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Studies of Heterocyclic Compounds. I. Structures of Acetylated Products of 3-Methylpyrazol-5-one

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Acetylation of 3-methylpyrazol-5-one (I) with acetic anhydride produces five acetates according to the reaction condition: by heating in the presence of concentrated sulfuric acid 4-acetyl-3-hydroxy-5-methylpyrazole (II); by heating several minutes crystalline monoacetate, 2-acetyl-3-hydroxy-5-methylpyrazole (IV) and oily diacetate, 3-acetoxy-2-acetyl-5-methylpyrazole (V); by heating for several hours crystalline diacetate, 3-acetoxy-1-acetyl-5-methylpyrazole (VI); and by heating in the presence of pyridine monoacetate, 1-acetyl-3-hydroxy-5-methylpyrazole (VII). Basic hydrolysis of the acetates (IV, V, VI, and VII) gives the starting pyrazolone (I). The enol-acetate moiety of the diacetate (V or VI) is more susceptible to hydrolysis under mild condition to give the corresponding N-monoacetate (IV or VII). Inspection by nuclear magnetic resonance spectroscopy of the acetates reveals that the chemical shift of C_5-methyl grouping is observed at approximately 0.3 ppm lower field when acetylated at the adjacent nitrogen atom.

While acylation of 3-phenylpyrazol-5-one was precisely discussed by Weissberger and Porter in 1943,[2] almost none has been reported on the acylated products of 3-methylpyrazol-5-one since Curtius commented on the structure of a monoacetate in 1896.[3] Curtius' procedure has now been re-examined and it has been revealed that acetic anhydride works as an acetylating reagent under various conditions to produce several kinds of acetyl derivatives.

After 3-methylpyrazol-5-one (I) was heated in acetic anhydride in the presence of concentrated sulfuric acid or polyphosphoric acid at 140° for half an hour afforded, after treatment of the mixture with ice-water, monoacetyl compound (II) [$C_6H_8O_2N_2$, mp 260° (35% yield)], which resisted against alkaline hydrolysis and showed only two methyl magnetic resonance peaks at δ 2.27 and 2.30 ppm and no resonance absorption at around the olefinic proton resonance region. These properties suggested that acetylation had taken place at the nuclear carbon, C_4. The unambiguous determination of the structure was performed by direct comparison with the authentic 4-acetyl-3-hydroxy-5-methylpyrazole (II) synthesized from I through 3-methyl-4-(1-aminoethylidene)pyrazol-5-one (III).[4]

Suspension of I in acetic anhydride was heated at 100° for about 10 minutes to give a clear solution, from which fine crystals separated after cooling. Recrystallization from benzene and then from methanol afforded monoacetate (IV) [$C_6H_8O_2N_2$, mp 147—148.5° (40% yield)]. A syrupy oil obtained from the filtrate by careful distillation *in vacuo* turned out to be diacetate (V) [$C_8H_{10}O_3N_2$, $bp_{0.6}$ 70—72° (35% yield)]. When the same suspension was heated at 140° for 3 hours, crystalline diacetate (VI) [$C_8H_{10}O_3N_2$, mp 48—49° (92.5% yield)] was obtained.

Treatment of I with hot acetic anhydride in pyridine afforded another monoacetate (VII) [$C_6H_8O_2N_2$, mp 153—154° (88% yield)], which presented reddish brown coloration with ferric chloride in methanol, one absorption maximum in the infrared (IR) spectrum and a sharp carbonyl band [ν_{max} 1725 cm^{-1} ($CHCl_3$)] in the IR spectrum. In contrast to that, IV gave intense

1) Location: *1-5-8, Hatanodai, Shinagawa-ku, Tokyo, 142, Japan.*
2) A. Weissberger and H.D. Porter, *J. Am. Chem. Soc.*, **65**, 1495 (1943).
3) Th. Curtius, *J. Prakt. Chem.*, **2**, **50**, 508 (1896).
4) F. Korte and K. Störiko, *Chem. Ber.*, **94**, 1956 (1961).

