Reactions of 3-Acetyltropolone and Its Methyl Ethers with Methylhydrazine

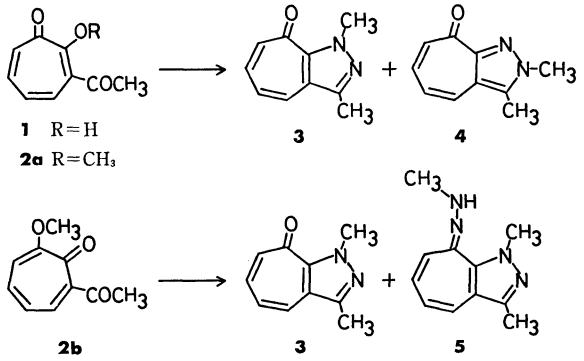
Akio YAMANE,† Kimiaki IMAFUKU,* and Hisashi MATSUMURA

Department of Chemistry, Faculty of Science, Kumamoto University, Kurokami, Kumamoto 860

(Received August 27, 1979)

Synopsis. The reactions of 3-acetyltropolone and 3-acetyl-2-methoxytropone with methylhydrazine gave 1,3-dimethyl-1,8-dihydrocycloheptapyrazol-8-one (**3**) and 2,3-dimethyl-2,8-dihydrocycloheptapyrazol-8-one. 7-Acetyl-2-methoxytropone reacted with methylhydrazine to afford 1,3-dimethyl-1,8-dihydrocycloheptapyrazol-8-one methylhydrazone, besides a small amount of **3**.

In a previous paper,[1] we reported that 3-acetyltropolone (**1**) and 3-acetyl-2-methoxytropone (**2a**) reacted with hydrazine to afford 3-methyl-1,8-dihydrocycloheptapyrazol-8-one and that 7-acetyl-2-methoxytropone (**2b**) gave the hydrazone and azine of the above cycloheptapyrazolone. In this note, we wish to report the synthesis of 1,8- (**3**) and 2,8-dihydrocycloheptapyrazol-8-one (**4**), which have an additional methyl group at N_1 or N_2 atom, by the reactions of **1**, **2a**, and **2b** with methylhydrazine.



Scheme 1.

Results and Discussion

The refluxing of a mixture of 3-acetyltropolone (**1**) and methylhydrazine, which has two different nucleophilic nitrogen atoms, in methanol for 2 h gave two isomeric products, **3** (mp 96—98 °C) (60%) and **4** (mp 178—179 °C) (8%). The IR spectra of **3** and **4** show absorptions at 1643 and 1650 cm^{-1} respectively for the tropone carbonyl group. The UV spectra of the two isomers (**3** and **4**) are very similar to that of 3-methyl-1,8-dihydrocycloheptapyrazol-8-one,[1] as are shown in Fig. 1. The NMR spectra of **3** and **4** show peaks at δ 4.39 and 4.05 ppm respectively for the *N*-CH_3 group. The *N*-CH_3 peak of **3** is seen to shift to a lower field than that of **4** as a result of the anisotropic effect of the tropone carbonyl group. Thus, **3** and **4** were assigned to 1,3-dimethyl-1,8-dihydrocycloheptapyrazol-8-one and 2,3-dimethyl-2,8-dihydrocycloheptapyrazol-8-one respectively.

The refluxing of 3-acetyl-2-methoxytropone (**2a**) with methylhydrazine for 2 h gave the same products, **3** and **4** in 49 and 2% yields respectively.

† Present address: Wakunaga Pharmaceutical Co., Ltd., Koda-machi, Takata-gun, Hiroshima 729-64.

