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SOME REACTIONS OF 3-BROMO-4-BROMOMETHYL-7-METHOXYCOUMARIN AND 3-BROMO-4-METHYL-7-METHOXYCOUMARIN WITH REFLUXING N,N-DIETHYLANILINE.

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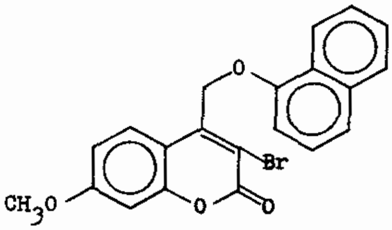
Abstract - N,N-diethylaniline effectively debrominated 3-bromo-4-methyl-7-methoxycoumarin and 3-bromo-4-bromomethyl-7-methoxycoumarin, at reflux. This and other reactions of the above-mentioned coumarins in refluxing N,N-diethylaniline provided supporting evidence for the mechanism of the fragmentation of simple 4-aryloxy-2-bromobut-2-enoates which occurred during their attempted Claisen rearrangement in refluxing N,N-diethylaniline.

Our interest in the synthesis of (2H,1)-benzopyrans has led us to develop simple methods for preparing these benzopyrans which are fully substituted on the pyran ring.

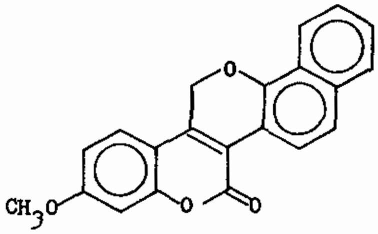
The successful conversion of the 3-bromo-4-(1-naphthoxymethyl)-7-methoxycoumarin (1) into the benzopyran-benzopyran (2), ref. 2, was one of a series of reactions[3] which demonstrated the efficacy of the general method of preparing (2H,1)-benzopyrans, which is outlined in the scheme 1. The synthetic value of this approach arose from the fact that not only can R_1, R_2 and R_3 be alkyl, hydrogen, aryl, or other compatible groups, but also from the ease with which the alkoxycarbonyl group can be transformed into a variety of other functional groups[4].

While these reactions, scheme 1, were generally successful, we observed that the simplest butenoate member of the series of compounds (3), where R_1, R_2, and R_3 were hydrogen, did not produce the desired benzopyran on refluxing its solution in N,N-diethylaniline. Instead, a complex mixture was produced, of which the phenol, derived by the fragmentation of the ether, was the major component.

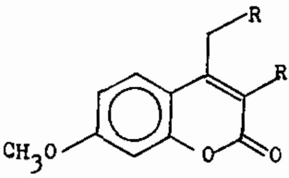
While it was obvious that several undesirable reactions were occurring, the paths of these reactions were not clear. In order to ascertain the role of the solvent in these reactions, and the fate of the but-2-enoate moiety, the more manipulable



(1)



(2)

