OXIDATION OF 1-ACYLINDOLES WITH MOLYBDENUM PEROXO COMPLEX (MoO₅·HMPA): PREPARATION OF 1-ACYL-trans- AND cis-2,3-DIHYDROXYINDOLINE DERIVATIVES

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Oxidation of 1-acylindoles with MoO_5 ·HMPA in methanol gave a mixture of 1-acyl-trans- and <u>cis</u>-2,3-dihydroxyindoline derivatives in good yields, while 1-acyl-2-substituted indole was oxidized to a corresponding 2-hydroxyindoxyl.

Although several mehtods have been reported for the preparation of 1-acy1-2,3dihydroxyindoline derivatives by the oxidation of 1-acylindoles,¹⁾ most of these methods are limited to the oxidation of 1-acy1-2,3-disubstituted indoles and yields are usually poor.

It is known that readily available molybdenum peroxo (MoO_5) complexes are excellent mild oxidizing reagents. The reagents have been utilized in the epoxidation of olefins,²⁾ the hydroxylation of enolate anions,³⁾ carbanions⁴⁾ and N-silyl amides,⁵⁾ and in the oxidation of dihydropyrane.⁶⁾ However, the use of MoO_5 complexes for the oxidation of indole nucleus has not been reported. We now wish to report that oxidation of 1-acylindoles with MoO_5 ·HMPA in methanol gives rise to 1-acyl-2,3-dihydroxyindoline derivatives in good yields, and that oxidation is affected by the presence of a substituent at 2-position of indole.

A solution of 1-acetylindole (1a) (3 mmol) in dry methanol (30 ml) was allowed to react with MoO_5 ·HMPA (3.3 mmol) under nitrogen at room temperature for a week,



and concentrated under reduced pressure to give a syrup, from which 1-acety1-<u>trans</u>-3-hydroxy-2-methoxyindoline (2a) and <u>cis</u>-isomer (3a) were obtained in 56% and 15% yields, respectively, by using a silica-gel column chromatography. The structure of <u>2a</u> was determined by its elemental analysis and spectral data, and by conversion of <u>2a</u> with CrO_3 -pyridine-H₂O⁷) into 1-acety1-2-methoxyindoxy1 (4).⁸) The elemental and spectral data of <u>3a</u> were strikingly similar to those of <u>2a</u>, and CrO_3 oxidation of <u>3a</u> also gave <u>4</u>. The stereochemistry of hydroxy and methoxy groups in <u>2a</u> and <u>3a</u> was confirmed by comparison of the coupling constants between 2-H and 3-H of the corresponding 0-acetates, (5) and (6) $[J_{2,3}=0$ Hz for <u>5</u>, $J_{2,3}=6$ Hz for <u>6</u>].⁹)



Similarly, 1-benzoylindole (1b), 1-methoxycarbonylindole (1c), and 1-tosylindole (1d) gave the corresponding indolines, (2b-d) and (3b-d) in good yields; the structures were determined by their elemental and spectral data. The results are shown in Table 1.

Reactant	Yiel <u>2</u>	d $\binom{\$}{3}^{a}$	Product Mp(°C)	$\frac{2^{b}}{NMR(\delta)^{c}}$	Product Mp(°C)	$\frac{3^{b}}{NMR(\delta)^{c}}$
<u>1a</u>	56	15	98-99	5.01 (s,2-H)	121-122	5.0-5.4
				4.80 (d,3-H) ^{d)}		(m,2-H and 3-H)
<u>1b</u>	56	18	178-180	5.13 (s,2-H)	116-117	5.45 (d,2-H) ^{e)}
				4.82 (s,3-H)		5.28 (d,3-H)
<u>1c</u>	69	19	98-100	5.35 (s,2-H)	102-104	5.43 (d,2-H) ^{e)}
				4.78 (d,3-H) ^{d)}		5.18 (dd,3-H)
<u>1d</u>	69	7	oil	5.23 (s,2-H)	oil	5.27 (d,2-H) ^{e)}
				4.60 (s,3-H)		4.70 (d,3-H)

Table 1. Physical Data of 1-Acy1-3-hydroxy-2-methoxyindolines

a) Isolated yield. b) All <u>trans</u>-isomers showed smaller Rf-values than the corresponding <u>cis</u>-isomers. c) Measured in deuterochloroform using tetramethyl-silane as internal standard. d) The coupling with hydroxy proton was observed. e) Coupling constant $J_{2,3}$ =6 Hz. Treatment of 1-acety1-3-methylindole (1e) with $MoO_5 \cdot HMPA$ under the same conditions gave a mixture of 1-acety1-<u>trans</u>-2-hydroxy-3-methoxyindoline (7) and the <u>cis</u>-isomer (8) in 75% yield, which could not be separated by chromatography and recrystallization.¹⁰⁾ The structures were assigned as <u>7</u> and <u>8</u> on the basis of their spectral data and the conversion to oxindole (9)¹¹⁾ by oxidation with CrO_3 -pyridine. The reaction of 1-acety1-2,3-dimethylindole (1f) with $MoO_5 \cdot HMPA$ afforded a mixture of 1-acety1-<u>trans</u>- and <u>cis</u>-2,3-dihydroxy-2,3-dimethylindoline, (10) and (11)¹²⁾ in 51% yield. In contrast, 1-acety1-2-methylindole (1g) was oxidized with $MoO_5 \cdot HMPA$ to give 1-acety1-2-hydroxy-2-methylindoxy1 (12)¹³⁾ in 63% yield.



The 2,3-epoxides (13) are expected to be produced initially by the oxidation of $\underline{1}$ and the methoxy derivatives, $\underline{2}$ and $\underline{3}$ or $\underline{7}$ and $\underline{8}$, should be formed by the subsequent methanolysis of $\underline{13}$ from $\underline{1a-d}$ and $\underline{1e}$, respectively. Further studies are being continued to clarify these oxidation mechanisms.

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