ment with rat liver homogenates. The formation of MHPL from MHPP was inhibited by pyruvate, the natural substrate of lactate dehydrogenase, but not influenced by α-ketoglutarate which is not a substrate of the enzyme. These results demonstrate that MHPP formed from 3-O-methylDOPA is then reduced to MHPL by liver lactate dehydrogenase. We recognized a small amount of homovanillate (HVA) on TLC along with MHPL suggesting an oxidative decarboxylation of MHPP to HVA. Furthermore, in isolated rat perfused liver, we have found that MK-486 increases the formation of 3-O-methylDOPA from L-DOPA and that 3-O-methylDOPA is metabolized mainly to MHPP, MHPL, and HVA, while no L-DOPA was detected.[5] Consequently, we have concluded that 3-O-methylDOPA is first transaminated to MHPP with liver tyrosine aminotransferase and then MHPP is reduced to MHPL with liver lactate dehydrogenase along with the concurrent oxidative decarboxylation of MHPP to HVA (chart 1). A more detailed study is now under investigation in our laboratory.

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5) K. Hattori, K. Tanaka, T. Maeda, and H. Shindo, the 18th Local Meeting of Pharmaceutical Soc. Japan, Tokyo, November 1974.

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Reaction of 4-(*o*-Nitrobenzylidene)-3,5-dimethylisopyrazole with Acyl Chlorides

4-(*o*-Nitrobenzylidene)-3,5-dimethylisopyrazole (**1**) was converted to 1-acyl-4-(α-hydroxy-*o*-nitrobenzyl)-3,5-dimethylpyrazoles (**2**, **3**) or 3-(1'-acyl-3',5'-dimethylpyrazolo)-5-chloroanthranils (**6**, **7**) by treatment with acyl chlorides with or without pyridine.

The literature on the reactivity of isopyrazole is extremely scanty, and recently we reported[1] some reactions of 4-(*m*-nitrobenzylidene)-3,5-dimethylisopyrazole, which exists in a betaine form.[2] In this communication, we describe the behaviors of 4-(*o*-nitrobenzylidene)-3,5-dimethylisopyrazole (**1**) in acyl chlorides with or without pyridine.

The reaction of **1** with slight excess of acetyl chloride or benzoyl chloride in pyridine at 50° for 20 hours followed by treatment with ice water afforded 1-acetyl-4-(α-hydroxy-*o*-nitrobenzyl)-3,5-dimethylpyrazole (**2**) in 72% yield, mp 152—153°, IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1740 (CO), NMR (DMSO-d_6) δ: 1.96 and 2.43 (C_3– and C_5–C<u>H</u>$_3$), 2.75 (O<u>H</u>), 2.62 (COC<u>H</u>$_3$), 6.45 (C<u>H</u>) or 1-benzoyl derivative (**3**) as oil in 55% yield, IR $\nu_{max}^{CHCl_3}$: 3650 (OH), 1700 (CO), NMR ($CDCl_3$) δ: 1.95 and 2.50 (C_3– and C_5–C<u>H</u>$_3$), 3.32 (O<u>H</u>), 6.45 (C<u>H</u>).

The introduction of hydroxy group at benzyl position can be explained by postulating the formation of pyridinium chloride (**4**), as reaction intermediate, because 1-acetyl-4-(α-chloro-*m*-nitrobenzyl)-3,5-dimethylpyrazole (**5**)[3] is stable against the treatment with water at room temperature. In contrast, treating a solution of **1** in acetyl chloride without pyridine at 50° for 10

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2) T. Kurihara, M. Sugiyama, H. Hirano, K. Tomita, and T. Sakaki, *J. Heterocyclic Chem.*, **12**, 541 (1975).
3) T. Kurihara, to be published.