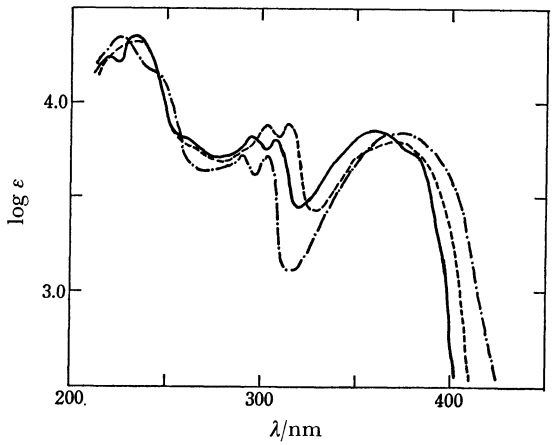
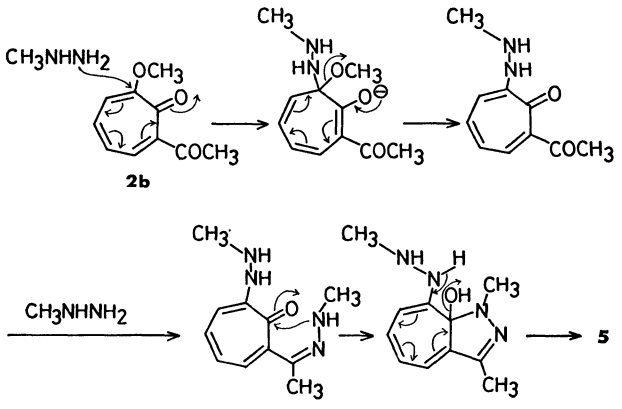


Fig. 1. UV Spectra.
——— 3-Methyl-1,8-dihydrocycloheptapyrazol-8-one,
------ **3**, —·—·— **4**.

A mixture of 7-acetyl-2-methoxytropone (**2b**) and methylhydrazine in methanol was refluxed for 2 h and then chromatographed on silica gel to afford **3** (trace) and **5** (29%). The IR spectrum of **5** shows no band near 1600 cm^{-1} for tropone, but it shows an NH band at 3260 cm^{-1}. Its UV spectrum is very similar to that of 3-methyl-1,8-dihydrocycloheptapyrazol-8-one hydrazone.[1] The NMR spectrum of **5** shows three singlet peaks at δ 2.16 for *C*-CH_3 and 3.72 for *N*-CH_3 in the pyrazole ring and 3.12 ppm for *N*-CH_3 of the methylhydrazono group. Consequently, **5** was assigned to 1,3-dimethyl-1,8-dihydrocycloheptapyrazol-8-one methylhydrazone.

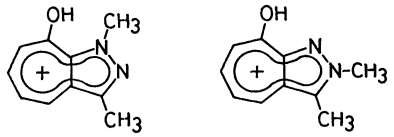
No methylhydrazone (**5**) was obtained from the reaction of **1** and **2a** with methylhydrazine. Furthermore, **3** did not react with methylhydrazine either. It is thoguht that the methylhydrazone (**5**) was directly formed from **2b** by the mechanism shown in Scheme 2. In addition, the formation of the minor product (**3**) from **2b** might be considered to proceed as follows. The nucleophilic attack of methanol (*i.e.*, the solvent) on a C_2-atom of **2b** would give 3-acetyl-



Scheme 2.

tropolone (**1**) which then reacts with methylhydrazine to afford **3**.

The NMR spectra of **3** and **4** in trifluoroacetic acid show a shift of the seven-membered ring protons by *ca.* 1.0—1.2 ppm, and one of the *N*- and *C*-CH_3 protons by *ca.* 0.4 ppm, towards a lower field. This indicates that the positive charge of the cations of **3** and **4** is delocalized over both the seven-membered ring and the pyrazole ring, as is shown in **3′** and **4′**:



3′ **4′**

Experimental

Measurements. The melting points were determined with a Yanagimoto MP-S2 melting-point measuring apparatus and are uncorrected. The IR spectra were taken on a JASCO IRA-1 spectrophotometer, and the UV spectra on a Hitachi EPS-3T spectrophotometer. The NMR spectra were recorded with a Hitachi R-24 spectrometer (60 MHz), with TMS as the internal standard.

