SYNTHESIS AND REDUCTION OF 2H-CYCLOHEPTA[c]PYRROL-6-ONES[1]

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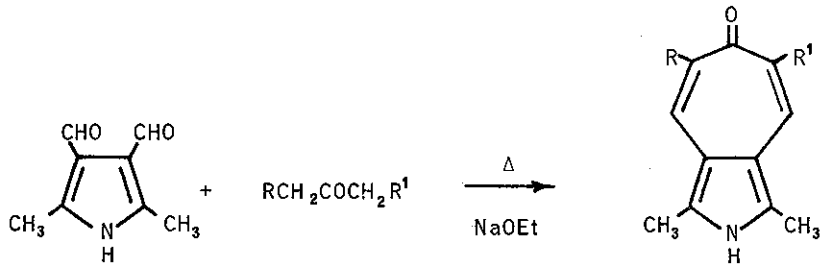
The base catalysed condensation of 3,4-diformyl-2,5-dimethylpyrrole with propanone derivatives to give 2H-cyclohepta[c]pyrrol-6-ones is described. The reaction of the intermediate 1-(2,5-dimethyl-3-pyrrolyl)prop-1-en-3-ones with hydrazine yields 5,7-dimethyl-6H-pyrrolo[3,4-d]pyridazine. Catalytic hydrogenation of the 2H-cyclohept[c]pyrrol-6-ones produces the 4,5,7,8-tetrahydro ketones and the corresponding alcohols.

The recently reported synthesis of 2H-cyclohepta[c]pyrrol-6-one and several 5,7-disubstituted derivatives[2] prompts us to communicate our observations.

3,4-Diformyl-2,5-dimethylpyrrole (I) reacts over a period of 1.5h with the propanones (IIa-e) in the presence of ethanolic sodium ethoxide at ca. 78°C to give the 2H-cyclohepta[c]pyrrol-6-ones (IIIa-e) in good yield (60 - 85%)(cf. ref. 2). The parent compound (IIIf) was obtained in only 37% yield from the corresponding reaction of acetone with (I), but when the condensation was

conducted in aqueous methanol at 25°C in the presence of sodium hydroxide over a period of 24h the yield was improved to 66%. (III<u>f</u>) was also obtained from the copper catalysed decarboxylation of (III<u>g</u>) in quinoline (<u>cf</u>. ref. 2).

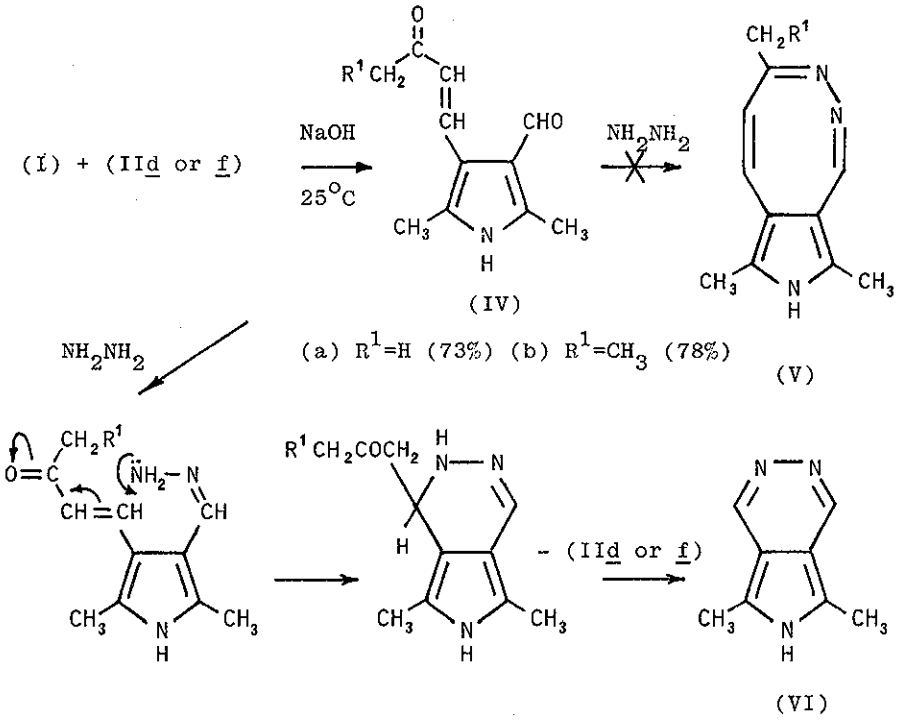


(I) (II) (III)