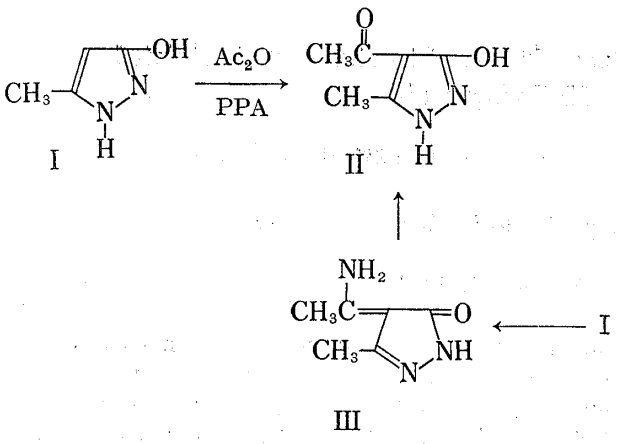


Chart 1

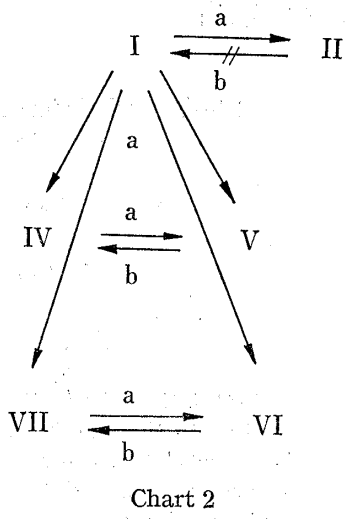


Chart 2

a : acetylation
b : basic hydrolysis

purple coloration with ferric chloride in methanol, distinct two absorption maxima in the ultraviolet (UV) spectrum and overlapped broad carbonyl band [ν_{max} 1700 cm^{-1} ($CHCl_3$)]. Coloration with ferric chloride indicated the presence of a free enol group in the structures of IV and VII and therefore they differed each other in the position of the nitrogen of the pyrazole nucleus to which the acetyl group attached. Treatment of VII with diazomethane furnished a methylated acetate (VIII) [$C_7H_{10}O_2N_2$, mp 32—33° (85% yield)], which was identical in every respect with the specimen prepared from 3-methoxy-5-methylpyrazole (IX)[5] by heating in acetic anhydride.

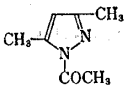
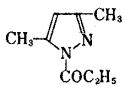
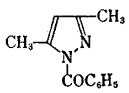
As the acetates (IV, VII, V and VI) all gave rise to the starting pyrazolone (I) by alkaline hydrolysis, every acetyl group was considered to be bound to nitrogen or to oxygen to form acetamide or enolacetate grouping, respectively. Further acetylation of the monoacetate (IV) with acetyl chloride and triethylamine in tetrahydrofuran produced the oily diacetate (V) [*Rf* value on the thin-layer chromatography (TLC) plate: 0.37 (CH_2Cl_2)]. On the other hand, the monoacetate (VII) afforded the crystalline diacetate (VI) [*Rf* value on the TLC plate: 0.45 (CH_2Cl_2)] by the same procedure. The partial hydrolysis of the diacetates, V and VI, was carried out with sodium carbonate solution to get back the monoacetates (IV and VII) respectively.

Now that chemical transformations under mild conditions established the relationships between the pairs of mono- and di-acetates, it followed that which one of the pair should have contained N_1-acetyl group. Literatures concerning proton magnetic resonance of acylated imidazoles[6] and pyrazoles[7] assert that the chemical shift of C-methyl group on the nitrogen heteroaromatic nucleus is lowered in case it is adjacent to N-acyl group in the same nucleus. Thus, the peaks at 2.18 and 2.48 ppm of 1-acetyl-3,5-dimethylpyrazole were assigned to C_3-methyl and C_5-methyl signals respectively. Broad singlet peaks of VII, VI and VIII at 2.42, 2.58 and 2.40 ppm turned out to be actually doublet peaks (J=0.9—1.0 Hz) by expanding the sweep-width of the spectra. The olefinic proton signals at 5.83, 6.16 and 5.80 ppm respectively were also expanded into broad quartets. These data supproted that VII, VI and VIII contained N_1-acetyl bonding and H-Ç=Ç-CH_3 grouping as the common structural units and that IV and V, on the contrary, contained N_2-acetyl bonding.

