

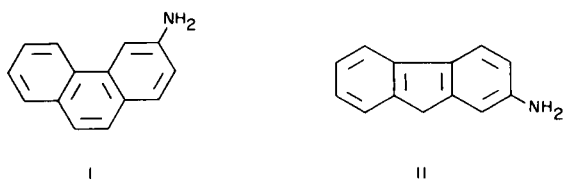
The Orientation in the Ullmann-Fetvadjian Acridine Cyclizations with 2-Aminofluorene

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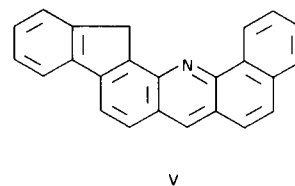
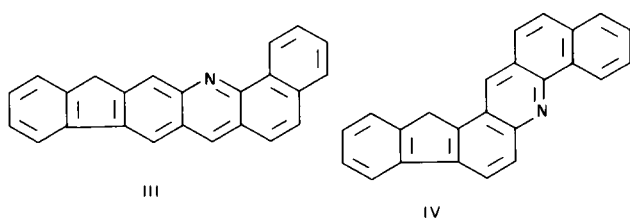
2-Aminofluorene is shown to undergo the Ullmann-Fetvadjian acridine cyclization with α -naphthol and paraformaldehyde at position 3, to give the linear indenoacridine; a similar reaction performed with β -naphthol afforded a mixture of the corresponding linear and angular indenoacridines.

It has recently been shown (1) that, at variance with Skraup's quinoline syntheses which closely follow Marckwald's rule (2), the Ullmann-Fetvadjian acridine cyclizations [*i.e.* the reaction, at high temperature, of a primary arylamine having a free *ortho*-position with α - or β -naphthol in the presence of paraformaldehyde (3)] sometimes fail to conform to that rule. This is for instance the case with 3-phenanthrylamine (I), which undergoes Ullmann-Fetvadjian reactions at both positions 4 and 2,



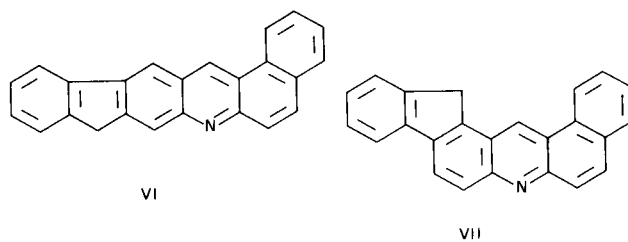
although the Skraup reaction with this amine is known to affect exclusively position 4 (4), and this departure from Marckwald's rule was ascribed to steric factors (5).

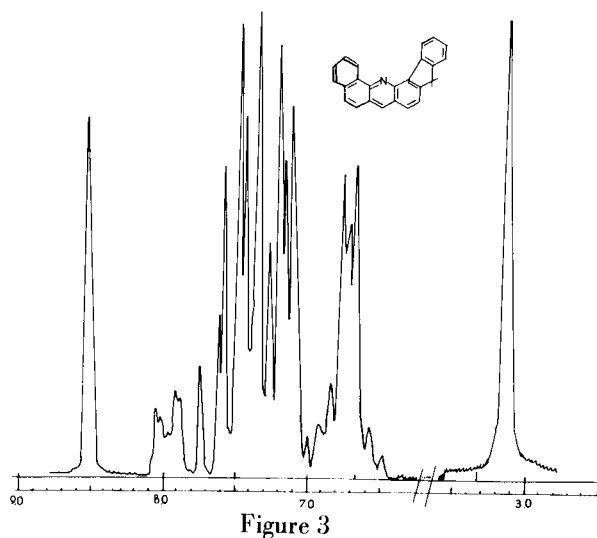
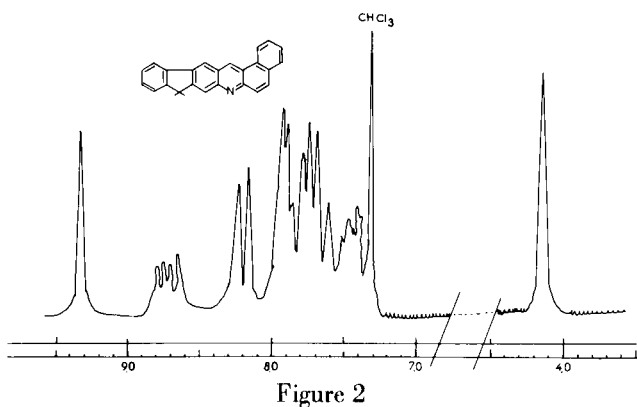
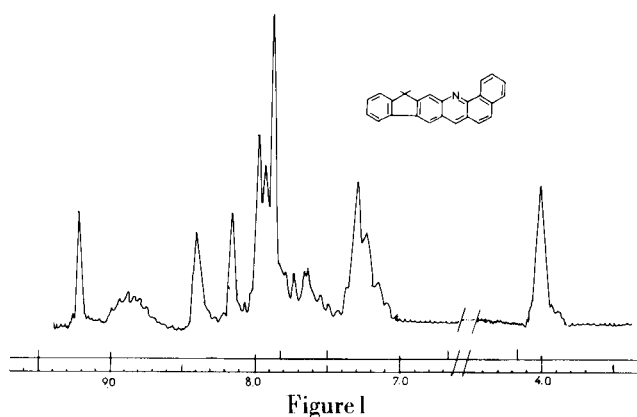
It was interesting to investigate the behavior in Ullmann-Fetvadjian reactions, of 2-aminofluorene (II), an amine which is structurally very close to 3-phenanthrylamine. From 2-aminofluorene, α -naphthol and paraformaldehyde, we obtained an acridine which was identical to the compound prepared by Austin (6) by a similar condensation reaction in which paraformaldehyde was replaced by methylene iodide; Austin, however, left undecided whether the indenoacridine he thus obtained possessed the linear structure (III) or the bisangular one (IV). Later, Hughes, Lions



