[CONTRIBUTION FROM THE DEPARTMENT OF PATHOLOGY, UNIVERSITY OF SHEFFIELD]

CHRYSOFLUORENE AND DERIVATIVES, WITH NOTES ON THE ULTRAVIOLET ABSORPTION SPECTRA OF THESE AND RELATED FLUORENE COMPOUNDS

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In an earlier publication (1), the syntheses of a number of 9-aminofluorene derivatives were described. The methods used in that work have now been employed for the preparation of 11-aminochrysofluorene hydrochloride, 11-carbethoxyaminochrysofluorene, and chrysofluorene.

Reduction of 11-chrysofluorenone oxime by sodium amalgam under alkaline conditions yielded 11-aminochrysofluorene from which were obtained by reaction with ethyl chloroformate the required 11-carbethoxyamino compound and the amine hydrochloride. If, however, reduction of the oxime was carried out in acetic acid-alcohol medium, the oxime group was eliminated completely, chrysofluorene being formed. Similar behavior had already been observed with the oximes of fluorenone, 2-methoxy- and 3-methoxy-fluorenone (1). Experiments on the reduction of 11-chrysofluorenone under the above-mentioned acid conditions are not yet complete, but it may be said that chrysofluorene has not been found in the product.

As a check on the purity of the chrysofluorene preparation, its ultraviolet absorption spectrum in chloroform was determined for comparison with the spectrum of an authentic sample of chrysofluorene recorded by Mayneord and Roe (2). At the same time, the absorption spectrum of 11-carbethoxyaminochrysofluorene was examined. The close resemblance between the two spectra (see Figure 1) prompted a comparison of the spectra of fluorene, 2-methoxy- and 3-methoxy-fluorene, and their 9-carbethoxyamino derivatives, which were available from previous work (1). These absorption spectra, determined in chloroform at 20° using a Unicam Quartz Spectrophotometer, Model SP 500, are shown in Figures 2, 3, and 4.

As was to be expected from previous work [see (1)], 11-aminochrysofluorene hydrochloride acted as a local anesthetic for the tongue. It is perhaps of interest to note that the hydrochloride of 2,2′-diamino-1,1′-dinaphthyl is said to possess strong local anesthetic activity (3) and the base is also known to be carcinogenic (4). A survey of 9-aminofluorene compounds for carcinogenic activity might profitably be undertaken, bearing in mind also the powerful carcinogenic properties of 2-aminofluorene.

Reactions studied are summarized in the flowsheet. Nitrogen analyses were carried out by Drs. Weiler and Strauss of Oxford, England. All m.p.'s are uncorrected.

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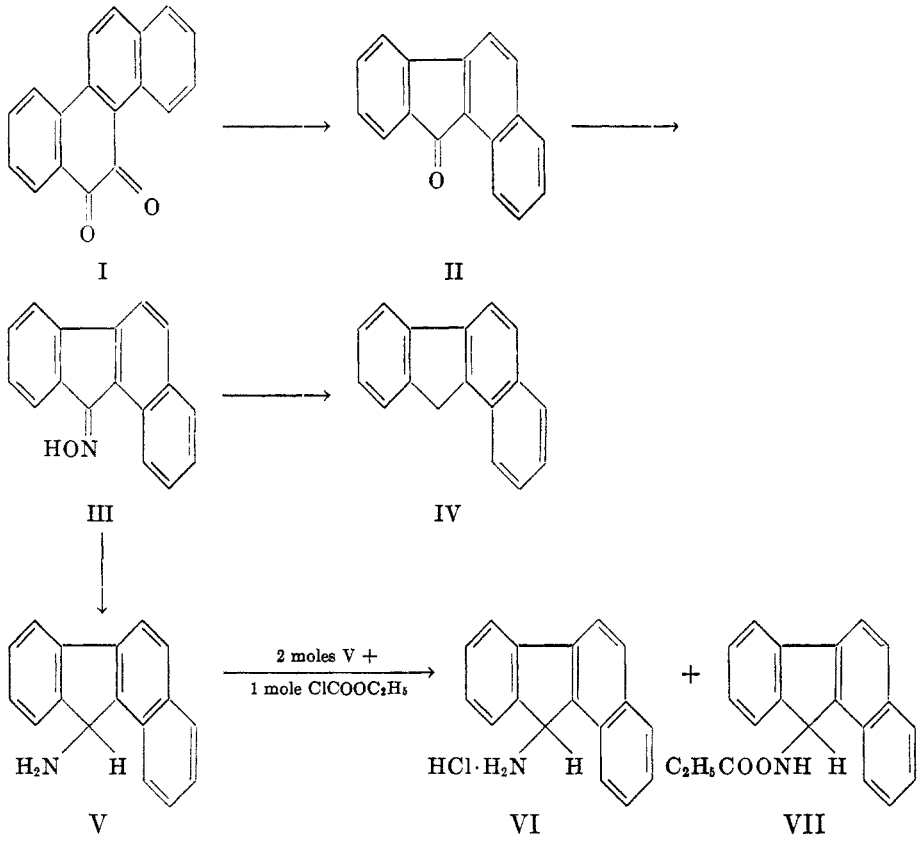
FLOWSHEET



EXPERIMENTAL

5,6-Chrysenedione (I) was prepared from commercial chrysene by the method of Graebe and Honigsberger (5).