Table II summarizes the physical properties of acetylated products of 3-methylpyrazol-5-one (I). Of the newly determined structures, 2-acetyl-3-hydroxy-5-methylpyrazole (IV),

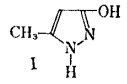
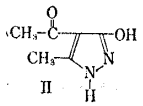
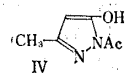
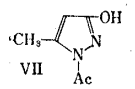
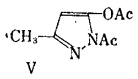
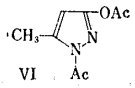
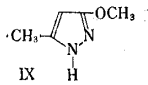
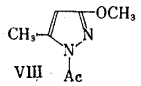
5) H.J. Backer and W. Meijer, *Rec. Trav. Chim.*, **45**, 428 (1926).
6) G.S. Reddy, L. Mandell, and J.H. Goldstein, *J. Chem. Soc.*, **1963**, 1414.
7) M. Ochiai and T. Kamikado, *Chem. Pharm. Bull.* (Tokyo), **14**, 628 (1966).

TABLE I. Methyl Proton Chemical Shifts of 1-Acyl-3,5-dimethylpyrazoles[a]

Compounds			
C_3-CH_3	2.18	2.18	2.21
C_5-CH_3	2.48	2.50	2.63
Difference Δ C_3-C_5	−0.30	−0.32	−0.42

a) Figures cited are δ values in CCl_4 (ppm from TMS as the internal reference).

TABLE II. Physical Properties of 3-Methylpyrazol-5-one and Its Derivatives

Compounds	mp (°C)	IR ν_{max}^{KBr} (cm^{-1})	UV λ_{max}^{MeOH} mμ (log ε)	NMR δ (ppm, in DMSO-d_6)[a] C_5-CH_3	-$COCH_3$	-$NCOCH_3$	C_4-H	O-CH_3
 I	216 (decomp.)	1620, 1555 1458	220(3.680) 242(3.628)	2.15			5.30	
 II	260 (decomp.)	1638, 1580 1555, 1532	249(3.872)	2.27	2.30			
 IV	147—148	1705,[b] 1650 1558	223(4.111) 289(3.919)	2.17		2.43	5.00	
 VII	153—154	1723,[b] 1615 1528	253(4.060)	2.42 (d, 1.0 Hz)		2.46	5.83 (q, 1.0 Hz)	
 V	oil[c]	1795,[d] 1747	238.5 (4.124)	2.30	2.24	2.57	5.87[e]	
 VI	48—49	1785,[d] 1750	239(4.176)	2.58 (d, 0.9 Hz)	2.31	2.62	6.16[e] (q, 0.9 Hz)	
 IX	49—50[f]	1580, 1500 1445		2.12			5.37	3.67
 VIII	32—33	1720, 1595 1515		2.40 (d, 1.0 Hz)		2.47	5.80 (q, 1.0 Hz)	3.80

a) The NMR spectra were taken with TMS as the internal reference using a 60 Mc spectrometer.
b) $\nu_{max}^{CHCl_3}$ (cm^{-1}) of IV and VII: 1700 and 1725 each
c) $bp_{0.6}$ 70—72°
d) $\nu_{max}^{CCl_4}$ (cm^{-1}) values are shown.
e) δ (ppm in $CDCl_3$) values are shown.
f) *cf.* reference (4)

1-acetyl-3-hydroxy-5-methylpyrazole (VII), 3-acetoxy-2-acetyl-5-methylpyrazole (V), 3-acetoxy-1-acetyl-5-methylpyrazole (VI) and 1-acetyl-3-methoxy-5-methylpyrazole (VIII), N_2-monoacetyl structure (IV) has already been proposed by Curtius[3] for the compound "$C_6H_8O_2N_2$ (mp 140°)." We could not isolate any trace of Curtius' compound except the monoacetate, IV (mp 147—148°). We consider the discrepancy with respect to the melting point of the former might be due to some contamination with the another monoacetate, VII (mp

