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A VERSATILE NEW SYNTHESIS OF QUINOLINES AND RELATED FUSED PYRIDINES. PART IV.[1]

A SIMPLE ONE-POT ROUTE TO PYRIDO[2,3-b]QUINOLIN-2-ONES FROM ANILIDES.

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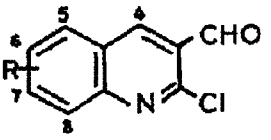
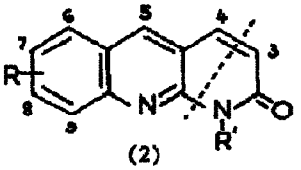
Abstract: *The title pyridoquinolin-2-ones are readily made by sequential treatment of an acetanilide firstly with DMF and $POCl_3$ and then with another secondary amide.*

In earlier papers in this series we have outlined a versatile approach to 2-chloro-3-formylquinolines (1) from acetanilides under Vilsmeier conditions.[2] A minor by-product from



(1)

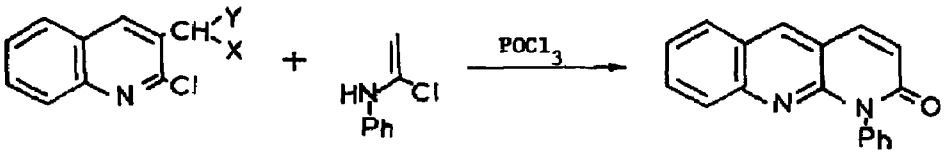


(2)

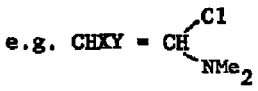
acetanilides under these conditions (readily observed by its bright blue fluorescence under u.v. during t.l.c. examination) was found to be the pyridoquinolinone (2; R=H, R'=Ph), formally derivable from (1) and acetanilide (dotted lines in 2). Although reaction of (1) with acetanilide under a variety of conditions failed to give any (2), the latter product formed in reasonable yield (25%) when 2 moles of acetanilide was reacted with DMF (2M) and $POCl_3$ (7M) at 75° for 18 h, suggesting that the protected chloro-aldehyde (1) indeed reacts with a derivative of acetanilide, probably the bidentate nucleophilic enamine (3) (Scheme). We have demonstrated already that this enamine is a key intermediate in the conversion of acetanilide to 2-chloroquinoline-3-aldehyde.[2b]

The pyridoquinolinones (2) are best made as follows: A 2-chloroquinoline-3-aldehyde (1)

Dedicated to Professor B. Suschitzky on his 65th birthday.



(3)

e.g. CHXY = 

Scheme

is prepared as described previously[2] by the action of DMF (2M) and $POCl_3$ (7M) on an acetanilide (1M). To this reaction mixture is added a secondary amide (1M) in $POCl_3$ (7M) solution containing one drop of DMF and the mixture heated for a further 2-3 h at 75°. The mixture is poured into ice-water, make alkaline (pH 9) and the crude product extracted and triturated with ice-cold methanol. By this means a variety of pyridoquinolinones have been generated in a simple one-pot procedure.

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Table

Starting Acetanilide	Derived Quinoline (1) R=	Added Amide	Product (2) R	Product (2) R'	Yield (%)	M.p. (°C)
PhNHAc	H	PhNHAc	H	Ph	59	256-6
m-MeC_6H_4NHAc	7-Me	p-$MeOC_6H_4NHAc$	8-Me	p-$MeOC_6H_4$	33	270-2
m-MeC_6H_4NHAc	7-Me	p-ClC_6H_4NHAc	8-Me	p-ClC_6H_4	25	300-1
m-MeC_6H_4NHAc	7-Me	EtNHAc	8-Me	Et	22	169-172
m-MeC_6H_4NHAc	7-Me	$PhCH_2NHAc$	8-Me	$PhCH_2$	26	210-11
PhNHAc	H	PhNHCOEt	3-Me	Ph	27	244-5

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References

1. Part III, O. Meth-Cohn, S. Rhouati and B. Tarnowski, Tetrahedron Letters, 1979, 4885.

2. (a) B. Narine and O. Meth-Cohn, Tetrahedron Letters, 1978, 2045;

(b) O. Meth-Cohn, B. Narine and B. Tarnowski, Tetrahedron Letters, 1979, 3111.

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