11-Chrysofluorenone (II) was obtained by the rapid distillation of 4 g. of I over lead monoxide in a partial vacuum according to Bamberger (6); yield, 2 g. of orange-red needles, m.p. 132° from ethanol.

11-Chrysofluorenone oxime (III) was prepared from II and hydroxylamine hydrochloride in pyridine (1), m.p. 189°.

11-Aminochrysofluorene hydrochloride (VI) and *11-carbethoxyaminochrysofluorene* (VII). 11-Chrysofluorenone oxime (100 mg.) was suspended in 95% ethyl alcohol (5 ml.) and with shaking, the flask being open to the air, 25 g. of 2.5% sodium amalgam was added gradually over 1 hour and reduction allowed to proceed for another 2 hours at room temperature. The base (V) was then isolated as the hydrochloride (63.5 mg.), a salmon-pink product; compare 2-methoxy-9-aminofluorene preparation (1). For purification, it was dissolved in warm water and the cooled solution filtered. The base was isolated by making the colorless filtrate alkaline and extracting with ether. After drying over sodium sulfate, the ether extract was concentrated to 5 ml. and 13 mg. of ethyl chloroformate was added. This gave almost immediately a precipitate of VI which was filtered, washed with ether, and dried. Yield 20 mg., m.p. indefinite, decomposition beginning at 185°.

Anal. Calc'd for $C_{17}H_{13}N \cdot HCl$: N, 5.23. Found: N, 5.02.

The *urethan* (VII) was isolated by evaporating the ether filtrate from VI to dryness and dissolving in hot 70% ethyl alcohol. It crystallized as long colorless needles, 12 mg., m.p. 219–220°.

Anal. Calc'd for $C_{20}H_{17}NO_2$: N, 4.62. Found: N, 4.77.

The *hydrochloride* (VI) dissolved readily in cold concentrated sulfuric acid to give a colorless solution, while crystals of 11-carbethoxyaminochrysofluorene darken and dissolve slowly in the acid yielding a bright blue solution. Traces of VI placed on the tongue produce local anesthesia of short duration.

Chrysofluorene (IV). 11-Chrysofluorenone oxime (120 mg.) was suspended in ethanol (10 ml.) and 50 g. of 2.5% sodium amalgam was added gradually (1 hour) along with sufficient glacial acetic acid to maintain acidity. Sodium acetate which separated during the reduction was redissolved by the addition of small amounts of water. The buff-colored precipitate which resulted when the supernatant fluid was poured into water weighed 100 mg. after drying. Crystallized twice from aqueous ethanol (charcoal as decolorizer), the

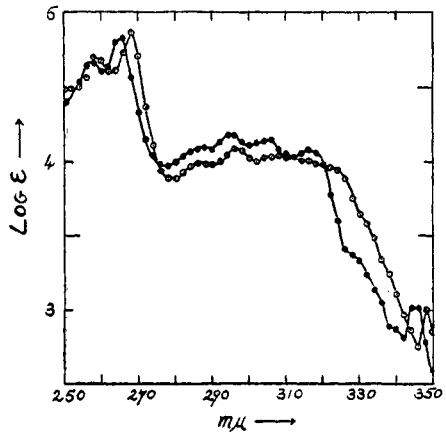


FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA OF CHRYSOFLUORENE (●) AND 11-CARBETHOXYAMINOCHRYSOFLUORENE (○) IN CHLOROFORM

compound was obtained as colorless platelets, 30 mg., m.p. 184°. Cook (7) gave m.p. 182–183° for chrysofluorene.

Figure 1 shows the ultraviolet absorption spectrum of this product, together with that of the urethan (VII), both in chloroform. Measurements were made at 2 mμ intervals. There is good agreement between the spectral data given by Mayneord and Roe (2) for chrysofluorene and those for product IV as may be seen from the following figures. Log ε values are shown in parenthesis following the wave length of the maximum expressed in mμ.

Data of Mayneord and Roe (2) for chrysofluorene. 247 (4.40); 256 (4.65); 265 (4.86); 285 (4.08); 295 (4.20); 306 (4.18); 318 (4.10); 330 (3.37); 345 (3.09).