153—154°) because treatment of IV with hot acetic acid readily causes migration of N-acetyl group to give a mixture of all the possible derivatives, I, IV, VII, V and VI.[8]

We could detect neither of the acetates of the other logically possible structure, 3-acetoxy-5-methylpyrazole nor 1,2-diacetyl-3-methylpyrazolin-5-one, probably due to its instability in the reaction mixture.[8]

Katritzky and co-workers predicted eight possible tautomeric forms for pyrazol-3-one[9,10] and anticipated difficulties to elucidate the tautomerism of its acylated derivatives owing to the instability of the structure.[10] We would postpone precise discussion on the tautomeric equilibration of these derivatives, however, a qualitative examination of the spectra of VII and IV in solutions revealed that the enol structure VIIa was much favored over structure VIIb, and the structures IVa and IVb were of nearly equal importance as shown in Chart 3.

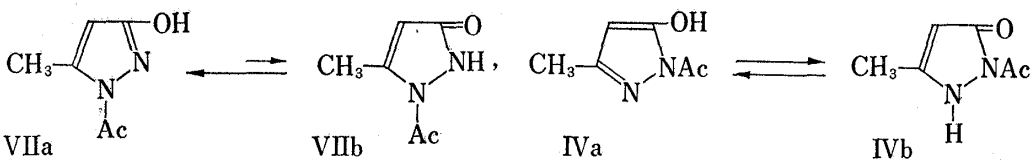


Chart 3

Experimental[11]

4-Acetyl-3-hydroxy-5-methylpyrazole (II)

(a) **Acetylation of 3-Methylpyrazol-5-one (I) with Ac_2O-Polyphosphoric Acid (PPA)**——A mixture of 3-methylpyrazol-5-one (I) (2 g), acetic anhydride (16 ml) and PPA (0.8 g) was heated on an oil-bath at 140° under nitrogen stream for 30 minutes. The reaction mixture was poured onto ice-water (80 g) and extracted with ether (100 ml) three times after decomposition of acetic anhydride was complete. Evaporation of the extracts afforded brown solid (2.6 g), which was heated under reflux in EtOH (10 ml). After cooling the solution deposited brown precipitate, which was collected by filtration and treated with decolorizing charcoal to give colorless needles. Recrystallization from water afforded colorless needles (II), mp 260° (decomp.), 1.0 g (35%). IR ν_{max}^{KBr} (cm^{-1}): 1638, 1580, 1555, 1532. UV $\lambda_{max}^{CH_3OH}$ nm (log ε): 249 (3.872). NMR δ ppm (in DMSO-d_6): 2.27 (3H, s), 2.30 (3H, s). *Anal.* Calcd. for $C_6H_8O_2N_2$: C, 51.42; H, 5.75; N, 19.99. Found: C, 51.53; H, 5.99; N, 19.78.

(b) **Acetylation of 3-Methylpyrazol-5-one (I) with Ac_2O-conc.H_2SO_4**——A mixture of 3-methylpyrazol-5-one (I) (2 g), acetic anhydride (16 ml) and conc.H_2SO_4 (0.4 g), was heated on an oil-bath at 140° under nitrogen stream for 30 minutes. The reaction mixture was worked up analogously as described above to give colorless needles, mp 260° (decomp.) (0.9 g, 31.5%). This material was proved to be identical with the specimen obtained according to the procedure (a) by the comparison of the IR and NMR spectra.

Attempted Hydrolysis of 4-Acetyl-3-hydroxy-5-methylpyrazole (II)——A solution of monoacetate (II) (0.1 g), NaOH (0.1 g) and H_2O (2 ml) in EtOH (3 ml) was heated under reflux for 2 hr. After evaporation of the solvent the pH value of the mixture was adjusted to 2 by adding diluted HCl. Colorless crystals separated, which were collected by filtration and recrystallized from water to give colorless needles, mp 260° (decomp.). The IR and NMR spectra were completely identical with those of the starting monoacetate (II).

