

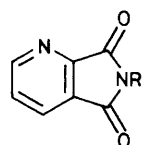
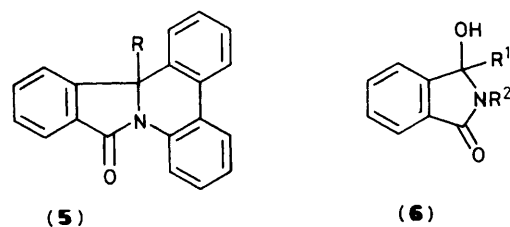
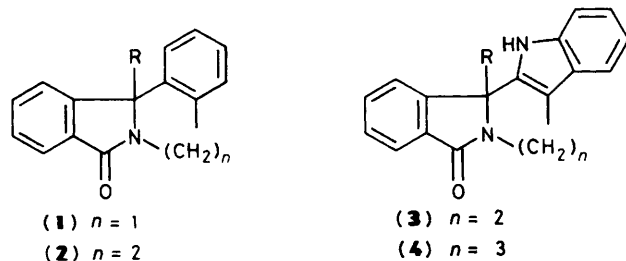
New Fused Heterocyclic Systems derived from Pyridine-2,3-dicarboximides

Gregory J. Hitchings and John M. Vernon*

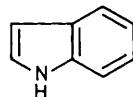
Department of Chemistry, University of York, Heslington, York YO1 5DD, U.K.

α -Hydroxylactams (**8**), formed by regioselective reduction or Grignard addition to pyridine-2,3-dicarboximides (**7**), undergo acid-catalysed cyclodehydration to give the new pyrido[2',3':3,4]-pyrrolo fused heterocyclic systems (**10**)—(**13**).

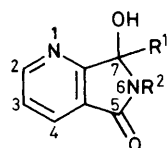
A widely used procedure for the synthesis of fused heterocyclic systems involves the cyclodehydration of α -hydroxylactams.¹ In particular, derivatives of the fused isoindole systems



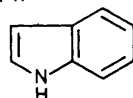
- (7) **a**: $R = \text{CH}_2\text{Ph}$
b: $R = \text{CH}_2\text{CH}_2\text{Ph}$
c: $R = \text{CH}_2\text{CH}_2$



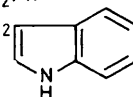
- d**: $R = o\text{-C}_6\text{H}_4\text{Ph}$



- (8) **a**: $R^1 = \text{H}, R^2 = \text{CH}_2\text{Ph}$
b: $R^1 = \text{H}, R^2 = \text{CH}_2\text{CH}_2\text{Ph}$
c: $R^1 = \text{H}, R^2 = \text{CH}_2\text{CH}_2$



- d**: $R^1 = \text{H}, R^2 = o\text{-C}_6\text{H}_4\text{Ph}$
e: $R^1 = \text{Ph}, R^2 = \text{CH}_2\text{Ph}$
f: $R^1 = \text{Ph}, R^2 = \text{CH}_2\text{CH}_2\text{Ph}$
g: $R^1 = \text{Ph}, R^2 = \text{CH}_2\text{CH}_2$



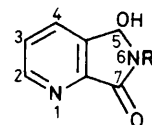
- h**: $R^1 = \text{Ph}, R^2 = o\text{-C}_6\text{H}_4\text{Ph}$

(**1**)—(**5**) have been obtained by acid treatment of *N*-substituted hydroxyphthalimidines (**6**)^{2,3} or, in some cases, by a one-step procedure from *o*-acylbenzoic acids and the appropriate amines.^{3,4} Our preparation of aza-analogues of the fused heterocyclic systems (**1**)—(**3**) and (**5**) *via* cyclodehydration of hydroxylactams derived from pyridine-2,3-dicarboximides (**7a—d**) represents a significant extension of the utility of this general method.

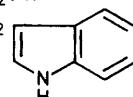
Reduction of the imides (**7a—d**) with sodium borohydride in ethanol gave mixtures of regioisomeric hydroxylactams (**8**) and (**9**) (Table 1). These were distinguished by ¹H and ¹³C n.m.r. evidence, which showed that the major product in each case was the 7-hydroxy-5-oxo-pyrrolo[3,4-*b*]pyridine (**8**) formed by attack at the more reactive carbonyl group in (**7**). For example, in the ¹H n.m.r. spectrum of (**9b**), irradiation at the frequency for the resonance of H-4 produced a nuclear Overhauser enhancement of the resonances due to H-3 and H-5. The corresponding experiment with the regioisomer (**8b**) showed no such interaction between H-4 and H-7.

Reaction of the imides (**7a—d**) with a four-fold excess of phenylmagnesium bromide gave in every case only a single adduct (Table 1). Comparison of ¹³C n.m.r. chemical shifts for the ring junction atoms C-4a and C-7a, which are distinctively different in (**8a—d**) and (**9a—d**), showed the Grignard adducts to be (**8e—h**). The regioselectivity observed in these reactions may be attributed to co-ordination of the pyridine nitrogen atom to magnesium, which directs the Grignard addition to the adjacent carbonyl group.

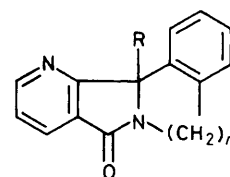
Cyclodehydration of the hydroxylactams (**8b—h**) occurred in refluxing trifluoroacetic acid to give the corresponding pyrido[2',3':3,4]pyrrolo fused heterocyclic products listed in



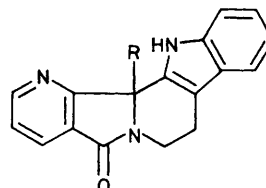
- (9) **a**: $R = \text{CH}_2\text{Ph}$
b: $R = \text{CH}_2\text{CH}_2\text{Ph}$
c: $R = \text{CH}_2\text{CH}_2$



- d**: $R = o\text{-C}_6\text{H}_4\text{Ph}$



- (10) **a**: $n = 1, R = \text{H}$
b: $n = 1, R = \text{Ph}$
a: $n = 2, R = \text{H}$
b: $n = 2, R = \text{Ph}$



- (12) **a**: $R = \text{H}$
b: $R = \text{Ph}$



- (13) **a**: $R = \text{H}$
b: $R = \text{Ph}$

Table 1. Hydroxylactam and fused heterocyclic products.^a

Imide	Reducing agent	Hydroxylactam(s)	% Yield	Cyclised product	% Yield
(7a)	NaBH ₄	(8a), (9a)	50, 18	(10a)	0
(7b)	NaBH ₄	(8b), (9b)	82, 14	(11a)	93
(7c)	NaBH ₄	(8c), (9c)	63, trace	(12a)	64
(7d)	NaBH ₄	(8d), (9d)	58, 19	(13a)	88
(7a)	PhMgBr	(8e) ^b	62	(10b)	40
(7b)	PhMgBr	(8f)	83	(11b)	73
(7c)	PhMgBr	(8g)	100	(12b)	56
(7d)	PhMgBr	(8h)	100	(13b)	64

^a All new compounds are characterised by appropriate spectroscopic evidence, including atomic composition of the molecular ion by mass spectrometry. ^b Molecular ion absent in the mass spectrum of (8e), but atomic composition C₂₀H₁₆N₂O verified for the peak at highest *m/z* corresponding to [M - O]⁺.

Table 1. Ring closure failed only in the case of (8a), as reported previously for the related *N*-benzylphthalimidine derivative (6; R¹ = H, R² = CH₂Ph);² under more forcing conditions (hot polyphosphoric acid) only tars were obtained.

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