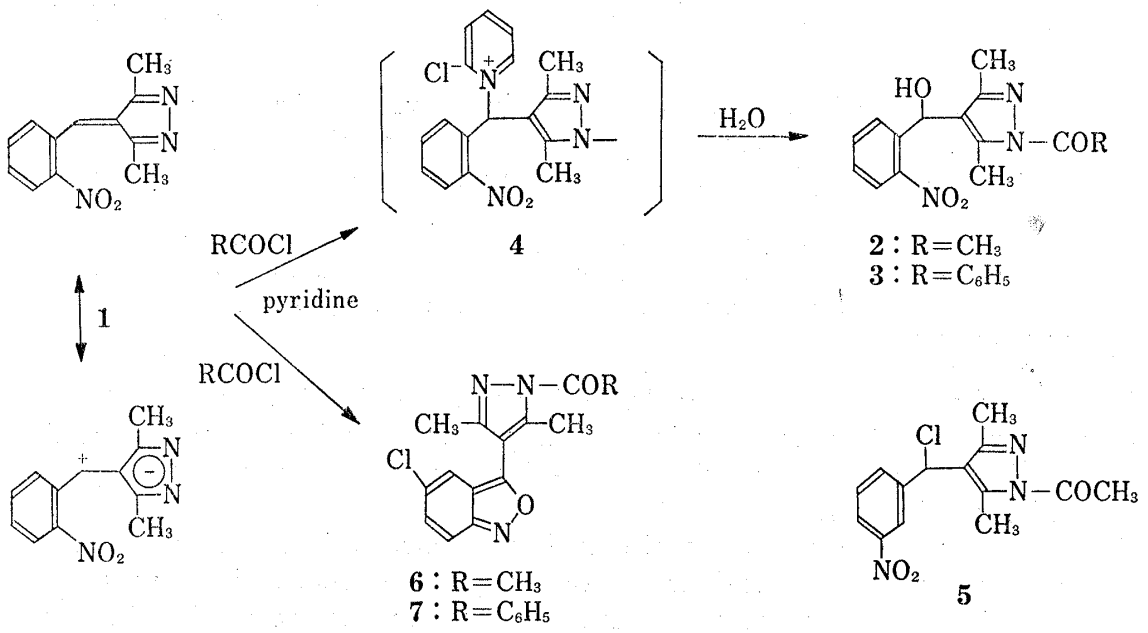

Chart 1

hours resulted in isolation of crystalline **6** as single product, mp 130—131°, in 92% yield, whose structure was assigned as 3-(1′-acetyl-3′,5′-dimethylpyrazolo)-5-chloroantharanil, $C_{14}H_{12}O_2N_3Cl$, IR ν_{max}^{KBr} cm^{-1}: 1740 (CO), no NO_2, UV λ_{max}^{EtOH} nm (log ε): 261 (3.86), 342 (4.06), NMR (DMSO-d_6) δ: 2.42 and 2.72 (each 3H, each s, C$\underline{H}_3$), 2.80 (3H, s, COC$\underline{H}_3$), 7.20—7.75 (3H, m, aromatic H). Dieckinson[4] has reported that *o*-nitrobenzhydrol cyclizes with introduction of a chlorine atom on heating with thionyl chloride in chloroform, forming 5-chloro-3-phenylanthranil. On the basis of these data, a possible mechanism of the formation of **6** was postulated as following scheme, in which include the unique 1,7-addition of acetyl chloride.

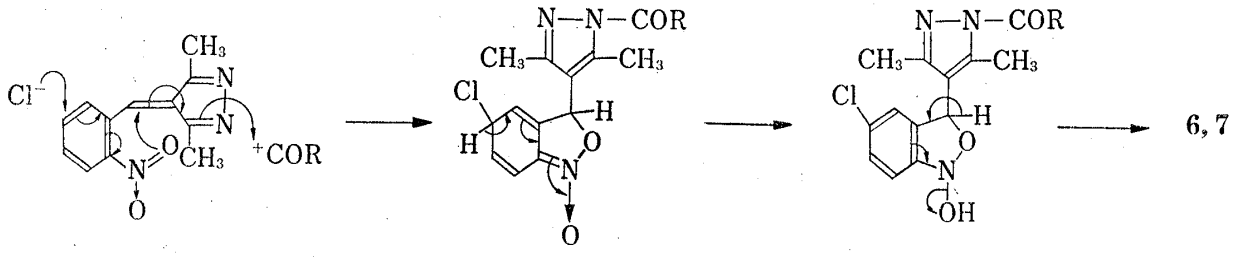

Chart 2

Similarly **1** was converted to 1′-benzoyl analog (**7**) as white needles by treatment with benzoyl chloride at 80° in 57% yield, mp 155—157°, IR ν_{max}^{KBr} cm^{-1}: 1700 (CO), UV λ_{max}^{EtOH} nm (log ε): 248 (4.07), 342 (4.07), NMR (DMSO-d_6) δ: 2.30 and 2.70 (each 3H, each s, C$\underline{H}_3$), 7.30—8.00 (8H, m, aromatic H).

Further work in the reactivity of isopyrazole system is now under way.

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4) W.B. Dieckinson, *J. Am. Chem. Soc.*, **86**, 3580 (1964).