Preparation of 4-Acetyl-3-hydroxy-5-methylpyrazole (II) from I and Acetamidine Hydrochloride[4]

3-Methyl-4-(1-aminoethylidene)pyrazol-5-one (III)——A mixture of I (11.76 g) and acetamidine hydrochloride (11.36 g) was heated on an oil-bath at 210°. The molten mixture solidified in about 20 minutes. After cooling the mixture was diluted with water, filtered and washed with small amount of sodium carbonate solution and then with water. The white needles obtained melted at 260° (10.56 g, 63%).

8) K. Arakawa, T. Miyasaka, and H. Ochi, *Chem. Pharm. Bull.* (Tokyo), **21**, 214 (1974), the following paper.
9) A.R. Katritzky and J.M. Lagowski, "Advances in Heterocyclic Compounds," Vol. II, Academic Press, New York and London, 1963, p. 44.
10) A.R. Katritzky and F.W. Maine, *Tetrahedron*, **20**, 299, 315 (1964).
11) All melting points were measured in capillary tubes and were uncorrected. Nuclear magnetic resonance (NMR) spectra were measured by a HITACHI R-20 60 MC spectrophotometer, using tetramethylsilane as the internal reference. IR and UV spectra were measured on a JASCO IRS spectrophotometer and on a HITACHI EPS-3 UV spectrophotometer, respectively.

4-Acetyl-3-hydroxy-5-methylpyrazole (II)——3-Methyl-4-(1-aminoethylidene)pyrazol-5-one (III) (1.39 g) was, without further purification, dissolved in 10% KOH solution (10 ml) and heated under reflux for 30 minutes. After evolution of ammonia had subsided, the mixture was cooled and acidified with 15% HCl. The separated crystals were collected by filtration and washed with cold water several times. Recrystallization from water–ethanol (1: 1) afforded white needles (II), mp 260 (decomp.) (1.33 g, 95%). The IR and NMR spectra were identical with those of the material obtained according to the procedure (a) described above.

2-Acetyl-3-hydroxy-5-methylpyrazole (IV) and 3-Acetoxy-2-acetyl-5-methylpyrazole (V), Treatment of I in Acetic Anhydride at 100°——A suspension of I (9.81 g) in acetic anhydride (100 ml) was heated on a boiling water-bath until the starting material dissolved completely. Vigorous agitation was necessary to obtain clear solution within 5 to 10 minutes. After cooling, crystals separated, which were collected by filtration and recrystallized from benzene and then from methanol to give colorless pillars, mp 147—148.5° (5.60 g, 40%). The material showed deep purple coloration with 1% anhydrous ferric chloride solution in methanol. IR $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1700. UV $\lambda_{max}^{CH_3OH}$ nm (log ε): 223 (4.111), 289 (3.919). NMR δ ppm (in DMSO-d_6): 2.17 (3H, s), 2.43 (3H, s), 5.00 (1H, s). *Anal.* Calcd. for $C_6H_8O_2N_2$: C, 51.42; H, 5.75; N, 19.99. Found: C, 51.33; H, 5.51; N, 20.19.

The filtrate of the reaction mixture was carefully evaporated under reduced pressure to remove acetic acid and acetic anhydride. The oily residue was then distilled *in vacuo* to give colorless oil (V), bp 70—72° (0.6 mmHg) (6.35 g, 35%). The material was negative to ferric chloride test in methanol and showed one spot on the silica gel TLC plate (Rf=0.37, solvent: CH_2Cl_2). IR $\nu_{max}^{CCl_4}$ (cm^{-1}): 1795, 1747. UV $\lambda_{max}^{CH_3OH}$ nm (log ε): 238.5 (4.124). NMR δ ppm (in $CDCl_3$): 2.24 (3H, s), 2.30 (3H, s), 2.57 (3H, s), 5.87 (1H, s). *Anal.* Calcd. for $C_8H_{10}O_3N_2$: C, 52.74; H, 5.53; N, 15.38. Found: C, 52.69; H, 5.68; N, 15.32.