Product IV. 258 (4.66); 266 (4.83); 288 (4.09); 294 (4.18); 306 (4.15); 316 (4.08); 345 (3.02). Contrary to Mayneord and Roe, product IV showed no maximum at 247 mμ (not shown in graph) and gave only an inflexion in the curve at 330 mμ (log $\epsilon \sim 3.38$). Nevertheless, agreement is sufficiently good to warrant the conclusion that product IV and chrysofluorene are identical.

Product VII. 258 (4.71); 268 (4.87); 286 (3.99); 296 (4.09); 310 (4.05); 320 (3.98); 348 (3.00). Introduction of the group—$NH.COOC_2H_5$ at position 11 of chrysofluorene produces a slight bathochromic shift of the chrysofluorene max-

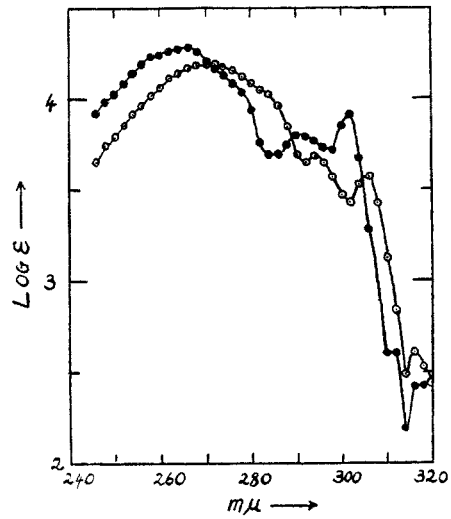


FIG. 2

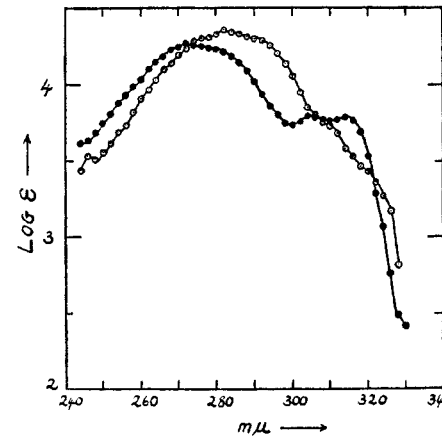


FIG. 3

FIG. 2. ULTRAVIOLET ABSORPTION SPECTRA OF FLUORENE (●) AND 9-CARBETHO XYAMINO FLUORENE (○) IN CHLOROFORM

FIG. 3. ULTRAVIOLET ABSORPTION SPECTRA OF 2-METHOXYFLUORENE (●) AND 9-CARBETH OXYAMINO-2-METHOXYFLUORENE (○) IN CHLOROFORM

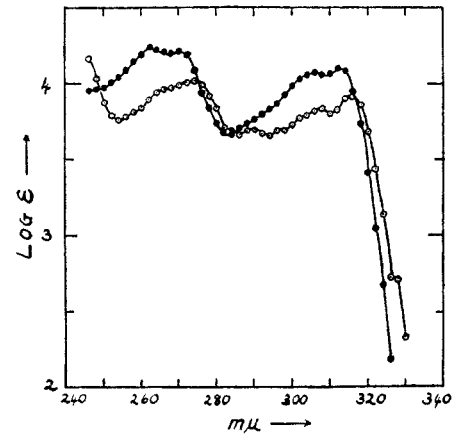


FIG. 4. ULTRAVIOLET ABSORPTION SPECTRA OF 3-METHOXYFLUORENE (●) AND 9-CARBETHOXYAMINO-3-METHOXYFLUORENE (○) IN CHLOROFORM

ima, which is more pronounced at the longer wave lengths. It increases slightly the intensities of the absorption bands in the 250 to 270 mμ region but causes a small reduction in intensity of bands above 270 mμ.

Bathochromic shifts are also observed when the carbethoxyamino group is attached to the 9-position of fluorene compounds as shown in Figures 2, 3, and 4. In the case of 2-methoxyfluorene (Figure 3) which exhibits 3 maxima, the two longer wave length absorption bands are suppressed by the introduction of $—NH.COOC_2H_5$ at the 9-position, while the intensity of the first broad band is increased.

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SUMMARY

The syntheses of two new compounds, 11-aminochrysofluorene hydrochloride (a local anesthetic for the tongue) and 11-carbethoxyaminochrysofluorene, are described. Chrysofluorene has been prepared from 11-chrysofluorenone oxime by a reduction process previously applied to other fluorenone oximes (1). Ultraviolet absorption spectra data are given for chrysofluorene and its 11-carbethoxyamino derivative and for 2-methoxy- and 3-methoxy-fluorene and their 9-carbethoxyamino derivatives.

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