

## METHYL GROUP AT 1-POSITION OF STABILIZED INDOLE AS A PROTECTIVE GROUP

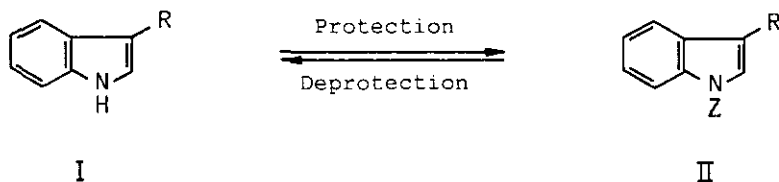
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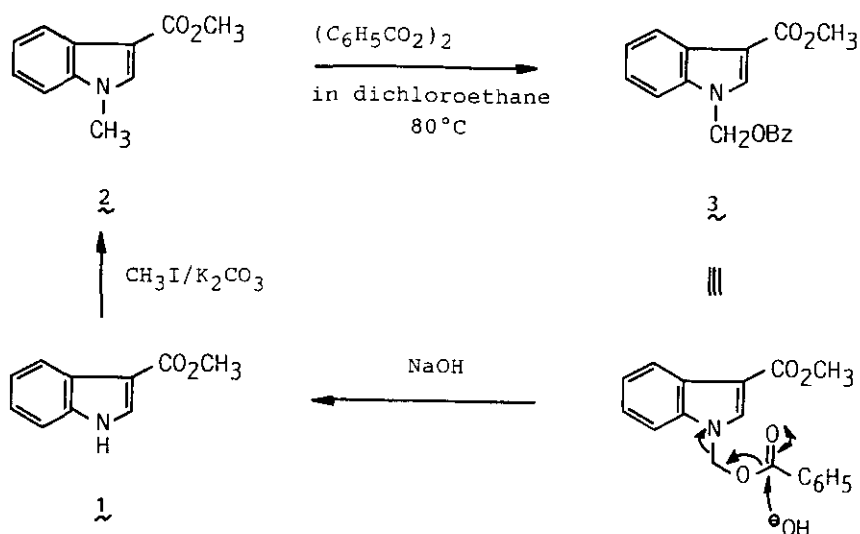
**Abstract**—Methyl group at 1-position of indole derivative **2** was removed by oxidation with benzoyl peroxide and subsequent hydrolysis.

Many protective groups (acyl<sup>1,2</sup>, sulfonyl<sup>1,2</sup>, methoxymethyl<sup>3</sup> etc.) for 1-position (NH) of indole derivatives have been used in the syntheses of indole alkaloids (Scheme 1). But acyl or sulfonyl type protection cause great influence upon the reactivity of indole nucleus. So, if a simple alkyl group can be removed in mild reaction condition, it must be very useful as a protective group. Now, we report a new method to remove a methyl group at 1-position of indole-3-carboxylic ester **2**.

Scheme 1.



We have examined the reactivities of methyl 1-methylindole-3-carboxylate **2**<sup>4</sup>, such as acylation<sup>4,5</sup>, nitration<sup>6</sup>, and so on.<sup>7,8</sup> In the course of these studies, we found out that the methyl group at 1-position of **2** was oxidized with benzoyl peroxide in dichloromethane at 80°C for 2 h to give 1-benzoyloxymethyl derivative **3** in 50% yield [**3**: MS  $m/z$  309( $M^+$ );  $^1H$ -NMR  $\delta$ ( $CDCl_3$ ) ppm 3.90(3H, s), 6.32(2H, s), 7.16-7.66 (6H, m), 7.84-8.04(2H, m), 8.05(1H, s), 8.06-8.22(1H, m)]. In this reaction, 2-benzoyloxy derivative of **2** was also produced as a minor component, but these were easily separated on preparative silica gel TLC [**2**: MS  $m/z$  309( $M^+$ );  $^1H$ -NMR  $\delta$ ( $CDCl_3$ ) ppm 3.67(3H, s), 3.76(3H, s), 7.16-7.70(6H, m), 8.03-8.20(1H, m), 8.18-8.37(2H, m)]. Subsequent hydrolysis of benzoyl ester group of **3** with 1N NaOH in methanol at 25°C afforded methyl indole-3-carboxylate **1** in quantitative yield. Thus, 1-methyl derivative **2** was converted to NH compound **1** by oxidation with benzoyl peroxide and subsequent hydrolysis in 50% overall yield. Compound **1** was methylated by treatment with  $CH_3I/NaH$  or  $CH_3I/K_2CO_3$  in dimethylformamide(DMF) in over 95% yield to give 1-methyl derivative **2**. These results suggest that methyl group at 1-position



of indole nucleus is applicable as a protective group in the synthetic studies of indole alkaloids. Further application of this method for the synthesis of indole alkaloids (for instance, tumor promoter teleocidins<sup>9</sup>) is now in progress.

#### REFERENCES

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