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LETTERS

Formation of 6,13-dimethyl-5,12-diazachrysene by oxidative coupling of 2-methylindole followed by base-induced ring-expansion.

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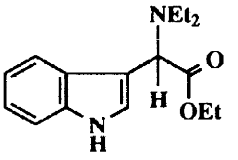
Abstract: Oxidative coupling of 2-methylindole with $FeCl_3$ gave, in addition to a trimeric coupling product, also the ring-expanded product 6,13-dimethyl-5,12-diazachrysene. © 1998 Elsevier Science Ltd. All rights reserved.

We have previously shown that oxidation of esters of indole-3-acetic acid with $FeCl_3$ in the presence of simple secondary amines, such as dimethylamine and diisopropylamine, yielded e.g. **1** (from methyl indole-3-acetate and diethylamine).[1] The formation of **1** is readily explained in terms of initial formation of an indolic radical cation [2-4] which subsequently will lead to a conjugated dehydro derivative of methyl indole-3-acetate, which in turn finally will add the secondary amine in a Michael fashion.

The reaction of various simple indoles with $FeCl_3$ in ether in the presence of simple secondary amines was first studied by von Dobeneck and Lehnerer.[5] To get rid of inorganic residues and to decompose complexes after completed reaction, the reaction mixtures were subjected to basic (aqueous sodium hydroxide) work-up followed by an extraction procedure involving distribution between an ether phase and an aqueous acid (HCl) phase. In this fashion the German workers usually isolated a "neutral" and a "basic" product. The quite stable colourless "slightly basic" product obtained after subjecting 2-methylindole, in the presence of diethylamine, to this procedure was assigned the unlikely structure **2**. Unlikely because as an indolenine such a molecule should be expected to quickly tautomerize to 2,2'-dimethyl-3-3'-biindolyl, a known compound[6], which during the present work was conveniently, although in a modest yield, obtained, quite expectedly[7, 8] by oxidative coupling of the 2-methylindole Grignard reagent with $FeCl_3$.[9]



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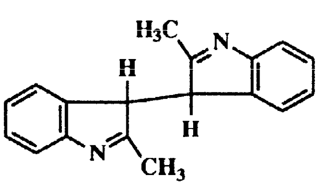

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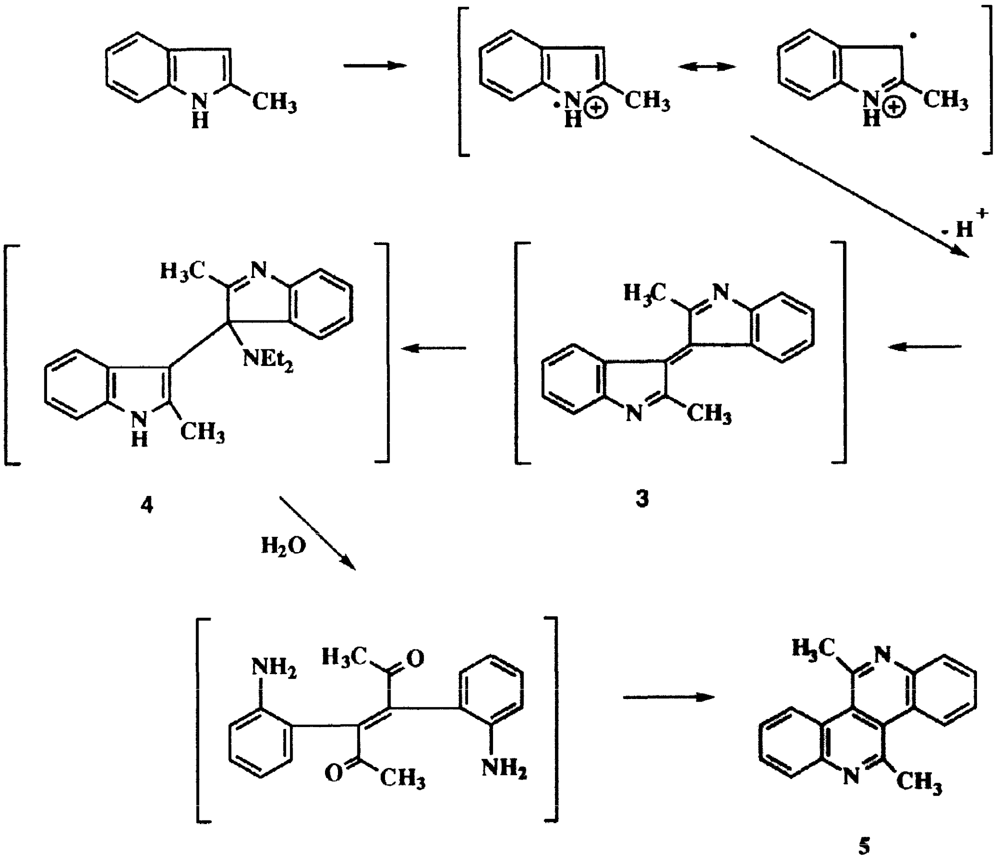
The IR spectrum, which clearly showed the absence of NH functions, in conjunction with the elemental analysis and mass spectrometry, which indicated the composition $C_{18}H_{14}N_2$ rather than $C_{18}H_{16}N_2$, are incompatible with the previously assumed structure. NMR data confirmed the symmetrical nature of the product. All these information would reasonably fit with the 3,3'-dehydro derivative of **2** (i.e. **3**), but as such a derivative should be unstable and highly coloured,[10, 11] the ring-expanded structure **5**[12] was suggested after some mechanistic considerations outlined in Scheme 1. It was also argued that **3** should readily add diethylamine and hence be present as the adduct **4**.



