Reactions of 3-Acetyltropolone and Its Methyl Ethers with Hydrazine

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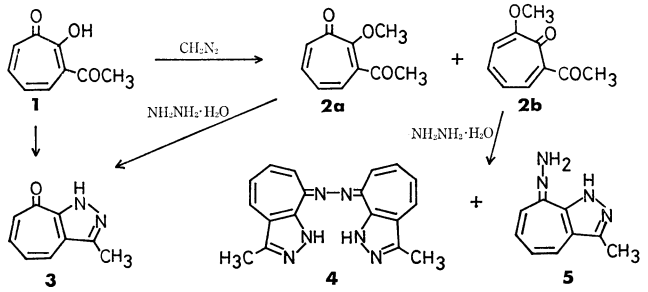
3-Acetyltropolone (**1**) was synthesized from 3-isopropenyltropolone by treatment with sodium azide in concentrated sulfuric acid. Methylation of **1** by diazomethane gave two isomers, 3-acetyl-2-methoxytropone (**2a**) and 2-acetyl-7-methoxytropone (**2b**). **1**, **2a**, and **2b** reacted with hydrazine to give some 1,8-dihydrocycloheptapyrazol-8-one derivatives.

Doi reported that 4-isopropenyltropolone affords 4-acetyltropolone by treatment with one equivalent of hydrazoic acid in concentrated sulfuric acid.[1] By the application of this reaction to 3-isopropenyltropolone, we successfully obtained 3-acetyltropolone (**1**). Schenck *et al.* synthesized chloro-substituted 3-acetyltropolone by another method.[2] Since 3-acetyltropolone (**1**) has an active methyl group and β-diketone structure, several interesting reactions are expected. Its two isomeric methyl ethers, **2a** and **2b**, would behave as active troponoid. On the other hand, Matsumoto obtained 1,8-dihydrocycloheptapyrazol-8-one derivatives by the reactions of 3-formyltropolone derivatives with hydrazines.[3] We have investigated the reactions of **1**, **2a**, and **2b** with hydrazine.



Scheme 1.

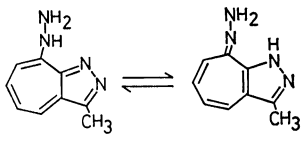
Results and Discussion

*Synthesis of 3-Acetyltropolone (**1**) and Its Methyl Ethers (**2a** and **2b**).* 3-Isopropenyltropolone was obtained by the method of Asao *et al.*[4] Treatment of 3-isopropenyltropolone with 1.5 equivalents of sodium azide in concentrated sulfuric acid gave 3-acetyltropolone (**1**) in a fairly good yield (70%). The structure was confirmed by means of spectral and analytical data. The IR spectrum showed a strong acetyl carbonyl band at 1715 cm^{-1} and a characteristic band for tropolone at 1620 cm^{-1}. The UV and NMR spectra also supported the structure of 3-acetyltropolone (**1**).

Being a β-diketone, 3-acetyltropolone (**1**) reacts with diazomethane to give two methyl ethers (**2a** and **2b**). As to the two methyl ethers, one is 3-acetyl-2-methoxytropone and the other 2-acetyl-7-methoxytropone. Generally, in ^1H NMR spectrum the signal of the proton situated in a β-position to a carbonyl group appears in a lower field. The NMR spectrum of **2a** showed a multiplet for seven-membered ring protons at 6.9—7.3 ppm, while that of **2b** showed a doublet of doublets for H-3 at 7.58 ppm. Thus, **2a** was assigned to 3-acetyl-2-methoxytropone and **2b** to 2-acetyl-7-methoxytropone.

