A New Preparative Route to Quinolines

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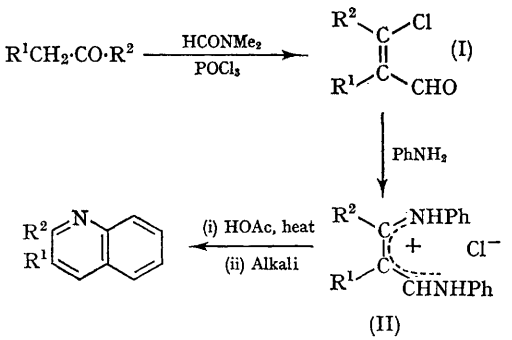
ESTABLISHED syntheses of quinoline derivatives such as the Skraup, Döbner–von Miller, and Combes reactions involve cyclisation of a carbonyl or imine group on to the activated *o*-position of a secondary arylamine.

A very simple related method is available using β-chlorovinyl aldehydes as intermediates; the latter are readily prepared from α-methylene ketones by formylation with *NN*-dimethylformamide and phosphoryl chloride.[1] These β-chlorovinyl aldehydes (I) react very readily with primary arylamines, giving imino-enamine salts (II), which in turn are cyclised to quinolines when heated in acetic acid:



(II)

Reaction appears to proceed directly from (II) to the quinoline with elimination of aniline, rather than by initial hydrolysis of (II) and ring-closure of the resultant oxo-enamine, since it takes place in anhydrous conditions. It appears to be accelerated by the presence of electron-donating groups attached to the benezne rings.

Alternatively the imino-enamine need not be isolated, and instead the chlorovinylaldehyde and amine are heated together in refluxing acetic acid to give the quinoline in one step.

When *N*-methylaniline reacts with a β-chlorovinyl aldehyde in 1 : 1 ethanol–benzene solution at room temperature a quinolinium salt is also obtained directly without separation of any intermediate (which in this case must be an oxo-enamine). For example *N*-methyl- and *N*-ethyl-aniline with 3-chloro-2-methylbut-2-enal give respectively *N*-methyl- and *N*-ethyl-2,3-dimethylquinolinium chlorides.

By these methods a number of quinolines have been prepared with great ease and in high yield. Examples are listed in the Table.

Iminoenamines analogous to (II) obtained from β-dicarbonyl compounds and primary aryl amines may also be cyclised in this way.

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TABLE

Quinoline	Overall % yield from ketone	
via Imino-enamine hydrochloride:		
2,3-Dimethyl-[2]	45	Hydrochloride, m.p. 248°; perchlorate, m.p. 182°
2-Phenyl-3-methyl-[3]	60	perhclorate, m.p. 192—195°; picrate, m.p. 208°
2,3-Cyclopenteno[4]	36	perchlorate, m.p. 188—190°; picrate, m.p. *ca.* 200° (decomp.)
2,3-Cyclohepteno[4a]	50	picrate, m.p. 195—196°
Directly:		
2,3-Cyclohexeno-[5]	54	m.p. 57—59°
1,2,3-Trimethylquinolinium chloride ..	59	m.p. 165°
2,3-Dimethyl-1-ethylquinolinium chloride ..	42	m.p. 119°
2,3-Dimethyl-5(7)-methoxy-	54	hydrochloride, m.p. 215—217° (decomp.)

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