INTRODUCTION OF A METHOXYL GROUP INTO THE 6-POSITION OF INDOLES

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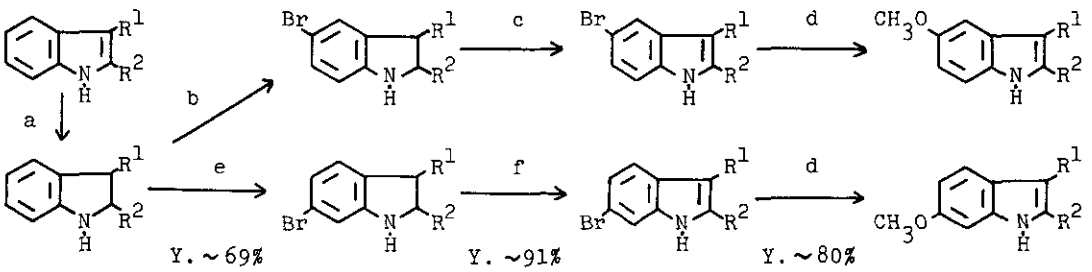
Methoxyindoles often have biological significance. Previously we reported the synthesis of 5-methoxyindoles from indoles as shown in Chart. This method has now been extended to the synthesis of 6-methoxyindoles. The key steps of this synthesis should be the regioselective C-6 bromination and the subsequent dehydrogenation of indolines.

a) Regioselective C-6 Bromination of Indolines: Treatment of indolines with bromine in sulfuric acid in the presence of silver sulfate or with bromine in superacid afforded the 6-bromoindolines.

b) Dehydrogenation of Indolines to Indoles: We report a dehydrogenation of indolines to indoles (1) via azasulfonium salts generated with indolines, dimethyl sulfide, and tert-butyl hypochlorite, and (2) via 1-chloroindolines generated with indolines and tert-butyl hypochlorite. In the latter case (2), solvent effects are discussed.

c) Application of This Method to the Synthesis of Natural Products: The synthesis of 11-methoxyyohimbine, which was isolated from Rauwolfia capuroni Mgf, from yohimbine is now in progress.

Chart



a, $Py \cdot BH_3$/20% HCl-EtOH; b, Br_2/AcOH; c, $CuCl_2$/pyridine, reflux; d, $NaOCH_3$/CuI/DMF, 120 °C; e, $Br_2/Ag_2SO_4/H_2SO_4$ or Br_2/HF-SbF_5(1:1)/CH_2Cl_2, -40 °C; f, (1) $Bu^tOCl/Me_2S/CH_2Cl_2$, -65 °C, (2) NaOEt or (1) Bu^tOCl/DBU/ether, (2) DMF.