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ARYL-ARYL COUPLING INDUCED BY n-TRIBUTYLSTANNYL HYDRIDE AN EFFICIENT PHENANTHRIDINE SYNTHESIS

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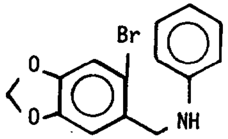
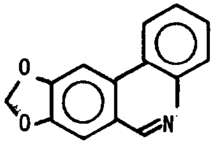
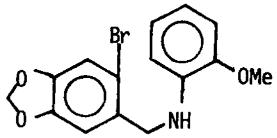
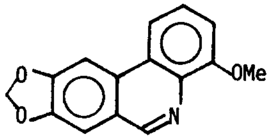
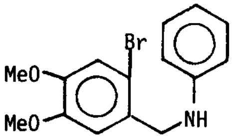
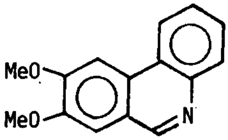
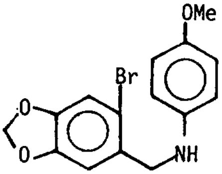
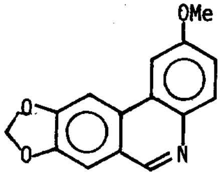
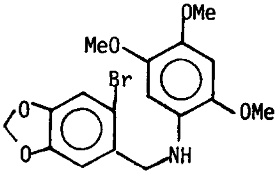
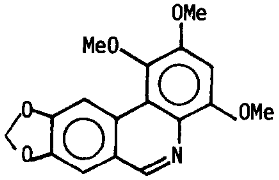
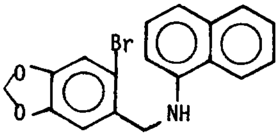
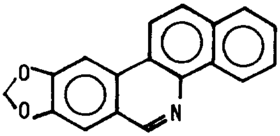
Abstract - N-(o-Bromobenzyl) anilines undergo smooth cyclisation, via dihydrophenanthridines, to phenanthridines by intramolecular addition of aryl radicals to the o-position of the aryl ring bearing the nitrogen atom.

Aryl radicals generated by the homolysis of the Ar-Br bond by n-Bu_3SnH - AIBN have been used extensively to establish a new $\underline{C}_{aryl}$-$\underline{C}_{alkyl}$ bond. The last few years have witnessed the application of this method to the construction of a variety of systems such as dihydroindoles,[1] benzofuran,[2] tetrahydro-β-naphthol[3] and oxindoles.[4] Recently a useful Pd^0 catalysed aryl-aryl cross coupling procedure involving aminoaryl boronic acids and o-bromobenzaldehydes leading to phenanthridines[5] was described but it appears to be limited[6] to aryl boronic acids with only one o-substituent.

Our interest in the synthesis of the cytotoxic alkaloid lycoricidine[7] (I) possessing a reduced phenanthridine system from a fully aromatic precursor led us to investigate the chemistry of aryl radicals formed by n-Bu_3SnH - AIBN treatment of N-(o-bromobenzyl) anilines. The expectation that the cyclisation would be facilitated by the additional stabilisation of the intermediate radical A was realised and thus made it possible to synthesise a variety of polyalkoxyphenanthridines (II) by direct intramolecular $\underline{C}_{aryl}$-$\underline{C}_{aryl}$ coupling[8] and subsequent aerial oxidation of the initially formed 5,6-dihydrophenanthridines (III).

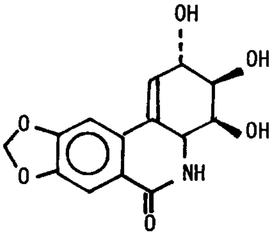
TABLE

Entry	$ArCH_2NHAr'$	Phenanthridine	Yield[a] (%)	m.p. (°C)
1			66	138-139 [b] (n-hexane)
2			63	229-231 (hexane)
3			68	165-166 [c] (benzene)
4			67	210-214 [d] (subl.)
5			61	188-190 (benzene)
6			70	235-236 [e] (benzene)

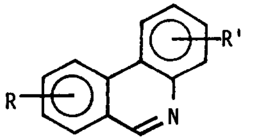
a) Represents yields of products obtained after evaporation of the solvent, washing the residue with cold n-pentane, followed by chromatography on SiO_2 to separate small amounts of unreacted starting material and debrominated product (total 15%); b) Lit.[8] 138-139°C; c) Lit.[8] 163-164°C; d) Lit.[5] 211-215°C; e) Lit.[5] 236-238°C.

The requisite starting materials, o-bromobenzyl anilines, were prepared in excellent overall yields from the appropriate Schiff's base [9] followed by $NaBH_4$ [10] reduction. The cyclisations were carried out in refluxing benzene with n-Bu_3SnH (1.2 eq.) and AIBN (0.5 eq.) added over a period of 12 - 16 h with a substrate concentration of 10 mmol/l and the results are collected in the TABLE.

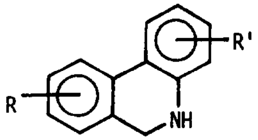
The simplicity of the procedure, its high yield and the lack of steric hindrance experienced by the attacking radical (cf. entry 5) make it a method of choice for the synthesis of a variety of substituted phenanthridines and related compounds.



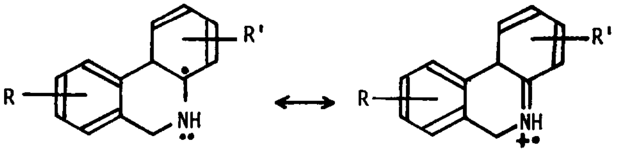
I



II



III



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