Tetrahedron Letters No. 50, pp 4885 - 4886. 0040-4039/79/1208-4885$02.00/0

A VERSATILE NEW SYNTHESIS OF QUINOLINES AND RELATED FUSED PYRIDINES. PART III.

Otto Meth-Cohn*, Salah Rhouati and Brian Tarnowski

The Ramage Laboratories, Department of Chemistry and Applied Chemistry

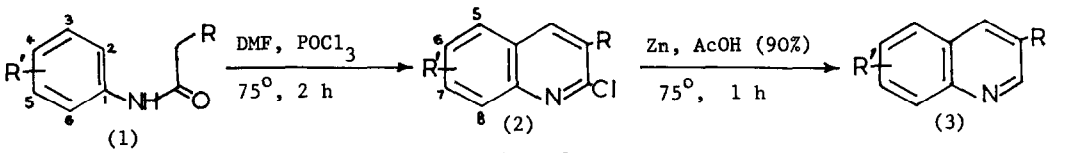
University of Salford, Salford M5 4WT, England

The action of dimethylformamide in phosphorus oxychloride on acylanilides gives 2-chloro-3-substituted quinolines, which may be dechlorinated to give 3-substituted quinolines in good yield. Similarly, N-nitrosodimethylamine in phosphorus oxychloride converts acylanilides into 2-chloro-3-substituted quinoxazolines.

In the earlier papers[1] in this series we showed that 2-chloroquinolines, 2-chloroquinoline-3-aldehydes and the thiophen analogues of these systems are readily available by the Vilsmeier formylation of acetanilides and acetamidothiophens, respectively. We now demonstrate the versatility of this method by applying it to the synthesis of 2-chloro-3-substituted quinolines (and hence 3-substituted quinolines by reductive dechlorination) and to quinoxalines.

Treatment of the acylanilides (1) with the Vilsmeier reagent in $POCl_3$ solution (1.5 M DMF in 7 M $POCl_3$) at 75° gave the products (2) as shown below. These 2-chloroquinolines were readily α-dechlorinated with zinc and 90% acetic acid to give pure 3-substituted quinolines.

Some of these quinolines (2) were shown to be versatile synthetic intermediates. Thus,



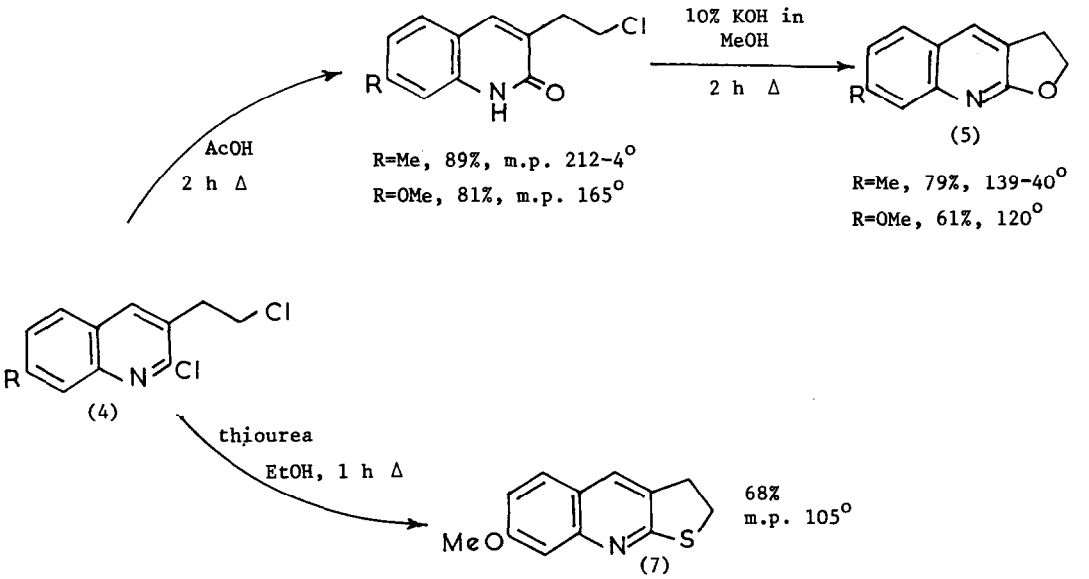
(1) (2) (3)

Scheme 1

(1)		(2)			(3)	
R	R'	Pos. of R'	%	M.p.(°C)	%	M.p.(°C)
Me	5-Me	7	78	94-5	98	78-80*
Ph	5-Me	7	95	86-7	72	83-4
Cl	5-Me	7	28	129-30	24	80
CH_2Cl	5-OMe	7	76	130	-	-
CH_2CH_2Cl	5-Me	7	95	92-3	-	-
CH_2CH_2Cl	5-OMe	7	76	90	-	-

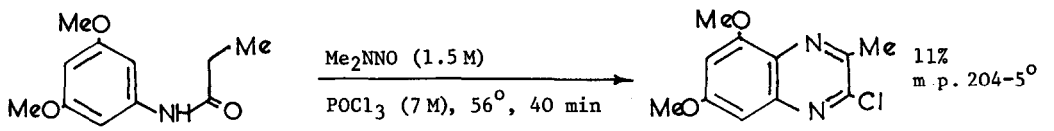
* Lit.[2] m.p. 78.5°

the 2-chloro-3-chloroethylquinolines (4) analogues of which have been prepared in a multi-step synthesis, are available in one step in high yield and allow ready synthesis of the parent of the furoquinoline alkaloids (5) in two further simple steps (Scheme 1). Similarly the thienoquinoline (7) is easily made. We feel these are the methods of choice for these systems. The remarkable specificity in the quinoline formation[1] is once more evident since the meta substituted acylanilides gave solely the one product.



Scheme 2

The second development is depicted in Scheme 2 being a novel, though as yet not optimised approach to quinoxalines. This utilises the aza-analogue of dimethylformamide which could behave as an electrophilic nitrosating agent in $POCl_3$ (i.e. $Me_2\overset{+}{N}{=}N{-}Cl$ or equivalent species). Albeit quinoxalines are formed and we are developing the reaction.



Scheme 3

We thank the S.R.C. and Clayton Aniline Company for grants to B.T. and the Algerian Government for a grant to S.R..

References

1. B. Narine and O. Meth-Cohn, Tetrahedron Letters, 1978, 2045;
O. Meth-Cohn, B. Narine and B. Tarnowski, Tetrahedron Letters, 1979, 3111.

2. M. Murugesan, N. Soundararajan, K. Ramasamy, and P. Shanmugam, Synthesis, 1979, 352.

(Received in UK 4 October 1979)