*Reactions of 3-Acetyltropolone (**1**) and 3-Acetyl-2-methoxytropone (**2a**) with Hydrazine.* Refluxing of a mixture of **1** and 2 equivalents of hydrazine hydrate in methanol afforded 3-methyl-1,8-dihydrocycloheptapyrazol-8-one (**3**) in 76% yield. The reaction at room temperature also gave **3** in 62% yield. Though **3** can be considered to be another tautomeric form, 3-methylcycloheptapyrazol-8-ol, its IR, NMR, and UV spectra support the form of 3-methyl-1,8-dihydrocycloheptapyrazol-8-one. **2a** also reacted with hydrazine hydrate to give **3**, the difference between the reactivities of **1** and **2a** not being observed.

*Reaction of 2-Acetyl-7-methoxytropone (**2b**) with Hydrazine.* When a mixture of **2b** and 2 equivalents of hydrazine hydrate in methanol was refluxed, 3-methyl-1,8-dihydrocycloheptapyrazol-8-one azine (**4**) precipitated and 3-methyl-1,8-dihydrocycloheptapyrazol-8-one hydrazone (**5**) was obtained from the filtrate. The reaction with equimolar hydrazine hydrate gave only **4** (34%), **2b** being recovered (36%). The azine (**4**) was purple plates and insoluble in organic solvents except acetic acid. Nozoe *et al.*[5] obtained 3-phenyl-1,8-dihydrocycloheptapyrrol-8-one azine by the reaction of 8-chloro-3-phenylcycloheptapyrrole with hydrazine hydrate, the UV spectrum of which being very similar to that of **4**. The IR spectrum of **4** has a few absorption bands because of high symmetry but no bands at near 1600 cm^{-1} for tropone nor at near 1720 cm^{-1} for acetyl group. However, it has an absorption band near 3200 and 3400 cm^{-1} for NH. Mass spectrum of **4** shows a molecular ion peak at 326. The structure of **4** is reasonable from the above-mentioned evidence and analytical data. **5** has two tautomeric forms such as A and B. The UV spectrum of **5** in visible region shows absorption maxima at fairly shorter wavelength[6] and the NMR spectrum the signal for NH of pyrazole ring at *ca.* 12.4 ppm, indicating that **5** exists mainly in the form B.



A B

Treatment of **5** with acetone yielded a tricyclic compound (**6**). The NMR spectrum of **6** showed the

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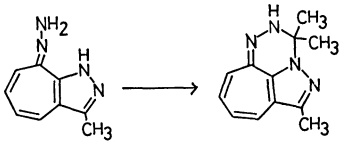
presence of three methyl group [δ 1.61 (6H), 2.36 (3H)]. Two methyl groups at 1.61 ppm suggest that they exist at sp^3 carbon atom. The mass spectrum showed the parent peak at 214 and the elemental analysis also gave a satisfactory result. Accordingly, **6** was identified as 1,3,3-trimethyl-3,4-dihydro-2,2a,4,5-tetraazabenz[*cd*]azulene.



5 **6**

Experimental

The melting points were determined with a Yanagimoto hot-stage apparatus and are uncorrected. All ^1H NMR spectra were recorded with a Hitachi R-24 spectrometer (60 MHz) with TMS as an internal standard. The IR and UV spectra were recorded with a JASCO IRA-1 and a Hitachi EPS-3T spectrophotometer, respectively. The mass spectra were taken on a JEOL JMS-OI-SG-2 spectrometer.

*Preparation of 3-Acetyltropolone (**1**).* Sodium azide (10 g) was added to a stirred mixture of 3-isopropenyltropolone (16.2 g), concentrated sulfuric acid (50 ml) and chloroform (50 ml) under cooling with water. The mixture was stirred at 60—70 °C for 2 h. After removal of the chloroform layer, the acid layer was diluted with water and then left to stand overnight. The crystals deposited were recrystallized from methanol to give 11.6 g (70%) of 3-acetyltropolone (**1**) as pale yellow needles: mp 131—132 °C; λ_{max}^{MeOH} nm (log ε): 245 (4.25), 350 (3.80), 415 (3.75); IR ($CHCl_3$): 1715 (C=O), 1620 cm^{-1} (C=O); NMR ($CDCl_3$): δ 9.0 (br, s, 1H, OH), 7.76 (d, 1H, J=9.0 Hz, H-4), 6.9—7.6 (m, 4H), 2.69 ppm (s, 3H, CH_3). Found: C, 65.68; H, 4.94%. Calcd for $C_9H_8O_3$: C, 65.85; H, 4.91%.