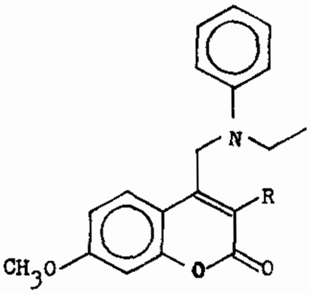


(4) R : H, R$_1$: Br

(5) R : R$_1$: Br

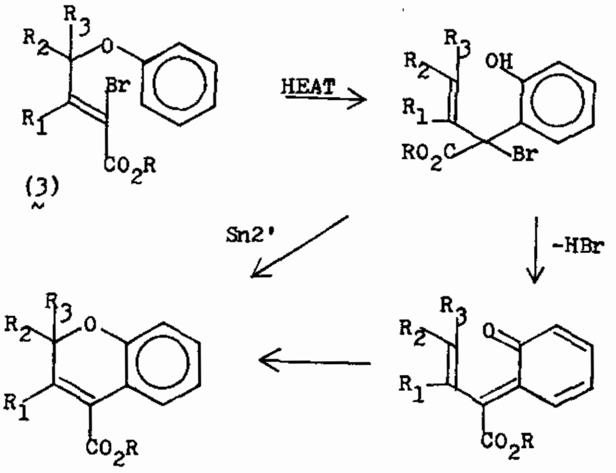
(6) R : R$_1$: H

(9) R : Br, R$_1$: H

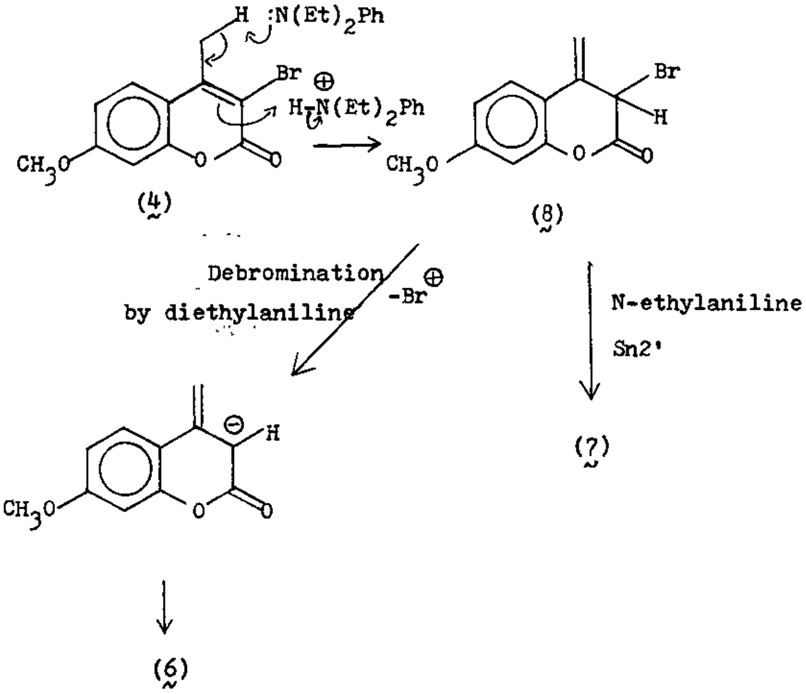


(7) R : H

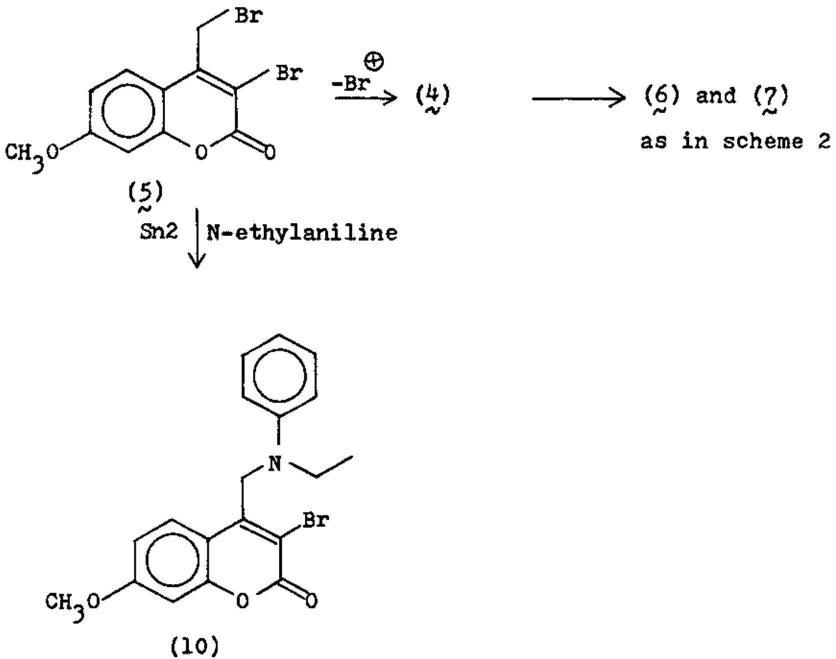
(10) R : Br



SCHEME 1.



SCHEME 2.



SCHEME 3.

compounds (4) and (5) were refluxed in N,N-diethylaniline and the reaction mixtures examined.

The reaction products detected were isolated and fully characterised, but no attempt was made to obtain the optimum yields of the produced materials. Since the yields and the relative amounts of the reaction products varied with the duration of the reactions, the yields quoted are intended to indicate that these reactions were not trivial side-reactions. As will be seen, the derived materials were all simple transformation products which can be prepared more efficaciously by other methods, and so the transformations were of mechanistic interest, rather than of synthetic value.

