α- and β-Pyrrolenines *via* a Pyrrole Grignard Reaction

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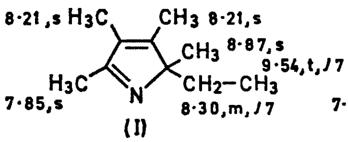
Summary β-Pyrrolenines, hitherto unknown but widely speculated, have been prepared and characterized along with the α-isomers.

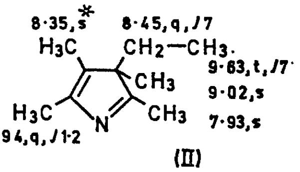
THE α- and β-pyrrolenines, two tautomeric formulations of pyrrole, are often invoked[1] in fundamental pyrrole chemistry and are of vital interest to the biosynthesis[2] of pyrrole pigments. However, all the known pyrrolenines are 2*H*-isomers.[3,4] It has been reported by Johnson and his co-workers[4] that alkylation of *C*-alkylpyrrole Grignard derivatives led to α-pyrrolenines exclusively. We report the first isolation, structural assignments, and characterization of several β-pyrrolenines obtained from alkylation of the Grignard derivatives of 2,3,4,5-tetramethylpyrrole, 3-ethyl-2,4,5-trimethylpyrrole (phyllopyrrole), and 3-ethyl-2,4-dimethylpyrrole (cryptopyrrole). The 3*H*-pyrroles described here provide the long-sought models for the studies of the electrophilic reactions of pyrroles[5] and the biogenesis of corrinoids[6] as in Vitamin B_{12}.

The Grignard derivatives of the above pyrroles were produced by an exchange reaction with methylmagnesium iodide and subsequently treated with an alkyl iodide.[4] The basic pyrrolenine fraction, obtained from the reaction mixture by extraction, was analysed and separated by g.l.c.† Satisfactory analyses were obtained for the liquid bases as picrates. All of the β-pyrrolenines isolated so far possess what may be described as camphoraceous odours whereas the α-isomers give pungent amine-like odours. The picrates of the isomeric pairs showed similar m.p.'s and almost no mixed-m.p. depression. The spectral properties‡ of the isomers are quite distinct. Thus, treatment of the Grignard derivative of tetramethylpyrrole with ethyl iodide gave an 83% yield of pyrrolenines of which 77% was the amine-like 2*H*-pyrrole (I), λ_{max} nm (ε) 242 (3610), pH 1, 266 (5070); ν_{max} cm^{-1} 1660, 1570, and 23% of the camphoraceous 3*H*-isomer (II), λ_{max} (ε) 264 (2160), pH 1, 286 (2240); ν_{max} 1650, 1580. Confirmation of structure (II) for the camphoraceous pyrrolenine was sought in the methylation of the Grignard derivative of phyllopyrrole. The reaction yielded a mixture of four pyrrolenines (41% of 2*H*-pyrroles and 59% of the 3*H*-isomers) which were resolved on an Apiezon L–KOH column. The major β-pyrrolenine obtained from preparative g.l.c. was found to be identical with (II) derived from tetramethylpyrrole in all respects (u.v., n.m.r., m.p. of the picrate, and superimposable i.r. and mass spectra). Since structure (II) is unequivocally established for the camphoraceous material obtained from ethylation of tetramethylpyrrole, the isomeric 2*H*-pyrrole (I) is correctly assigned on the basis that it is the only other isomeric pyrrolenine possible.

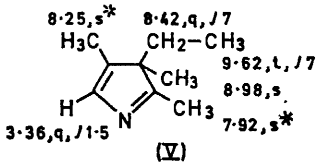
Methylation of the Grignard derivative of tetramethylpyrrole provided the pyrrolenines in 77% yield, of which 41% was the 2*H*-pyrrole (III): λ_{max}(ε) 240 (3940), pH 1, 264 (5410); ν_{max} 1665, 1570; n.m.r.: τ 7·83 (s,3), 8·18 (s,6), 8·83 (s,6), and 59% the 3*H*-isomer (IV): λ_{max}(ε) 262 (2600), pH 1, 283 (2650); ν_{max} 1650, 1580; n.m.r.: τ 7·88 (s,3), 7·99 (q,3, *J* 1), 8·29 (s*,3), 9·01 (s,6). The assignments of structures are made by analogy in respect to i.r., u.v., n.m.r., mass spectra, and odour with the ethylated pyrrolenines (I) and (II). Ozonolysis[4] of the bases from methylation of tetramethylpyrrole gave biacetyl in 23% yield and is compatible with the present results.



(I)



(II)



(V)

The alkylation of cryptopyrrole is of interest because of its connection with the biogenesis of porphyrins.[2] Alkylation was postulated[4] at the α-position to yield a 2*H*-pyrrole. We have re-examined the products obtained from methylation of cryptopyrrolylmagnesium iodide. Phyllopyrrole was isolated in 49% yield as a result of C-5 methylation. A monomethylated cryptopyrrole accounted for 80% of the basic components; the remaining 20% was made up of the methylation products of phyllopyrrole. The major pyrrolenine after separation by g.l.c. had a camphoraceous odour, λ_{max}(ε) 254 (3110), pH 1, 272 (3160); ν_{max} 1615, 1575, and an n.m.r. spectrum only consistent with the 3*H*-pyrrole structure (V). An analogy to the assignment of the high triplet at τ 9·62 can be found in the ethyl-CH_3 (τ 9·46) of 3,3-diethylindolenine.[7] Methylation of cryptopyrrole with trideuteriomethyl iodide produced trideuteriomethyl-pyrrolenine in the same manner, n.m.r.: τ 3·36 (q,1, *J* 1·5), 7·92 (s*,3), 8·25 (s*,3), 8·43 (q,2, *J* 7), and 9·61 (t,3, *J* 7). The spectrum is virtually superimposable on the nondeuteriated one except for the disappearance of the singlet at τ 8·98, thus completing the structural assignment.

The mass spectra of all the pyrrolenines obtained thus far showed strikingly similar fragmentation pattern. However, within the various isomer pairs, the $M - 1$ peak in the 2*H*-isomer relative to the molecular ion peak is larger (usually twice as intense) than in the corresponding 3*H*-isomer, hence is a useful feature which indicates the pyrrolenine as being the 2*H*- or 3*H*-isomer.

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† Columns effective in separating the pyrrolenine isomers include: 20% THEED on Anachrom, 60—70 mesh, and 20% Apiezon L on KOH-treated Chromosorb-W, 70—80 mesh. Column temperature ranged from 100—120°, isothermal.

‡ U.v. spectra were taken in 95% EtOH, i.r. as 10% CCl_4 solution, n.m.r. in $CDCl_3$ (reported as τ values from internal Me_4Si, *J* in Hz) and s* refers to broadened singlet due to unresolved multiplet.

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