and Wright (7) suggested for this compound the formula (IV), without furnishing any convincing reason for their choice. This problem has now been solved unequivocally by nuclear magnetic resonance spectroscopy, which shows Austin's compound to be the linear benzo[c]indeno[1,2-*i*]acridine (III); the spectrum of this substance (Fig. 1) comprises four singlets: one at 4 p.p.m., corresponding to the methylene protons, one at 9.22 p.p.m., representing the *meso*-acridinic proton, and the two remaining ones (at 8.15 and 8.4 p.p.m.) which denote the presence of protons 8 and 14. This was further confirmed by comparison with benzo[c]indeno[1,2-*h*]acridine (V), which we had previously prepared from 4-aminofluorene, α -naphthol, and paraformaldehyde (8), and whose angular structure is unequivocal; as could be expected, the n.m.r. spectrum of V showed only two singlets, corresponding to the methylene protons and to the *meso*-acridinic proton, respectively (Fig. 3). It can therefore be concluded that in the Ullmann-Fetvadjian reaction of 2-aminofluorene with α -naphthol, cyclization has taken place at position 3, in contrast with Marckwald's rule, and at variance with the choice made by Hughes and coworkers.

However, when a similar cyclization was effected with β -naphthol, the reaction-product afforded, after purification by chromatography on a column of silicium dioxide, two isomeric acridines. The higher-melting compound,





which constituted 20% of the mixture of the two isomers, showed an n.m.r. spectrum (Fig. 2) very similar to that of compound III, with a singlet for the methylene protons at 4.15 p.p.m., a singlet at 9.35 p.p.m. for *meso*-acridinic proton, and two further singlets (at 8.2 and 8.4 p.p.m.)

characteristic of the protons 8 and 14 in Formula VI. The bulk of the reaction-product was made up of a lower-melting isomer, whose n.m.r. spectrum with only two singlets (one at 4.05 p.p.m. for the methylene protons, the other at 9.12 p.p.m. for the *meso*-acridinic proton) is consistent with structure VII. In the case of β -naphthol, the Ullmann-Fetvadjian reaction had led, therefore, predominantly to the angular benzo[*a*]indeno[1,2-*j*]acridine (VII), in conformity with Marckwald's rule, although some of the linear isomer, *i.e.* benzo[*a*]indeno[1,2-*i*]acridine (VI) was also formed.

The behavior of 2-aminofluorene, which much resembles that of 3-phenanthrylamine, thus confirms the inapplicability of Marckwald's rule for predicting the course of Ullmann-Fetvadjian heterocyclizations, although that same rule had proved its general validity insofar as Skraup reactions are concerned (9).

EXPERIMENTAL

Benzo[*a*]indeno[1,2-*i*]acridine (VI).

To a mixture of 3.2 g. of 2-aminofluorene and 2.9 g. of β -naphthol heated in a Claisen flask at *circa* 250°, 0.7 g. of paraformaldehyde was added in small portions; when evolution of steam had subsided, the reaction-mixture was heated to *circa* 300° for a further fifteen minutes, then vacuum-distilled. The red resin, b.p. 280°/12 mm. (3 g.), was collected, and solidified on trituration with cyclohexane, giving fine pale yellow needles which, however, proved on thin layer chromatography to be a mixture of two substances. By chromatography on an activated silicium dioxide column (preheated at 110° for two hours) and using benzene for elution, benzo[*a*]indeno[1,2-*i*]acridine (VI) was obtained, recrystallizing from benzene in fine colorless prisms, m.p. 251°, giving a fluorescent greenish yellow halochromism in concentrated sulfuric acid, yield, 20% of the mixture of isomers.

Anal. Calcd. for $C_{24}H_{15}N$: C, 90.8; H, 4.8; N, 4.4. Found: C, 91.1; H, 5.0; N, 4.6.

The corresponding picrate crystallized from toluene in orange-yellow microneedles, m.p. 265° (dec. > 240°).

Anal. Calcd. for $C_{30}H_{18}N_4O_7$: N, 10.3. Found: N, 10.5.

Benzo[*a*]indeno[1,2-*j*]acridine (VII).

Further elution of the chromatographic column with benzene + ethanol (9:1) afforded the main isomeric acridine VII, which crystallized from benzene in pale yellow needles, m.p. 210°, giving an orange-yellow halochromism in sulfuric acid.

Anal. Calcd. for $C_{24}H_{15}N$: C, 90.8; H, 4.8; N, 4.4. Found: C, 90.2; H, 4.8; N, 4.6.

The corresponding picrate crystallized from xylene in orange-yellow microprisms, m.p. 298° (dec. > 240°).

Anal. Calcd. for $C_{30}H_{18}N_4O_7$: N, 10.3. Found: N, 10.1.

Nmr Determinations.

These were performed in the Nmr spectroscopy Department of this Institute (Mrs. Alais, to whom our thanks are due). A Varian A-60 spectrometer was used, with tetramethylsilane as internal reference. The acridines VI and VII were dissolved in deuteriochloroform, and the spectra of compounds III and V were determined in deuterated trifluoroacetic acid.

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