*Methylation of 3-Acetyltropolone (**1**).* An ethereal solution of diazomethane was slowly added to a solution of **1** (11.1 g) in chloroform until the resulting mixture gave no coloration with iron(III) chloride. After removal of the solvents *in vacuo*, the residue was chromatographed on a silica gel column (Wakogel C-100, 900 g) using ethyl acetate as eluant. The former fractions were combined and recrystallized from hexane–benzene to give 5.37 g (45%) of 3-acetyl-2-methoxytropone (**2a**) as colorless needles: mp 45—46 °C; λ_{max}^{MeOH} nm (log ε): 235 (4.21), 330 (3.87); IR ($CHCl_3$): 1730 (C=O), 1587 cm^{-1} (C=O); NMR ($CDCl_3$): δ 6.9—7.3 (m, 4H), 4.00 (s, 3H, OCH_3), 2.53 ppm (s, 3H, $COCH_3$). Found: C, 67.34; H, 5.69%. Calcd for $C_{10}H_{10}O_3$: C, 67.40; H, 5.66%. The latter fractions were also combined and recrystallized from hexane–benzene to give 4.92 g (41%) of 2-acetyl-7-methoxytropone (**2b**) as pale yellow needles: mp 105—106 °C; λ_{max}^{MeOH} nm(log ε): 235 (4.24), 330 (3.84), 365 (3.83); IR ($CHCl_3$): 1716 (C=O), 1601 cm^{-1} (C=O); NMR ($CDCl_3$): δ 7.58 (dd, 1H, J=11.2 and 2.0 Hz, H-3), 6.7—7.4 (m, 3H), 3.96 (s, 3H, OCH_3), 2.53 ppm (s, 3H, $COCH_3$). Found: C, 67.22; H, 5.72%. Calcd for $C_{10}H_{10}O_3$: C, 67.40; H, 5.66%.

*Reaction of 3-Acetyltropolone (**1**) with Hydrazine.* a) A mixture of **1** (213 mg, 1.30 mmol) and 80% hydrazine hydrate (167 mg, 2.67 mmol) in methanol (10 ml) was refluxed for 1 h. After removal of the solvent the residue was recrystallized from benzene to give 158 mg (76%) of 3-methyl-1,8-dihydrocycloheptapyrazol-8-one (**3**) as orange plates: mp 183—184 °C; λ_{max}^{MeOH} nm (log ε): 235 (4.35), 296 (3.82), 308 (3.81), 365 (3.85); IR ($CHCl_3$): 3200 (NH), 1580 cm^{-1} (C=O); NMR ($CDCl_3$): δ: 12.0—13.5 (br, 1H, NH), 6.6—7.3 (m, 4H), 2.60 ppm (s, 3H, CH_3). Found: C, 67.35; H, 5.07; N, 17.74%. Calcd for $C_9H_8ON_2$: C, 67.48; H, 5.03; N, 17.49%. b) At room temperature, the reaction of **1** (205 mg, 1.25 mmol) with 80% hydrazine hydrate (80 mg, 1.28 mmol) in methanol (10 ml) gave the same product **3** (124 mg, 62%) after 48 h.

*Reaction of 3-Acetyl-2-methoxytropone (**2a**) with Hydrazine.* a) A mixture of **2a** (330 mg, 1.85 mmol) and 80% hydrazine hydrate (295 mg, 4.72 mmol) in methanol (10 ml) was refluxed for 1 h. After removal of the solvent the residue was recrystallized from benzene to give 206 mg (68%) of **3**. b) The same reaction of **2a** (206 mg, 1.26 mmol) with 80% hydrazine hydrate (67 mg, 1.07 mmol) at room temperature for 48 h also gave **3** (90 mg, 51%).

