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TRANSFORMATION OF 3-FORMYLCHROMONES INTO PYRIDINES AND PYRROLES

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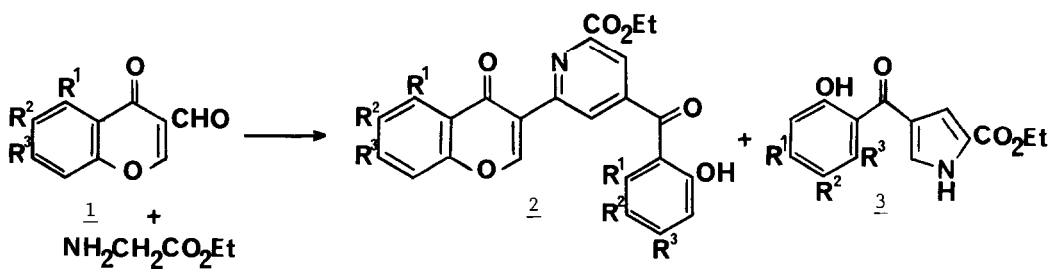
Summary Interaction of 3-formylchromones with ethyl aminoethanoate provides a novel route to pyridines and pyrroles

The use of 3-formylchromone in the synthesis of heterocyclic systems is well-known[1-5] and examples include several closely related pyridine syntheses[6-8] We now report a novel synthesis of both pyridines and pyrroles via the unusual reaction of 3-formylchromones with ethyl aminoethanoate (glycine ester)

In a typical experiment, interaction of 3-formylchromone 1a with ethyl aminoethanoate in the presence of a trace of p-toluene sulphonic acid in refluxing toluene using a Dean and Stark water-trap gave a mixture of ethyl 4-(2-hydroxybenzoyl)-6-(4-oxo-4H-1-benzopyran-3-yl)-pyridine-2-carboxylate 2a and ethyl 4-(2-hydroxybenzoyl)pyrrole-2-carboxylate 3a which was separated chromatographically



a, $R^1 = R^2 = R^3 = H$

b, $R^1 = R^3 = H$, $R^2 = Me$

c, $R^1 = R^3 = H$, $R^2 = Cl$

d, $R^1 = R^3 = H$, $R^2 = NO_2$

e, $R^1 = R^3 = Me$, $R^2 = H$

f, $R^1 = OMe$, $R^2 = R^3 = H$

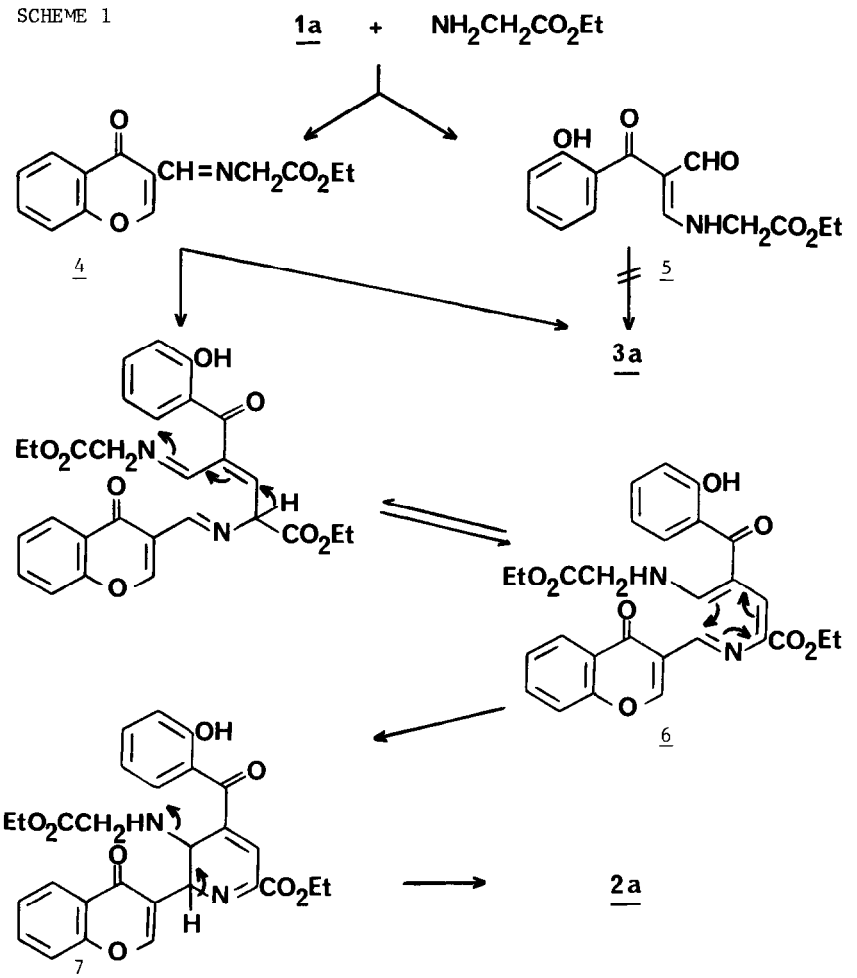
The products obtained from various substituted 3-formylchromones are shown in the Table

