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4-OXO-2-PYRROLINES CARRYING NO SUBSTITUENTS ON THE RING CARBON: SUBSTITUENT EFFECTS IN THE TAUTOMERISM BETWEEN 4-OXO-2-PYRROLINES AND 3-HYDROXYPYRROLES

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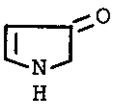
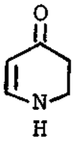
Syntheses of 4-oxo-2-pyrrolines having no substituents on the ring carbon were accomplished, and the substituent effects governing the tautomerism between hydroxypyrroles and pyrrolinones were investigated in a series of 3-hydroxypyrroles synthesized.

4-Oxo-2-pyrroline (I) is the smallest of vinylogous lactams. It is of interest to compare I with 4-oxo-1,2,3,4-tetrahydropyridine[1] (II) with respect to reactivities and spectral properties. It is also of interest to investigate the tautomerism between I and 3-hydroxypyrrole (III), because only theoretical treatment[2] has been given to this simple system whereas the derivatives of I and III have been synthesized and discussed[3] for the tautomerism on the basis of observed data. However, the nonsubstituted system of I or III has not been synthesized to date.


(I)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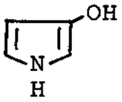
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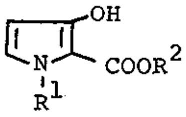
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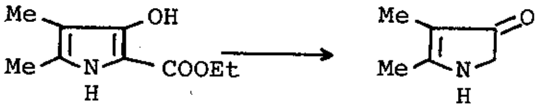
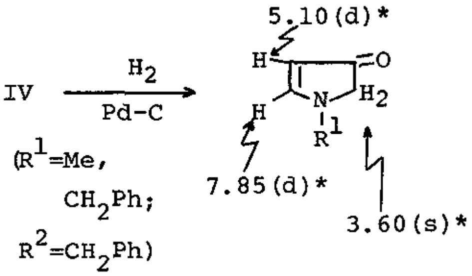
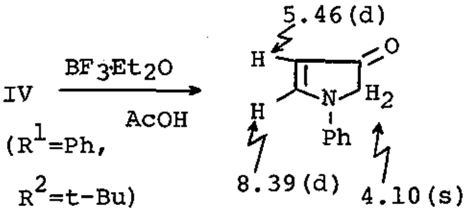

(V) (VI)

We attempted the synthesis of I starting from various alkyl 3-hydroxypyrrole-2-carboxylates (IV). In spite of the successful result[4] in 4,5-dimethyl derivative (V → VI), ketonic cleavage of IV (R^1=H, R^2=Et) or the acid cleavage of a t-butyl ester (IV; R^1=H, R^2=t-Bu) or the hydrogenolysis of a benzyl ester (IV; R^1=H, R^2=CH_2Ph) prepared from an ethyl ester (IV; R^1=H, R^2=Et) by ester exchange reaction resulted in formation of complex products, owing probably to extreme instability of nonsubstituted 4-oxo-2-pyrroline.

However, N-benzyl- and N-methyl-4-oxo-2-pyrrolines (VII) could be isolated by hydrogenolysis of IV (R^1=R^2=CH_2Ph and R^1=Me, R^2=CH_2Ph), respectively, and N-phenyl-4-oxo-2-pyrroline (VIII) could be obtained on the acid cleavage of IV (R^1=Ph, R^2=t-Bu) with boron trifluoride etherate. These compounds (VII and VIII) are the first instance of 4-oxo-2-pyrrolines having no substituents on the ring carbon, but unfortunately, they are extremely unstable in the presence of oxygen, especially in dilute solution at room temperature.



UV:327 nm*
(VII)

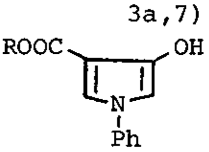


UV:243 nm
354 nm
(VIII)

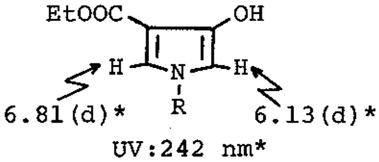
* : the value for $R^1=CH_2Ph$

Davoll[3a] has reported that N-phenyl-4-hydroxypyrrole-3-carboxylates (IX) exist as the hydroxy form owing to the interannular conjugation between the phenyl and pyrrole rings. But we have found that compound VIII does not exist as the hydroxy tautomer inspite of its ability of interannular conjugation. Differentiation between two tautomers was evidently furnished by examination of their ultraviolet and PMR spectra.

On the other hand, Chong and Clezy[3e] have pointed out two factors influencing the tautomerism of 3-hydroxypyrroles; intramolecular hydrogen bonding between the ring hydroxyl and neighboring substituents, and stabilization by conjugation of the enol system with a carbonyl group. They have also mentioned that 3-hydroxypyrroles substituted in the 2-position with carbonyl group usually exist as the hydroxy tautomer while the 4-hydroxypyrrole-3-carboxylates, e.g., X, are usually found as the keto form.

