

The oxidation of indole derivatives using dimethyl dioxirane

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INTRODUCTION

The oxidation of indoles is an important route for the formation of oxindoles. Popular methods employ DMSO/HCl, *N*-halosuccinimides or *t*-BuOCl.¹ Additionally, 2,3-disubstituted indoles undergo oxidative rearrangement to give *spiro*-pyrrolidine-2-oxindoles, a heterocyclic framework found in natural products and some currently interesting pharmaceutical compounds.²

The present study has investigated the use of dimethyl dioxirane (DMD) as an agent for promoting the oxidative rearrangement of tetrahydro- β -carboline to *spiro*-pyrrolidine-2-oxindoles.

RESULTS AND DISCUSSION

N-H indole substrates (**1**, **2** and **3**) were reacted with DMD generated *in situ* from NaHCO₃ and oxone® in acetone/H₂O (Figura 1) and gave products **4** and **5**.

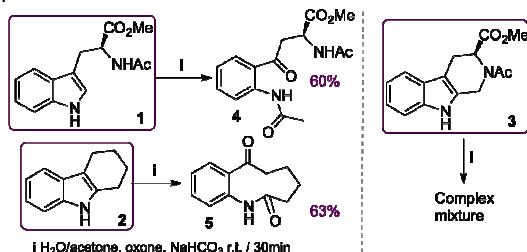


Figura 1. Oxidation of **1**, **2** and **3** with DMD.

Pictet-Spengler (PS) reactions:³ Compounds **3**, **6**, **7** and **8** were prepared by the PS reaction using tryptophan methyl ester (**9**): **3** by the reaction with formaldehyde (**10**),⁴ **6** and **7** using 2-oxoglutaric acid (**11**),⁵ and **8** by use of levulinic acid (**12**)⁶ (Figure 2).

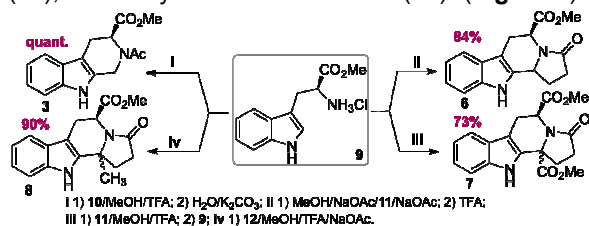


Figure 2. Preparation of tetrahydro- β -carboline by the Pictet-Spengler reaction.

In view of the results of the oxidation of *N*-H indoles a second approach where *N*-acetyl indoles were treated with DMD (Figure 3) was investigated.

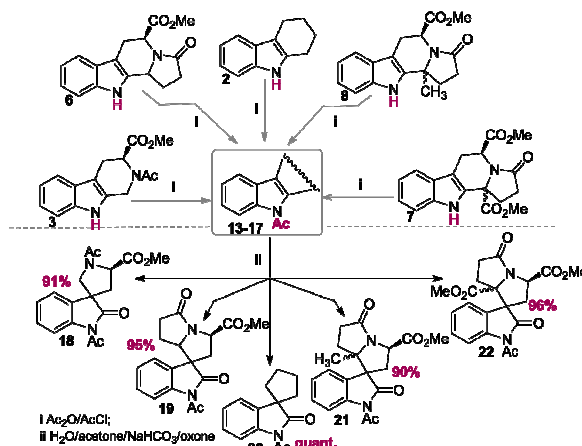


Figure 3. *Spiro*-Pyrrolidine-2-oxindoles from oxidative rearrangement of *N*-acetylindoles with DMD.

CONCLUSION

The oxidation of *N*-H indoles by DMD resulted in indole ring cleavage, as characterized by the products **4** (60%) and **5** (63%). The Pictet-Spengler reaction provided excellent yields of **3** (quant.), **6** (84%), **7** (73%) and **8** (90%). The tetrahydro- β -carboline derivatives were acetylated to give **13** to **17**. The *N*-acetylindoles reacted with DMD to give *spiro*-pyrrolidinyl-oxindoles as mixtures of diastereoisomers (except for **20**) via an oxidative rearrangement: **18** (91%), **19** (95%), **20** (quant.), **21** (90%) and **22** (96%).

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