Pergamon

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Photocyclization of Enaminoesters : Access to 2,3-Dihydroindoles Spiroimides[1]

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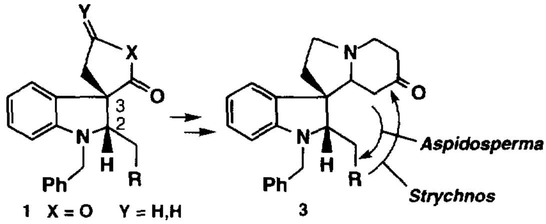
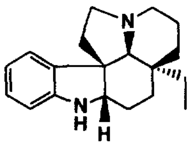
Abstract : The synthesis of spiroindolines imides **15a,b** using a photochemical reaction and their transformations into known precursors of pentacyclic *Aspidosperma* alkaloids is presented.

The synthesis of tetracyclic spiroindolines **3** is of considerable interest due to their potential as precursors of pentacyclic dihydroindolic *Aspidosperma* (*e.g.* aspidospermidine) or *Strychnos* (*e.g.* echitamidine) alkaloids. A possible approach to this substructure could use spiranic indolines **1** or **2** having the required stereochemistry at C-2 and C-3.

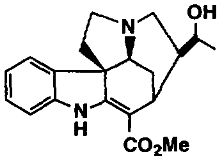


1 X = O Y = H,H
2 X = NR Y = O

3

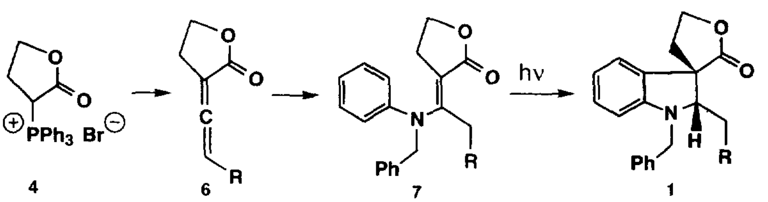


aspidospermidine

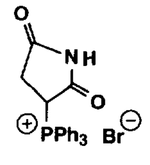


echitamidine

Recently[2], we have described the stereocontrolled synthesis of spiroindolinic lactones **1** by photocyclization of enaminolactones **7**, which were easily obtained through condensation of *N*-benzylaniline with allenic lactones **6**.

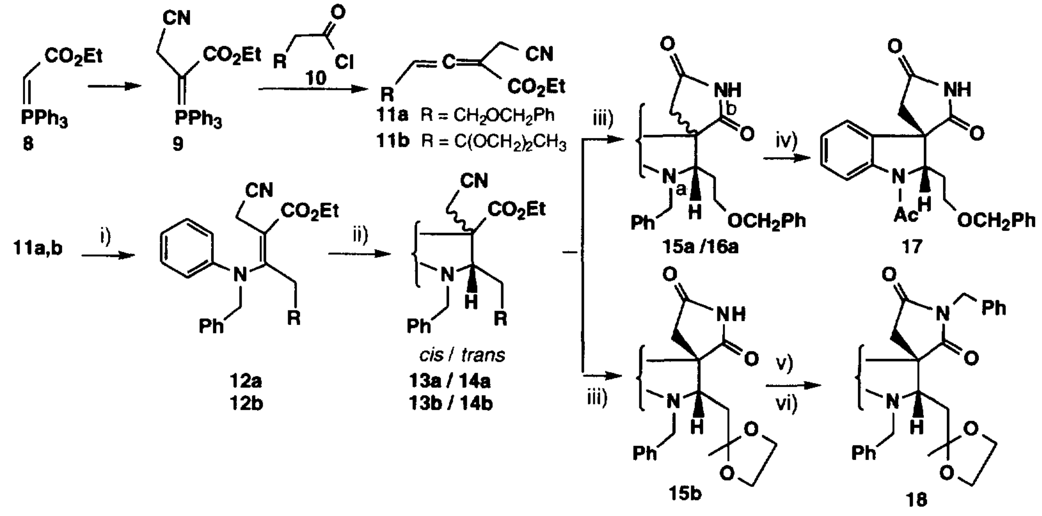


4 **6** **7** **1**



5

Although the lactone ring of **1** could be transformed into a *N*-substituted lactam ring, it would be faster to synthesize directly spiroimides **2**. Our photochemical approach involved the preparation of allenic imides. Unfortunately, all attempts to prepare allenic imides using the imidophosphorane precursor **5**[3] were unsucessful. Thus, we envisaged to overcome this difficulty by preparing allenic esters **11a,b** substitued by an acetonitrile side chain as precursor of the imide ring. Compounds **11a,b** were prepared in 83% and 88% yield respectively according to a Wittig reaction[2] between phosphorane **9** (obtained by alkylation[4] of **8**) and the corresponding acylchlorides **10**. Condensation of *N*-benzylaniline with **11a,b**[5] afforded enaminoesters **12a,b** in 82% and 85% yield, respectively. Irradiation of compound **12a** in acetonitrile[2] led quantitatively to a 1/2 ratio of *cis/trans*[6] spiranic indolines **13a** and **14a**[7].Compounds **13a/14a** which could not have been separated at this stage, were quantitatively transformed into spiranic imides **15a/16a**,by KOH/*t*-BuOH treatment [8].N_a-Debenzylation[9] of imide mixture, followed by acylation with acetic anhydride[10] provided the known intermediate **17**[11] in 84% yield. Photocyclization of enaminoester **12b**, using the same procedure, led to the mixture of *cis* and *trans* [6] indolines **13b/14b**[7], which were easily separated by flash chromatography (85% yield ; 3/2 ratio). Indoline **13b** was readily converted by basic treatment to the spiranic imide **15b** which was further transformed into the already described imide **18**[12], in two steps and 90% yield.



Reagents and conditions : i) $PhNHCH_2Ph$, C_6H_6, Δ; ii) hν, CH_3CN; iii) KOH, *t*-BuOH, Δ; iv) HCO_2NH_4, Pd/C, MeOH then Ac_2O, CH_2Cl_2; v) $PhCH_2OH$, DEAD, PPh_3, THF; vi) HCO_2NH_4, Pd/C, MeOH.

In conclusion, we have developed a short and efficient synthesis of tricyclic spiroindolines, useful intermediates in the synthesis of pentacyclic indole alkaloids.

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