

수피니딘의 효율적인 합성경로에 대한 연구

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An Efficient Transformation to the Structure of (±)-Supinidine

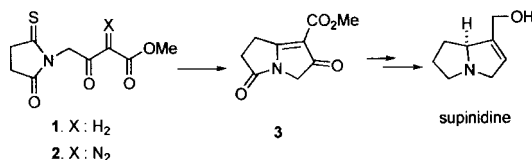
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Recently, we have reported the synthesis of (±)-supinidine.¹ In the synthesis an intramolecular carbonoid-thioimide coupling was exploited to afford 1-carbomethoxy- $\Delta^{1,8}$ -dehydro-2,5-dioxopyrrolizidine **3** from monothioimide **2** having a diazoketoester group. And the subsequent transformation to (±)-supinidine was carried out by 4 step sequence-hydrogenation, mesylation, elimination, and hydride reduction (Scheme 1).

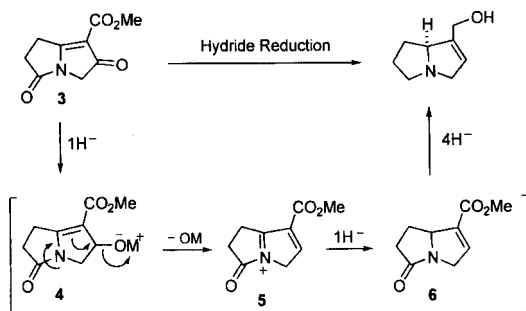
To make the process more concise and improve yield, we considered that cyclization reaction of **1** to **3** and transformation of **3** to supinidine would be steps for elaboration. At first, we have tried to make cyclize **1**. Cyclodehydration conditions which were employed in the formation of indole structure² have been applied. However, decomposition without any desired product was detected. Diradical intermediate formation via Norrish type II reaction of **1** under high-pressure mercury lamp^{3,4} was expected to undergo cyclization. But the condition gave rise to recover the starting material. Oxidative



Scheme 1.

radical generation reaction using such as silver carbonate⁵ yielded only desulfurized imide. Various other attempts to afford the compound **3** have failed. It is assumed that the trajectory for the formation of the ring is quite unfavorable in the structure **1**.

Secondly, we have tried to transform the intermediate **3**, which is obtained as described previously,¹ to (±)-supinidine in one pot. We assumed that 1, 2-reduction of keto group would be followed by elimination to afford acyliminium intermediate **5**, then 1, 2-reduction of acyliminium should give intermediate **6** (Scheme 2). Conversion of **6** to supinidine was already described. So several reduction conditions have been searched. The results are shown in Table 1. Only starting ma-



Scheme 2.

Table 1. The yields of reduction in several conditions

reagent	conditions	yield
NaBH ₄	MeOH/r.t.	no reaction
NaCNBH ₃	MeOH/r.t., pH=4	no reaction
LiAlH ₄	THF/0 °C	5%
DIBAL-H	Toluene/- 78 °C → r.t.	35%

terial was recovered by NaBH₄ or NaBH₃(CN) reaction. However, more powerful conditions such as LAH or DIBAL-H afforded the desired product. Especially, DIBAL-H reduction in toluene showed complete conversion of **3** to supinidine in NMR of the crude reaction mixture. Purification by column chromatography provided 35% yield of the product.

In conclusion, one pot reduction of **3** by DIBAL-H has made the transformation to supinidine more efficient, and hopefully would be applied to the synthesis of alkaloids containing an analogous structure.

EXPERIMENTAL

DIBAL-H (10 equiv.) was added to a solution of **3** (48.0 mg, 0.246 mmol) in 2 ml of toluene at

- 78 °C. The mixture was stirred for two hrs at - 78 °C and slowly warmed to room temperature. To the mixture was added 20% aqueous NaOH solution and the solid was filtered. The filtrate solution was concentrated and the crude product was purified by silica gel column chromatography to afford 36.2 mg of supinidine (35.0%).

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