*Reaction of 2-Acetyl-7-methoxytropone (**2b**) with Hydrazine.* a) When a mixture of **2b** (722 mg, 4.05 mmol) and 80% hydrazine hydrate (496 mg, 7.92 mmol) in methanol (40 ml) was refluxed, a purple precipitate was formed. After 1 h the precipitate was filtered off and recrystallized from dimethyl sulfoxide–water to give 82 mg (13%) of 3-methyl-1,8-dihydrocycloheptapyrazol-8-one azine (**4**) as purple plates: mp >300 °C; λ_{max}^{MeOH} nm (log ε): 224 (4.32), 283 sh (3.69), 450 (4.13); IR (KBr): 3300 (NH), 1540 cm^{-1}; NMR (CF_3COOH): δ 7.4—8.1 (m, 8H), 2.98 ppm (s, 6H, $CH_3\times2$). Found: C, 67.98; H, 5.10; N, 26.28%. Calcd for $C_{18}H_{16}N_6$: C, 68.33; H, 5.10; N, 26.57%. M^+ 316. The filtrate was evaporated and the red residue was recrystallized from methanol to give 479 mg (68%) of 3-methyl-1,8-dihydrocycloheptapyrazol-8-one hydrazone (**5**) as red needles: mp 199—202 °C; λ_{max}^{MeOH} nm(log ε): 215 (4.42), 335 (3.98); IR (KBr): 3340 (NH), 3200 (NH), 1640 cm^{-1}; NMR (DMSO-d_6): δ 12.4 (br, 1H, NH), 5.6—6.7 (m, 6H), 2.28 ppm (s, 3H, CH_3). Found: C, 61.98; H, 5.81; N, 31.90%. Calcd for $C_9H_{10}N_4$: C, 62.05; H, 5.79; N, 32.17%. b) Refluxing of **2b** (409 mg, 2.30 mmol) with 80% hydrazine hydrate (137 mg, 2.19 mmol) in methanol (20 ml) for 1 h afforded **4** (130 mg, 34%), **2b** (148 mg, 36%) being recovered. c) At room temperature, the reaction of **2b** (348 mg, 1.96 mmol) with 80% hydrazine hydrate (197 mg, 3.15 mmol) in methanol (20 ml) gave **4** (61 mg, 18%) and **5** (189 mg, 51%) after 24 h. d) At room temperature, **2b** (405 mg, 2.28 mmol) reacted with 80% hydrazine hydrate (135 mg, 2.16 mmol) in methanol (20 ml) for 72 h to afford **4** (133 mg, 31%), **2b** (127 mg, 31%) being recovered.

*Reaction of 3-Methyl-1,8-dihydrocycloheptapyrazol-8-one Hydrazone (**5**) with Acetone.* Acetone (117 mg) was added to a solution of **5** (160 mg) dissolved in hot methanol (10 ml), and the mixture was refluxed for 2 h. The resulting solution was concentrated to dryness and the residue was recrystallized from benzene–petroleum ether to afford 127 mg (66%) of 1,3,3-trimethyl-3,4-dihydro-2,2a,4,5-tetraazabenz[*cd*]-azulene (**6**) as orange prisms: mp 152—155 °C; λ_{max}^{MeOH} nm(log ε): 222 (4.48), 293 (3.68), 350 (4.01); IR ($CHCl_3$): 3270 (NH), 1630, 1600 cm^{-1}; NMR ($CDCl_3$): δ 5.8—6.6 (m, 4H), 5.7 (br, 1H, NH), 2.36 (s, 3H, CH_3), 1.61 (s, 6H, $CH_3\times2$). Found: C, 67.33; H, 6.56; N, 25.96%. Calcd for $C_{12}H_{14}N_4$: C, 67.26; H, 6.59; N, 26.15%. M^+ 214.

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