*Reaction of 3-Acetyltropolone (**1**) with Methylhydrazine.* A mixture of **1** (345 mg, 2.1 mmol) and methylhydrazine (185 mg, 4.1 mmol) in methanol (20 ml) was refluxed for 2 h. After the removal of the solvent, the residue was chromatographed on a Wakogel B-10 plate (30×30 cm^2) with ethyl acetate to give **3** (218 mg, 60%) and **4** (28 mg, 8%). 1,3-Dimethyl-1,8-dihydrocycloheptapyrazol-8-one (**3**): Pale yellow needles (from hexane); mp 96—98 °C; IR ($CHCl_3$): 1643, 1598 cm^{-1}; UV (MeOH): λ_{max} nm (log ε) 235 (4.33), 303 (3.89), 316 (3.89), 372 (3.80); NMR ($CDCl_3$): δ 2.50 (s, 3H, *C*-CH_3), 4.39 (s, 3H, *N*-CH_3), 6.4—7.5 ppm (m, 4H); NMR (CF_3COOH): δ 2.94 (s, 3H), 4.78 (s, 3H), 7.4—8.5 ppm (m, 4H). Found: C, 68.65; H, 5.76; N, 16.12%. Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08%. 2,3-Dimethyl-2,8-dihydrocycloheptapyrazol-8-one (**4**): Pale yellow needles (from benzene-petroleum ether); mp 178—179 °C; IR ($CHCl_3$): 1650, 1603 cm^{-1}; UV (MeOH): λ_{max} nm (log ε) 226 (4.36), 244 (4.17), 252 (4.04), 290 (3.72), 303 (3.71), 377 (3.84); NMR ($CDCl_3$): δ 2.51 (s, 3H, *C*-CH_3), 4.05 (s, 3H, *N*-CH_3), 6.3—7.4 ppm (m, 4H); NMR (CF_3COOH): δ 2.95 (s, 3H), 4.49 (s, 3H), 7.5—8.5 ppm (m, 4H). Found: C, 68.91; H, 5.87; N, 16.16%. Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08%.

*Reaction of 3-Acetyl-2-methoxytropone (**2a**) with Methylhydrazine.* A mixture of **2a** (423 mg, 2.4 mmol) and methylhydrazine (183 mg, 4.0 mmol) in methanol (20 ml) was refluxed for 2 h. The reaction mixture was then worked up as has been described above to afford **3** (205 mg, 49%) and **4** (8 mg, 2%).

*Reaction of 7-Acetyl-2-methoxytropone (**2b**) with Methylhydrazine.* A mixture of **2b** (357 mg, 2.0 mmol) and methylhydrazine (228 mg, 5.0 mmol) in methanol (20 ml) was refluxed for 2 h. After the removal of the solvent, the residue was chromatographed on two Wakogel B-10 plates (30×30 cm^2) with ether–chloroform (1:2) to give **3** (trace) and **5** (118 mg, 29%). 1,3-Dimethyl-1,8-dihydrocycloheptapyrazol-8-one methylhydrazone (**5**): Orange needles (from benzene-petroleum ether); mp 112—113 °C; IR ($CHCl_3$): 3260, 1530 cm^{-1}; UV (MeOH): λ_{max} nm (log ε) 260^{sh} (3.96), 270^{sh} (3.92), 350 (4.10); NMR ($CDCl_3$): δ 2.16 (s, 3H, *C*-CH_3), 3.12 (s, 3H, *NH*-CH_3), 3.72 (s, 3H, *N*-CH_3), 5.4—6.3 (m, 4H), 8.7—9.3 ppm (br, 1H, NH). Found: C, 65.31; H, 7.02; N, 27.79%. Calcd for $C_{11}H_{14}N_4$: C, 65.32; H, 6.98; N, 27.70%.

We wish to thank Dr. Tetsuo Nozoe, Professor Emeritus of Tohoku University, for his advice and encouragement.

Reference

1) A. Yamane, M. Nagayoshi, K. Imafuku, and H. Matsumura, *Bull. Chem. Soc. Jpn.*, **52**, 1972 (1979).