INTRAMOLECULAR CYCLIZATION OF 2,2'-DIPROPIONYLazoxybenzenes. X-RAY STRUCTURAL INVESTIGATION OF 1-(2-PROPIONYLphenylamino)-2-METHYL-2-METHoxyINDOLIN-3-ONE


X-ray structural analysis has revealed that the product of base-promoted intramolecular rearrangement of 2,2'-dipropionylazoxybenzenes has a 1-(2-propionylphenylamino)-2-methyl-2-methoxyindolin-3-one structure, not that of 3-[1-alkoxy-1-(2-propionylphenylamino)ethylbenzo[c]isoxazole, as was previously thought.

In previous studies [1, 2] of the base-catalyzed reactions of 2,2'-dipropionylazoxybenzenes in alcohol media the product formed in quantitative yield was assigned the 3-(1-arylamino)ethylbenzo[c]isoxazole structure (G, Scheme 1), based on its UV, IR, NMR, and mass spectral data.

Scheme 1

Since this type of transformation of azoxybenzenes had not been described previously, we initiated a series of experiments in order to determine a feasible mechanism for this reaction. We have established that rearrangement of 2,2'-dipropionylazoxybenzenes takes place in the presence of catalytic amounts of base, is intramolecular in nature, and involves a solvent molecule as reagent. We have also found that the size or volume of the alkyl radical in the alcohol participating in the reaction can be a restraining factor, and that there must be two propionyl groups present in the molecule, in the 2 and 2'-positions of the azoxybenzene for the reaction to occur, with one of the propionyl groups involved in intramolecular deoxygenation of one of the reaction intermediates.

Taking into account these experimental facts, as well as the proposed structure of the reaction product, we hypothesized an appropriate scheme for the transformation of dipropionylazoxybenzenes (Scheme 1).
This hypothetical heterocyclization scheme presumes regioselective attack of the carbanion C formed upon treatment with base at the distance nitrogen atom in the azoxy group, resulting in the formation of an intermediate with a cinnoline structure D; this appears to us to be the key step involved in the conversion of azoxy compounds into the reaction product G.

However, in another earlier study [3] it was shown that azoxybenzenes containing only one propionyl group gave, in addition to reaction products derived from intermediate cinnoline-type precursors (type E), compounds containing an indolinone ring. These results suggested to us that reactions of ortho-disubstituted azoxybenzenes could in principle proceed via an alternative pathway leading to a different final result.

As can be seen from Scheme 2, in this case attack of the intermediate carbanion I also occurs at the nitrogen atom carrying the oxygen group; however, the anion is formed initially from the propionyl group closer to this nitrogen atom.

Since the principal criterion underlying in each case the proposed rearrangement scheme of dipropionylazoxybenzenes is the structure of the final reaction product (other criteria, as will be shown, are common to both reaction variations), we decided to return to the question of its structure. Toward this end, the reaction of 2,2'-dipropionylazoxybenzene (A) was carried out in the presence of a catalytic amount of sodium hydroxide in methanol solution, and the structure of the resulting product was examined by x-ray analysis (XRA).

The IR, UV, and PMR spectral data were found to be identical to those reported in the literature [1] for the reaction product of azoxybenzene A under the same reaction conditions. However, based on x-ray structural analysis, we conclude that