Hydrolysis of 2-Acetyl-3-hydroxy-5-methylpyrazole (IV)——Monoacetate (IV) (140 mg) was added into a mixture of MeOH (5 ml) and 10% aq. NaOH solution (2 ml) and the mixture was heated on a water-bath for 10 minutes. After the pH value of the solution was adjusted to 2 by adding 2N HCl, the mixture was evaporated under reduced pressure. The residue was recrystallized from water to give colorless prisms, mp 266—268° (79 mg). The mixed melting point and the IR spectrum showed that it was identical with the authentic 3-methylpyrazol-5-one (I).

Hydrolysis of 3-Acetoxy-2-acetyl-5-methylpyrazole (V)——A solution of diacetate (V) (182 mg), MeOH (5 ml) and 10% aq. NaOH solution was heated on a water-bath for 10 minutes. After the pH value was adjusted to 2 by adding 2N HCl, the mixture was evaporated under reduced pressure. The residue was recrystallized from water to give colorless prisms mp 266—268° (71 mg). The mixed melting point and the IR spectrum showed that it was identical with the authentic specimen of 3-methylpyrazol-5-one (I).

3-Acetoxy-1-acetyl-5-methylpyrazole (VI), Treatment of I in Acetic Anhydride at 140°——A suspension of I (9.81 g) in acetic anhydride (100 ml) was heated under reflux on an oil-bath for 3 hr. After the solvent was evaporated to one-half of the volume, the reaction mixture was poured onto ice-water. The separated crystals were collected by filtration and recrystallized from a mixture of benzene–petroleum ether (30—60°) to give colorless plates, mp 48—49° (16.7 g, 92.5%). The material was negative to ferric chloride test in methanol and showed one spot on the silica gel TLC plate (Rf=0.45, solvent: CH_2Cl_2). IR $\nu_{max}^{CCl_4}$ (cm^{-1}): 1785, 1750. UV $\lambda_{max}^{CH_3OH}$ nm (log ε): 239 (4.176). NMR δ ppm (in $CDCl_3$): 2.31 (3H, s), 2.58 (3H, d, J=0.9 Hz), 2.62 (3H, s), 6.16 (1H, q, J=0.9 Hz). *Anal.* Calcd. for $C_8H_{10}O_3N_2$: C, 52.74; H, 5.53; N, 15.38. Found: C, 52.59; H, 5.61; N, 15.27.

Hydrolysis of 3-Acetoxy-1-acetyl-5-methylpyrazole (VI)——A solution of diacetate (VI) (182 mg), MeOH (5 ml) and 10% aq. NaOH solution was heated on a water-bath for 10 minutes. After the pH value was adjusted to 2 by adding 2N HCl, the mixture was evaporated under reduced pressure. The residue was recrystallized from water to give colorless prisms, mp 266—268° (75 mg). The mixed melting point and the IR spectrum showed that it was identical with the authentic specimen of the 3-methylpyrazol-5-one (I).

1-Acetyl-3-hydroxy-5-methylpyrazole (VII), Treatment of I in Acetic Anhydride in the Presence of Pyridine——Acetic anhydride (10.21 g) was added dropwise into a heated and agitated solution of I (9.81 g) in pyridine (30 ml) on an oil-bath (90—100°) in about half an hour. After another half-hour's heating the reaction mixture was cooled and poured onto ice-water. The separated crystals were collected by filtration and recrystallized from benzene to give long colorless needles (VII), mp 153—154° (12.3 g, 88%). The material showed reddish brown coloration with 1% solution of ferric chloride in methanol. IR ν_{max}^{KBr} (cm^{-1}): 1723, 1615, 1528; $\nu_{max}^{CHCl_3}$ (cm^{-1}); 1725. UV $\lambda_{max}^{CH_3OH}$ nm (log ε): 253 (4.060). NMR δ ppm (in DMSO-d_6): 2.42 (3H, d, J=1.0 Hz), 2.46 (3H, s), 5.83 (1H, q, J=1.0 Hz). *Anal.* Calcd. for $C_6H_8O_2N_2$: C, 51.42; H, 5.75; N, 19.99. Found: C, 51.38; H, 5.82; N, 20.05.