TABLE

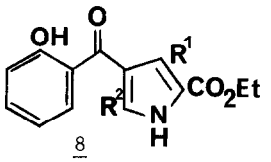
3-Formylchromone 1	Pyridine 2	(%)	Pyrrole 3	(%)
1a	2a	23.5	3a	22 4
1b	2b	33 5	3b	29 4
1c	2c	4 3	3c	51.5
1d	2d	—	3d	36 4
1e	2e	24 0	3e	11 0
1f	2f	34 0	3f	24 0

The pathways proposed for the formation of the products from ethyl aminoethanoate and e g 3-formylchromone are outlined in Scheme 1. (2,5-Dioxopiperazine which can be formed from ethyl aminoethanoate under similar reaction conditions was shown not to react with 3-formylchromone)

SCHEME 1



The reaction proceeds initially via the anil 4, cyclisation of which yields the pyrrole 3a Although this represents a disfavoured process[9], the alternative route (5 →3a) seems less likely since use of 3-acetylchromone in place of 3-formylchromone gave ethyl 4-(2-hydroxybenzoyl)-2-methylpyrrole-2-carboxylate 8a and not the 3-methyl isomer 8b. Pyrrole 8a was identified by comparison of its spin-decoupled ^{13}C n m r spectrum with those of related pyrroles[10]



8

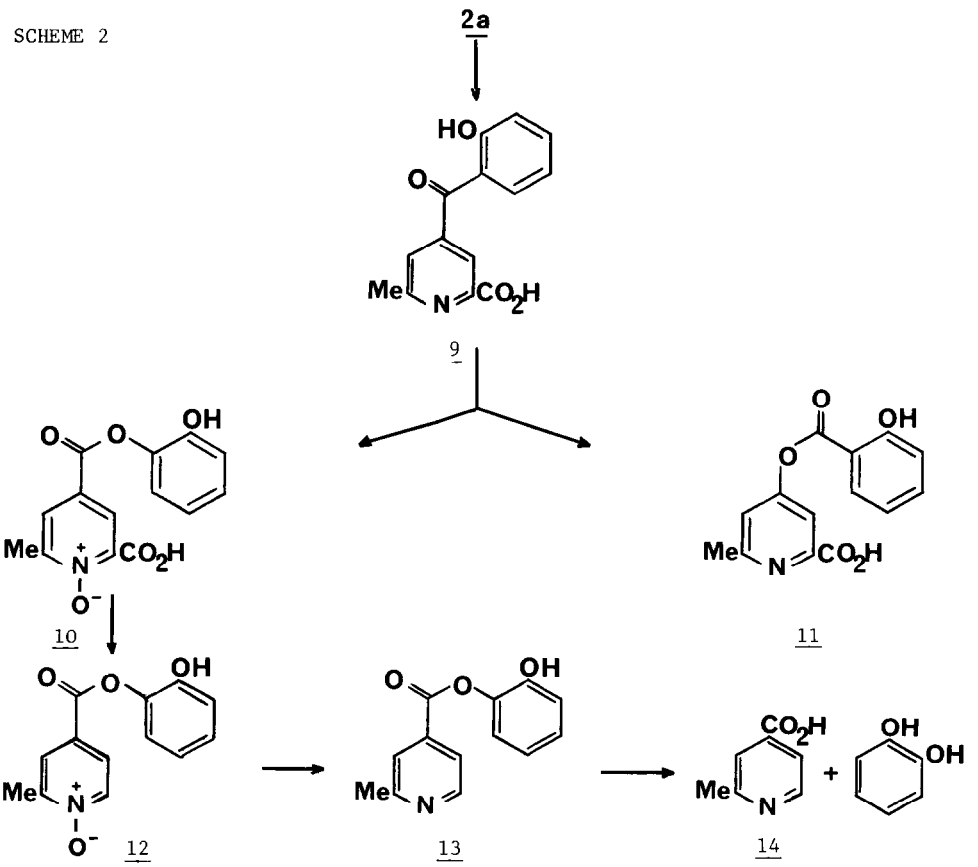
a R^1 = H, R^2 = Me

b R^1 = Me, R^2 = H

Formation of the pyridine is rationally explained via interaction of 2 molecules of the anil 4 with ring-opening at the chromone 2-position. The pyridine is formed on cyclisation of the resulting intermediate 6 followed by aromatisation of 7 by elimination of ethyl aminoethanoate.

Structural assignments were based largely on spectroscopic data, and confirmation of the pyridine structure was obtained (see Scheme 2) by degradation of pyridine 2a to the known[10] 2-methylpyridine-4-carboxylic acid 14

SCHEME 2



Thus, alkaline hydrolysis of the pyridine 2a gave derivative 9, and Baeyer-Villiger oxidation of the latter gave both 2-carboxy-4-(2-hydroxyphenoxycarbonyl)-6-methyl pyridine N-oxide 10 and 4-(2-hydroxybenzoyloxy)-2-methylpyridine 11. Treatment of the N-oxide 10 with triethyl phosphite in refluxing bromobenzene gave firstly the decarboxylated pyridine N-oxide 12 and then the deoxygenated pyridine 13. Acid hydrolysis of the latter gave catechol and 2-methyl-pyridine-4-carboxylic acid 14

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