrrole (IIc).

Treatment of the pyrimidine (IV) with the same reagent gave, after 20 min., the pyrrole (V). After removal of this pyrrole, the aqueous portion was basified with ammonium hydroxide, and extracted with benzene. The dihydropyrimidine (VI) was isolated from this extract.

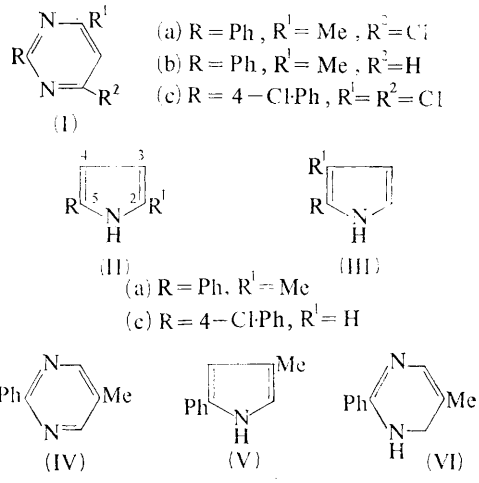
The structures of the pyrroles were assigned as follows: mass spectrum analysis gave the following molecular formulae: (IIa), (IIIa), and (V) (m.p. 150° with sublimation, lit.[2] 151–152°), $C_{11}H_{11}N$; and (IIc) (m.p. 137—139°, lit.[3] 136·5°) $C_{10}H_8ClN$. N.m.r. ($CDCl_3$) spectroscopy provided the most evidence for structure and is best presented in the form of a Table, which shows only the chemical shifts of protons assigned as pyrrole protons (H-2, H-3, and H-4).

TABLE

Chemical shifts of pyrrole protons (τ)

Compound	H-2	H-3	H-4
5-Phenylpyrrole	3·29	3·72	3·49
(IIc)	3·26	3·79	3·58
(IIa)	—	4·15	3·71
(IIIa)	3·35	3·94	—
(V)	3·53	—	3·75

The pyrrole protons of 5-phenylpyrrole appeared as multiplets. Treatment with D_2O caused collapse to broadened quartets, and the coupling constants J_{23}, J_{24}, and J_{34}, were found to be 2·75, 1·5, and 3·5 c./sec. respectively. The chemical shifts and band multiplicities of the pyrrole protons in (IIc) were very similar to those of 5-phenylpyrrole, and D_2O treatment again caused collapse to quartets. The coupling constants J_{23}, J_{24}, and J_{34}, were the same as for 5-phenylpyrrole. The pyrrole protons, in (IIa) and (IIIa), appeared



as triplets, slightly broadened by a small coupling with the methyl group and by slightly different coupling between the N–H and the ring protons. The triplet character of the protons of pyrrole itself is ascribed to equal coupling of the N–H with the other ring protons.[4] The pyrrole protons in (V) appeared as unresolved multiplets. Double resonance of the N–H signal in (IIa), (IIIa), and (V) removed all N–H coupling and the coupling constants J_{34}, J_{23}, and J_{24} were again found to be 3·5, 2·75, and 1·5 c./sec. respectively.

The remaining protons of pyrroles of types (II), (III), and (V) were assigned as follows: τ 1·7—2·1 (1H, very broad, N–H), τ 2·6—2·9 [4 or 5H (a or c types), m, phenyl protons], τ 7·81—7·91 (where present) (3H, s, Me). Thus n.m.r. spectroscopy provides very good evidence for the structures suggested.

The structure of the dihydropyrimidine (VI) was assigned as follows: the compound melted over the range 92—135°. T.l.c. on a melted

sample showed a spot identified as the pyrimidine (IV).

Further evidence that (VI) is oxidized by air to (IV) was obtained during purification of (VI) by preparative t.l.c. It was found that (VI) could not be obtained free of (IV) even though solvent systems giving large differences in R_F values for (VI) and (IV) were used. Such easy oxidation of a dihydropyrimidine is very unusual.[6]

The n.m.r. spectrum ($CDCl_3$) of (VI) ($C_{11}H_{12}N_2$ from mass spectrum) showed proton signals at τ 2·45 (2H, m, phenyl protons *ortho* to ring junction), τ 2·75 (3H, m, phenyl protons), τ 4·0 (1H, quartet, olefinic proton at C-4 in the pyrimidine ring), τ 5·55 (1H, broad, N–H), τ 5·98 (2H, s, H_2 at C-6 in the pyrimidine ring), τ 8·53 (3H, s, Me). This evidence is consistent with the structure suggested for (VI).

The nearest analogy found to the ring contraction described is the preparation of 2,4,5-triphenylimidazole from 2,4,6-triphenyl-1,3,5-triazine, by reduction with zinc in glacial acetic acid.[7]

The mechanism of the pyrimidine ring contraction is not yet clear and further work is in progress.

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