Refluxing a solution of 3-bromo-4-methyl-7-methoxycoumarin (4) in N,N-diethylaniline for 6 hours produced 4-methyl-7-methoxycoumarin (6) and, significantly, 4-(N-ethyl-N-phenylaminomethyl)-7-methoxycoumarin (7) as 27% and 37% respectively of the crude, isolated reaction products.

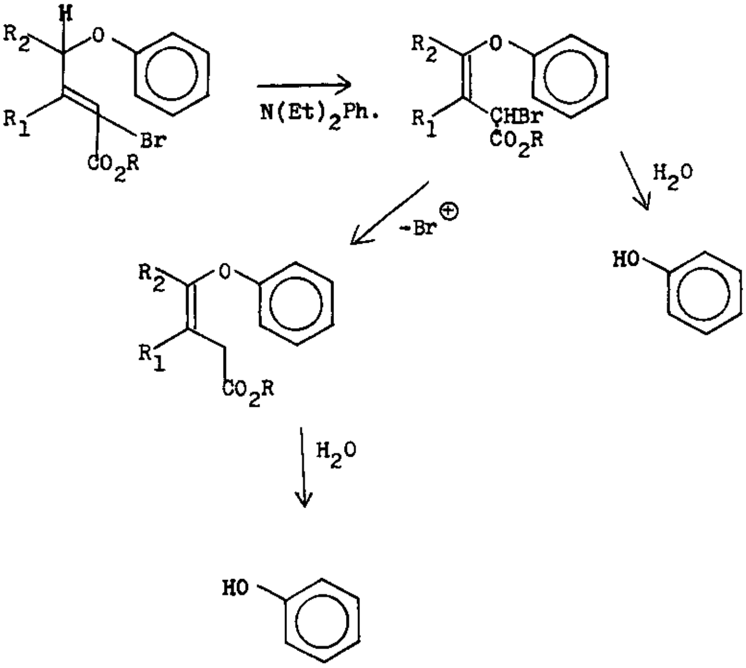
These compounds (6) and (7) must have been formed from the intermediate (8) as is outlined in the scheme 2, particularly because the compound (4) cannot be isomerised to the compound (9) by simply heating it. The compound (4) could be recovered almost totally from refluxing decalin, indicating its stability in an inert solvent even at 190°C.

The N-ethylaniline involved in the reaction was undoubtably generated by the fragmentation of N,N-diethylanilinium bromide at the high temperature of the reaction, in a similar fashion to that by which N,N-dimethylanilinium bromide underwent fragmentation to produce N-methylaniline at similar temperatures[5].

Thus, in addition to its role of solvent, N,N-diethylaniline performed the roles of base/acid, debrominating agent[5] **and a source of N-ethylaniline.**

Refluxing a solution of the dibromo-compound (5) in N,N-diethylaniline for 1.5 h produced the compounds (4), (6), (7) and (10) in 40%, trace, 15% and 11% yields respectively. The reaction of the compound (5) in N,N-diethylaniline containing 5% of 4-toluenesulphonic acid, at reflux for 20 minutes, produced the same mixture of compounds (4), (6), (7) and (10) in 30%, trace, 15% and 17% yields respectively. The presence of the acid had stimulated a marked acceleration of the reaction. These compounds (4), (6), (7) and (10) must have been formed as is shown in the scheme 3.

These reactions described above provided an insight into the reactivity of N,N-diethylaniline at its boiling point and hence a plausible explanation for the



SCHEME 4.

fragmentation, rather than rearrangement, of the but-2-enoates (**3**) which had R_1, R_2 and R_3 as hydrogen.

It seemed very likely that these but-2-enoates were rearranged to vinyl ethers, then were debrominated and cleaved by the traces of water usually present in the N,N-diethylaniline, as is shown in the scheme 4. The aldehydic fragment would be expected to undergo an array of fragmentation and condensation reactions at the temperature of the reaction, and so not survive the reaction.

The Claisen rearrangements of compounds like (**1**) were always accompanied by some cleavage to produce the phenolic entities. While the use of anhydrous N,N-diethylaniline seemed to be a possible way to minimise these side reactions, the great enhancement of the rates of Claisen rearrangements in N,N-diethylaniline by traces of water has been established[6].

The Claisen rearrangement of compounds like (**1**) and (**3**) were not successful in refluxing decalin and these compounds were recovered from these reactions. The use of a polar, high-boiling, inert solvent is neccessary.

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