Hydrolysis of 1-Acetyl-3-hydroxy-5-methylpyrazole (VII)——Monoacetate (VII) (140 mg) was added into a mixture of MeOH (5 ml) and 10% aq. NaOH solution (2 ml) and the mixture was heated on a water-bath for 10 minutes. After the pH value of the solution was adjusted to 2 by adding 2N HCl, the mixture was evaporated under reduced pressure. The residue was recrystallized from water to give colorless prisms mp 266—268° (80 mg). The mixed melting point and the IR spectrum showed that it was identical with the authentic specimen of 3-methylpyrazol-5-one (I).

3-Acetoxy-2-acetyl-5-methylpyrazole (V), Acetylation of 2-Acetyl-3-hydroxy-5-methylpyrazole (IV) with Acetyl Chloride and Triethylamine——Into a stirred solution of monoacetate (IV) (1.401 g) and acetyl chloride (800 mg) in dry tetrahydrofuran (100 ml), which was cooled below 5° with ice-water, there was added a solution of triethylamine (1.050 g) in tetrahydrofuran (10 ml) in one lot. The precipitated crystals of triethylamine hydrochloride were filtered off after further 30 minutes' stirring at the same temperature. The filtrate was passed through a short column of silica gel (15 g) and washed with dichloromethane. The filtrate and the washings were combined and evaporated to dryness to get colorless syrup, which was distilled to give colorless oil (V), bp 70—72° (0.6 mmHg) (1.640 g, 90%). This material was negative to ferric chloride test in methanol and showed one spot on the silica gel TLC plate (Rf=0.37, solvent: CH_2Cl_2). The IR and NMR spectra were identical with those of the material obtained directly from I and acetic anhydride at 100°.

Partial Hydrolysis of 3-Acetoxy-2-acetyl-5-methylpyrazole (V)——An aqueous solution of anhydrous sodium carbonate (110 mg, in 1 ml H_2O) was added into a solution of diacetate (V) (180 mg) in methanol (5 ml) and the mixture was stirred at room temperature for an hour. The reaction mixture was diluted with water (30 ml) and extracted with ether (10 ml) three times. The pH value of the water-layer was adjusted to 2 with 15% HCl solution. The precipitated crystals were collected by filtration and dried (45 mg). Recrystallization from benzene gave colorless pillars, mp 144—147°, which showed deep-purple coloration with ferric chloride in methanol. The mixed melting point and IR spectrum proved it to be identical with the monoacetate (IV).

Acetylation of 1-Acetyl-3-hydroxy-5-methylpyrazole (VII) into 3-Acetoxy-1-acetyl-5-methylpyrazole (VI)——(a) A solution of monoacetate (VII) (140 mg) in acetic anhydride (5 ml) was heated on a boiling water-bath for 30 minutes. After the solvent was evaporated under reduced pressure, the residue was recrystallized from benzene–petroleum ether (30—60°) to give colorless crystals (VI), mp 48—49° (172 mg). The mixed melting point and IR spectrum showed it was identical with the diacetate (VI) obtained directly from I by refluxing in acetic anhydride.

(b) Into a stirred solution of monoacetate (VII) (1.401 g) and acetyl chloride (800 mg) in dry tetrahydrofuran (100 ml), which was cooled below 5° with ice-water, there was added a solution of triethylamine (1.050 g) in tetrahydrofuran (10 ml) in one lot. After 30 minutes' stirring the precipitated crystals of triethylamine hydrochloride were filtered off. The filtrate was evaporated to dryness and the crystalline residue was recrystallized from benzene–petroleum ether (30—60°) to give colorless prisms (VI) mp 48—49° (1.710 g, 94%). The mixed melting point and IR spectrum showed it was identical with the diacetate (VI) obtained directly from I by refluxing in acetic anhydride.