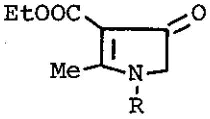


(IX)



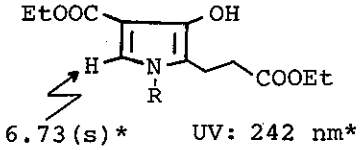
(R=Me, Ph, CH_2Ph)

(XI)



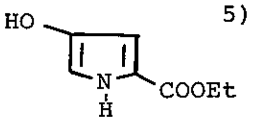
(R=H, Ph)

(X)

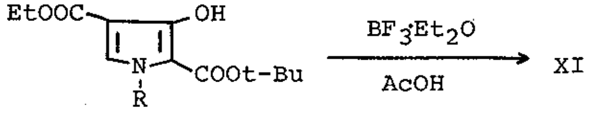


(R=Me, CH_2Ph)

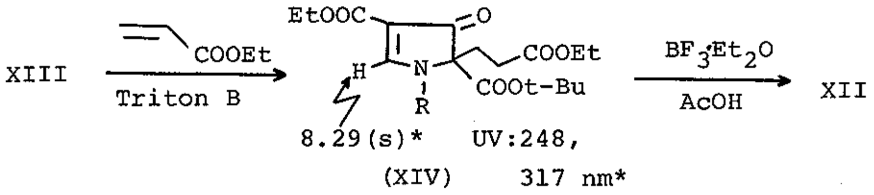
(XII)



(XV)



(XIII)

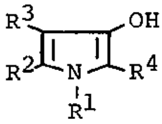
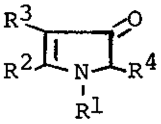


* : the value for $R=CH_2Ph$

But the present compounds, N-methyl- and N-benzyl-4-hydroxypyrrolecarboxylates (XI and XII) were found to exist as the hydroxy form. Compounds XI were prepared from the t-butyl esters of N-substituted 4-ethoxycarbonyl-3-hydroxypyrrole-2-

carboxylic acids (XIII) by acid cleavage with boron trifluoride etherate, and compound XII was obtained via acid cleavage of a triester (XIV) which was prepared from XIII by Michael addition with ethyl acrylate.

Table Influence of ring substituents on the tautomerism between 3-hydroxypyrroles and 4-oxo-2-pyrrolines

Substituents					
R^1	R^2	R^3	R^4		
H	Me	Me	H		VI[6]
Me, CH$_2$Ph	H	H	H		VII
Ph	H	H	H		VIII
H, CH$_2$Ph, Me, Ph	H	H	COOR	IV	
H	Me	Me	COOEt	V[3e]	
H, CH$_2$Ph, Me, Ph	H	COOEt	COOR	XIII	
Me, Ph, CH$_2$Ph	H	COOEt	H	XI	
Me, Ph, CH$_2$Ph	H	COOEt	CH$_2$CH$_2$COOEt	XII	
H, Ph	Me	COOR	H		X[3a]
Me, Ph	NMe$_2$	Ph	H		XVI[8]

The difference in favorable form of existence between IX and X would be derived from the ability of intramolecular hydrogen bonding. In the presence of a substituent at the C-2 position in X, steric repulsion between the carbonyl group at the C-3 position and the C-2 substituent would eliminate the possible conformation needed for hydrogen bonding between the C-3 carbonyl and the C-4 hydroxyl. Now, it is clear that this tautomerism is largely influenced both by the nature of substituents and by the mode of their substitution. Some examples are collected and listed in the table.

However, it is still difficult to understand the argument by Kuhn and Osswald[5] that 5-ethoxycarbonyl-3-hydroxypyrrole (XV) exists predominantly as the hydroxy tautomer.

REFERENCES

1 A. Haider, G. Cornuz and H. Wyler, Helv. Chim. Acta, 1975, **58**, 1287.

2 N. Bodor, M. J. S. Dewar and A. J. Harget, J. Am. Chem. Soc., 1970, **92**, 2929.

3 a) J. Davoll, J. Chem. Soc., 1953, 3802; b) A. Treibs and A. Ohorodnik, Ann., 1958, **611**, 139; c) Idem, ibid., 1958, **611**, 149; d) R. S. Atkinson and E. Bullock, Can. J. Chem., 1963, **41**, 625; e) R. Chong and P. S. Clezy, Aust. J. Chem., 1967, **20**, 935.

4 G. Pfeiffer and H. Bauer, Ann., 1976, 383.

5 R. Kuhn and G. Osswald, Ber., 1956, **89**, 1423.

6 H. Bauer, Ann., 1970, **736**, 1.

7 E. Benary and R. Konrad, Ber., 1923, **56**,44.

8 R. Fuks and H. G. Viehe, Tetrahedron, 1969, **25**, 5721.

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