Methylation in Ullmann-Fetvadjian Benzacridine Syntheses

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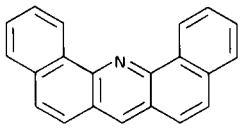
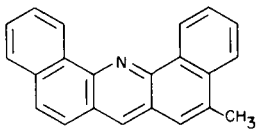
Sir:

The so-called Ullmann-Fetvadjian method for the synthesis of angular benzacridines and dibenzacridines consists of thermal condensation of paraformaldehyde with a mixture of α- or β-naphthol and an appropriate primary arylamine (1,2). For instance, Ullmann and Fetvadjian prepared dibenz[*c,h*]acridine (I) from 1-naphthol and 1-naphthylamine.

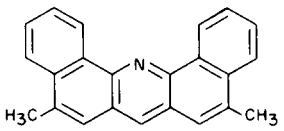
We have now found that this reaction is far more complex than had been thought, and that in addition to the expected acridine, mono- and dimethyl homologs can also be formed; indeed, in certain circumstances (*e.g.*, favorable ratio of paraformaldehyde to the other reactants) the Ullmann-Fetvadjian procedure provides a convenient and direct method for the preparation of such methylated acridines. Thus, when paraformaldehyde (2.5 g.) was made to react with a mixture of 1-naphthol (0.1 mole) and 1-naphthylamine (0.1 mole), the product obtained could be resolved by fractional crystallization from ethanol-benzene into: a) dibenz[*c,h*]acridine (I), m.p. 189°, identical with a sample prepared by an unequivocal



I



II



III

method (3) (mass spectrum, m/e = 279); b) 5,9-dimethyldibenz[*c,h*]acridine (III), m.p. 285° (mass spectrum, m/e = 307), identical with a sample prepared by condensation of paraformaldehyde with a mixture of 4-methyl-1-naphthol and 4-methyl-1-naphthylamine, and whose n.m.r. spectrum confirmed its structure. A third substance present in the reaction-product, which could not be isolated by fractional crystallization, was detected by g.l. chromatography and identified as 5-methyldibenz[*c,h*]acridine (II), m.p. 192°, which was synthesized independently by a Pfitzinger reaction of 4-methyl-1-oxo-1,2,3,4-tetrahydronaphthalene and α-naphthisatin, decarboxylation of the resulting cinchoninic acid to 5,6-dihydro-5-methyldibenz[*c,h*]acridine (m.p. 134°), and dehydrogenation of this last over palladized charcoal.

The ratio I:II:III determined by g.l. chromatography was circa 3:1.5:1.5; this was modified in favor of II and III when the proportion of paraformaldehyde was increased.

The mechanism of formation of methylated acridines in such Ullmann-Fetvadjian syntheses resides in an *in situ* thermal methylation by paraformaldehyde of the naphthol and/or naphthylamine used, *via* a process similar to the formation of 4-methyl-1-naphthylamine by pyrolysis of 4-anhydroamino-1-hydroxymethylnaphthalene (the product of condensation of formaldehyde with 1-naphthylamine) in the presence of calcium hydroxide (4). Indeed, 1-methyl-2-naphthol was readily obtained by reacting paraformaldehyde with boiling 2-naphthol.

Numerous other examples of direct synthesis of methylated acridines by "abnormal" Ullmann-Fetvadjian reactions will be reported at a later date.

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