(<u>a</u>) R=R^1= CH_3; (<u>b</u>) R=R^1= C_6H_5; (<u>c</u>) R=R^1= CO_2CH_3; (<u>d</u>) R= H, R^1= CH_3; (<u>e</u>) R= H, R^1= C_6H_5; (<u>f</u>) R=R^1= H; (<u>g</u>) R=R^1= CO_2H

The reaction of (I) with acetone and butan-2-one (II<u>d</u>) in the presence of sodium hydroxide over a period of 3h gave the intermediate α,β-unsaturated ketones (IV) which, upon heating in presence of sodium ethoxide, were converted into the bicyclic compounds (III<u>f</u> and <u>d</u>), respectively. Attempts to characterize (IV<u>a</u> and <u>b</u>) through the formation of their hydrazones or the bicyclic system (V) failed, as the hydrazone derivatives of both compounds underwent an intramolecular Michael addition reaction followed by a retro-aldol type reaction with the extrusion of the propanones (identified by glc) and the formation of 5,7-dimethyl-6<u>H</u>-pyrrolo[3,4-<u>d</u>]pyridazine (VI). Compound (VI) has also been obtained by the direct reaction of (I) with hydrazine[4] and similar reactions occur between (I) or (IV) and phenylhydrazine and

methylhydrazine to give 2-substituted 5,7-dimethyl-2H-pyrrolo-[3,4-d]pyridazines.[4]

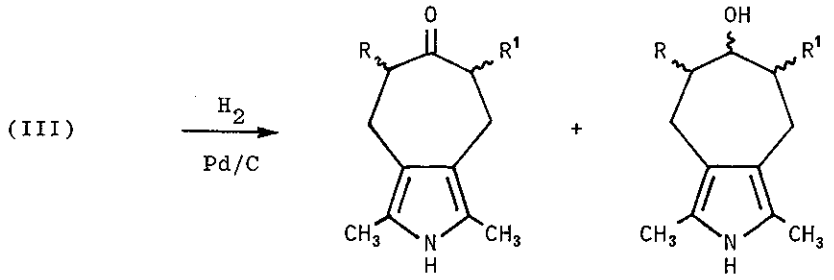


The condensation of (I) with cyclic ketones has also been examined[4] and will be described in the full paper.

Catalytic hydrogenation of 2H-cyclohepta[c]pyrrol-6-ones gave mixtures of the 4,5,7,8-tetrahydro derivatives (VII) and the corresponding alcohols (VIII), the highest yields of the alcohols being obtained from the least sterically hindered systems. Complete conversion of the ketones into the alcohols was effected by reduction with sodium borohydride.

Analysis of the relative configurations of the 5-, 6-, and 7-substituents and the preferred conformations of the seven-membered

rings are in hand and will be reported in the full paper.



		(VII)	(VIII)
(a)	$R=R^1= CH_3$	67%	13%
(b)	$R=R^1= C_6H_5$	88%	3%
(c)	$R=R^1= CO_2CH_3$	77%	0%
(d)	$R=R^1= H$	33%	66%
(e)	$R= H, R^1= CH_3$	22%	58%

REFERENCES

1. Pyrrole Studies Part XVIII. Part XVII C.F. Candy and R.A. Jones, J. Org. Chem., 1971, 36, 3993.
2. R. Kreher, G. Vogt and M-L. Schultz, Angew. Chem., Internat. Edn., 1975, 14, 821.
3. Elemental analysis for all new compounds were satisfactory and structures were confirmed by ir and nmr spectroscopy.
4. S. Singh, Ph.D. Thesis, University of East Anglia, 1975.

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