

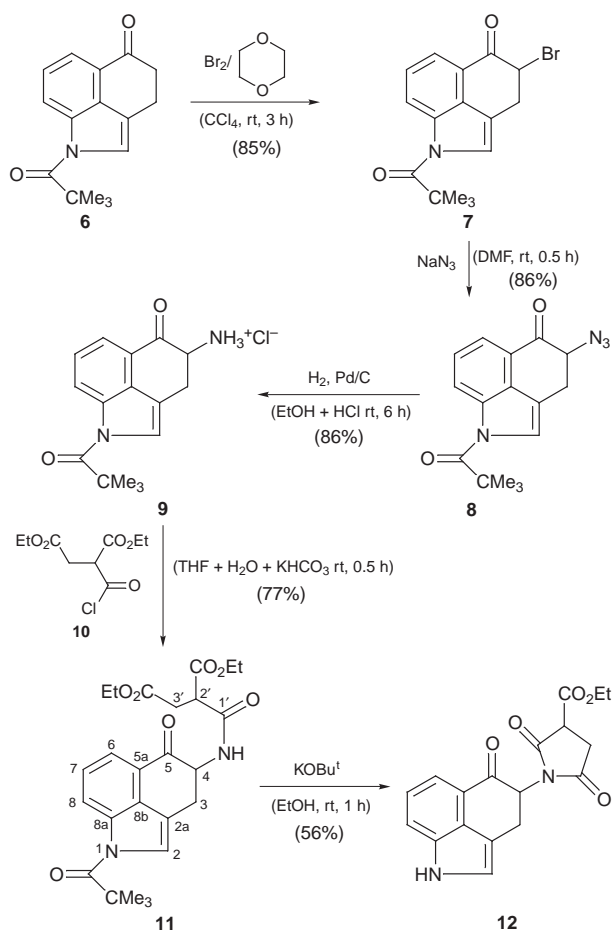
## Chemistry of Indoles carrying a Basic Function. Part 5.<sup>1</sup> Some Observations while Constructing an Ergoline Ring by Stobbe Reaction

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Tricyclic indole derivative **11** affords the imide **12** under Stobbe reaction conditions rather than the expected intermediate containing an ergoline ring.

Recently we reported the construction of D-norergoline and the ergoline ring system *via* Stobbe reaction starting from an indole derivative with a succinic diester side chain.<sup>1</sup> To continue investigations concerning the scope and limitation of the intramolecular Stobbe-like reaction, we hoped to prepare a modified side chain at C-4, which is appropriate for studying the possibility of D-ring closure. Our first goal was to prepare an amide derivative, expecting the formation of a carbanion in  $\alpha$  position to the farther (C-3') ester group.



**Scheme 2**

In our reaction sequence (Scheme 2) the starting material **6**, the *N*-pivaloyl derivative of Uhle's ketone<sup>7</sup> was treated with bromine–1,4-dioxane in  $\text{CCl}_4$  (3 h, rt) to yield

crystalline  $\alpha$ -bromoketone **7** (yield: 85%). In the further steps, the side chain was introduced starting from the C-4-bromide function. According to observations of Bowman *et al.* direct bromine–amine exchange did not lead to unambiguous results, therefore we had to choose an alternative procedure. Bromide **7** was transformed into azide derivative **8** (yield: 86%) with  $\text{NaN}_3$  in DMF (0.5 h, rt), which was then reduced by catalytic hydrogenation ( $\text{H}_2$ , Pd/C, rt, EtOH–HCl) to the appropriate amine hydrochloride **9** (86% yield). Treatment of the latter with diethyl chloroformylsuccinate **10**<sup>9</sup> in THF– $\text{NaHCO}_3$  (aq) (30 min, rt) led to the amide derivative **11** (yield: 77%) as a diastereomeric mixture. In the final step, amide **11** was reacted with  $\text{KOBU}^+$  (EtOH, 1 h, rt) under the conditions of Stobbe condensation.<sup>10</sup> Unfortunately the C-5-ketone did not participate in cyclisation; instead a tetracyclic ergoline imide derivative **12** (56%) was obtained as the end-product as a diastereomeric mixture.

Attempted Stobbe condensation with  $\alpha$ -bromoketone **7** or  $\alpha$ -aminoketone **9** failed owing to their facile oxidation. The resulting derivatives were always the  $\alpha, \beta$ -unsaturated carbonyl compounds.

Investigations concerning further methods for the construction of ergoline derivatives are in progress.

Techniques used: IR, NMR and mass spectrometry

References: 14

Schemes: 5 (structures of compounds, formation of imide **12**)

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### References cited in this is synopsis

- Part 4, see: I. Moldvai, E. Temesvári-Major, E. Gács-Baitz, O. Egyed and Cs. Szántay, *Heterocycles*, in press.
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- Compound **10** was prepared from diethyl formylsuccinate (C. G. Wermuth, *J. Org. Chem.*, 1979, **44**, 2406) by Jones oxidation and subsequent treatment of the obtained acid with thionyl chloride.
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