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SYNTHESIS OF QUINOLINES BY REACTION OF ANILINOBUTENOATES WITH VILSMEIER REAGENT

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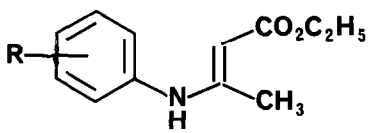
The synthesis of substituted carboethoxyquinolines is described by the reaction of ethylanilinobutenoates with Vilsmeier reagent.

As part of a programme directed toward the synthesis of potential antiparasitic agents various substituted carboethoxyquinolines were required as starting materials. This preliminary communication describes an efficient direct synthesis of substituted carboethoxyquinolines by subjecting ethyl anilinobutenoates (see Table 1) to Vilsmeier formylating conditions. Recently under similar conditions Meth-Cohn and co-workers have described a new synthesis of quinolines and related fused pyridines by using N-arylacetamides as starting materials[1]. However, the reaction was only effective with acetamido thiophens or with anilides which contained at least one activating substituent such as the 3-methoxy derivative. The utility of a procedure to obtain substituted carboethoxyquinolines using activated and deactivated substituted ethyl anilinobutenoates as starting materials, which is now reported, is illustrated with four examples (see Table 2).

Table 1 [2]

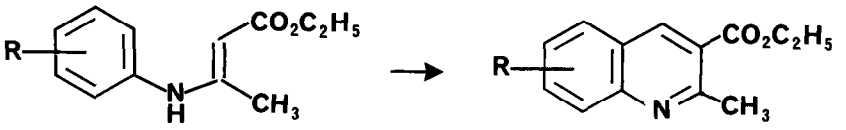


R	Yield %	bp/mp[+]
3-OMe	76	136°/0.8mm
4-OMe	87	130°/0.4mm
3-NO_2	86	50-51°
4-NO_2	94	109-110°

[+] The nitro derivatives were purified by sublimation under high vacuum.

The methoxy-substituted ethyl anilinobutenoates were prepared using a published method[3]. The nitro-derivatives were obtained by heating at 150°, the appropriate nitroamine with ethyl-3-ethoxy-but-2-enoate[4], cooling, subsequent precipitation of the product by mixing with hexane, filtration and drying. The product was then used without further purification.

Table 2 [2]



R (Substrate)	Solvent	Conditions Temp.	Time	Ratio (moles) $POCl_3$: DMF	Yield[+]	R (Product)	mp
3-OMe	$CHCl_3$	0°	2h	1 : 1	73	7-OMe	97-98°
4-OMe	$CHCl_3$	Reflux	4h	1 : 1	69	6-OMe	79-80°
3-NO_2	$CHCl_2CHCl_2$	Reflux	4h	3 : 1	61	7-NO_2	114-115°
4-NO_2	$CHCl_2CHCl_2$	Reflux	4h	3 : 1	60	6-NO_2	125-126°

[+]Isolated yield after recrystallization from hexane: isopropanol (R-OMe), from ethanol: water (R=NO_2).

In a typical run the Vilsmeier reagent was prepared by the slow addition of phosphoryl chloride to dimethyl formamide at 0-5°. The resultant reagent was stirred for a further 30 min at room temperature and then cooled to ca. 5°, the substituted ethyl anilinobutenoate was then added dropwise in the appropriate solvent. After being subjected to the reaction conditions (see Table 2), the cooled reaction mixture was poured into saturated sodium bicarbonate solution and extracted with chloroform. The combined organic extracts were washed with saturated sodium bicarbonate solution, dried ($MgSO_4$) and concentrated and the resultant product was crystallized after decolourisation with charcoal.

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