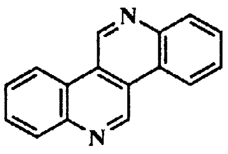
Scheme 1

In a separate experiment 2,2'-dimethyl-3,3'-biindolyl (1eq) was treated with 2,3-dichloro-4,5-dicyanoquinone, DDQ (1eq) in dioxane, which should lead to **3**. The reaction mixture obtained was however complex and **3** could not be isolated, presumably due to cyclization, *via* isomerization to indolo[2,3-*c*]-carbazoles e.g. **6** and consequtive dehydrogenation products.[13] Compound **5** was not observed in this experiment, which underlines the importance of the trapping reaction (**3** → **4**) in Scheme 1. In a similar experiment 3,3'-biindolyl[14] could, by dehydrogenation with DDQ followed by alkaline work up, be converted to 6,12-diazachrysene **7** in a good yield. Attempted thermal rearrangement of the dehydrogenation product to **7** was unsuccessful.[10]

The re-assigned structure **5** could readily be proven as its known parent compound **7** could be converted into **5** by addition of methyl lithium to the C=N double bonds followed by a work-up involving treatment with $K_3Fe(CN)_6$. The tetracycle 5,12-diazachrysene **7** was first prepared by Woodward and Harley-Mason in connection with their synthesis of calicanthine.[15] Interestingly the route used involved an acid-induced ring-expansion of 3,3'-bioxindolyl **9**, yielding **8**, which could be reduced to **7**.[15, 16] Mechanistically the transformation of **9** to **8** is similar to the conversion of **3** to **5**.

Oxidative coupling of 2-ethylindole induced by $FeCl_3$ and diethylamine in ether gave 6,13-diethyl-5,12-diazachrysene in a yield (30%) somewhat higher than that of the lower homologue **5**.

The oxidative coupling of 2-methylindole was finally repeated and the reaction mixture was worked up by chromatography on silica gel using CH_2Cl_2 as eluent. By this procedure the trimeric derivative **10** could be isolated in 35% yield and identified.[19] Formation of **10** is readily understandable in terms of a Michael addition of 2-methylindole to the intermediate **3**. Clearly **4** and **10** are competitive products. The coupled dimer **11**, which is readily obtained from 2-methylindole when exposed to peroxides or oxygen was however absent in the reaction mixture.[17, 18] The trimeric derivative **10** has recently been obtained also by electrochemical oxidation of 2-methylindole.[19, 20]



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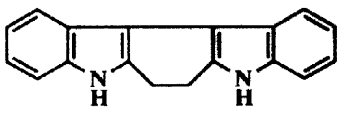

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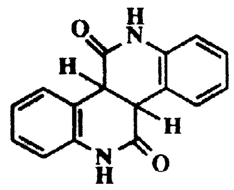

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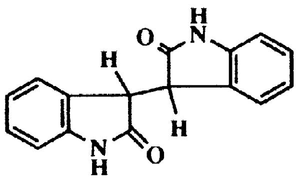

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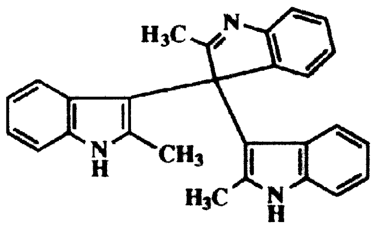

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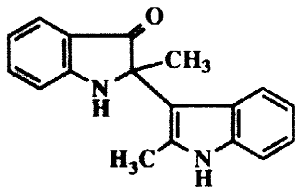

11

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