Partial Hydrolysis of 3-Acetoxy-1-acetyl-5-methylpyrazole (VI)——An aqueous solution of anhydrous sodium carbonate (110 mg in 1 ml H_2O) was added into a solution of diacetate (VI) (180 mg) in methanol (5 ml) and the mixture was stirred at room temperature for 7 hr. The reaction mixture was diluted with water (30 ml) and the pH value adjusted to 2 by adding 15% HCl. The separated crystals were collected by filtration. Recrystallization from benzene gave long colorless needles, mp 153—154° (110 mg), which showed reddish brown coloration with ferric chloride in methanol. The mixed melting point and IR spectrum proved it to be identical with the monoacetate (VII).

1-Acetyl-3-methoxy-5-methylpyrazole (VIII), Treatment of 1-Acetyl-3-hydroxy-5-methylpyrazole (VII) with Diazomethane——Into a stirred suspension of monoacetate (VII) (140 mg) in ether (20 ml) there was added a solution of diazomethane in ether prepared from N-methyl-N-nitroso-*p*-toluenesulfonamide (1 g) and KOH in ether–EtOH–H_2O.[12] When the evolution of nitrogen was complete, the solution was evaporated to dryness under reduced pressure and the residue was crystallized from ether–petroleum ether (30—60°) to give colorless plates (VIII), mp 32—33° (131 mg, 85%). IR ν_{max}^{KBr} (cm^{-1}): 1720, 1595, 1515. NMR δ ppm (in DMSO-d_6): 2.40 (3H, d, J=1.0 Hz), 2.47 (3H, s), 3.80 (3H, s), 5.80 (1H, q, J=1.0 Hz). *Anal.* Calcd. for $C_7H_{10}O_2N_2$: C, 54.53; H, 6.54; N, 18.17. Found: C, 54.45; H, 6.69; N, 18.30.

Preparation of 3-Methoxy-5-methylpyrazole (IX) accordig to Backer's Method[5]——A mixture of methyl acetoacetate (11.61 g) and hydrazine monohydrochloride (7.0 g) in MeOH (100 ml) was heated under reflux for 2 hr. After the solution was basified by adding aq. NaOH (4 g in 10 ml H_2O), the crystals which separated were collected by filtration and the crude crystals were digested with ether (100 ml). Filtration to remove insoluble 3-methylpyrazol-5-one gave rise to clear filtrate, which was passed through a short column of silica gel (20 g) in CH_2Cl_2–ether solution. The filtrate and washings were combined and evaporated *in vacuo* to give colorless syrup, which was dissolved in a mixture of ether and petroleum ether and left in a refrigerator to precipitate crystalline 3-methoxy-5-methylpyrazole (IX), mp 49—50° (0.91 g, 8.1%). This material was negative to ferric chloride test in methanol. IR ν_{max}^{KBr} (cm^{-1}): 1580, 1500, 1445. NMR δ ppm (in DMSO-d_6): 2.12 (3H, s), 3.67 (3H, s), 5.37 (1H, s). *Anal.* Calcd. for $C_5H_8ON_2$: C, 53.55; H, 7.19; N, 24.99. Found: C, 53.41; H, 7.35; N, 25.02.

1-Acetyl-3-methoxy-5-methylpyrazole (VIII), Acetylation of 3-Methoxy-5-methylpyrazole (IX)——A solution of 3-methoxy-5-methylpyrazole (IX) (112 mg) in acetic anhydride (5 ml) was heated at 100° on

12) Th. J. de Boer and H. J. Backer, "Organic Syntheses," Coll. Vol. IV ed. by N. Rabjohn, John Wiley and Sons, Inc., New York, 1963, p. 943; *idem*, *Rec. Trav. Chim.*, 73, 229, 582 (1954).

an oil-bath for an hour. After the solvent was evaporated under reduced pressure, the residue was recrystallized from ether–petroleum ether (30—60°) to give colorless plates, mp 32—33° (58 mg). The mixed melting point and IR and NMR spectra proved this material to be identical with the specimen obtained from monoacetate (VII) and diazomethane.

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