Reactions of 3-Acetyltropolone and Its Methyl Ethers with Aminoguanidine

Zhong-Tian Jin

Department of Chemistry, Yanbian University, Yanji, Jilin Province, People's Republic of China

and

Kimiaki Imafuku*

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

Received December 22, 1981

3-Acetyltropolone (**1**) reacted with aminoguanidine to afford its guanylhydrazone (**3**). The reaction of 3-acetyl-2-methoxytropone (**2a**) gave 4-methyl-1(2*H*)-phthalazinone (**5**), while the reaction of 7-acetyl-2-methoxytropone (**2b**) gave its guanylhydrazone (**6**) and 3-methyl-1,8-dihydrocycloheptapyrazol-8-one (**4**). The guanylhydrazones (**3** and **6**) were easily cyclized to **4** by heating in acetic acid.

J. Heterocyclic Chem., **19**, 969 (1982).

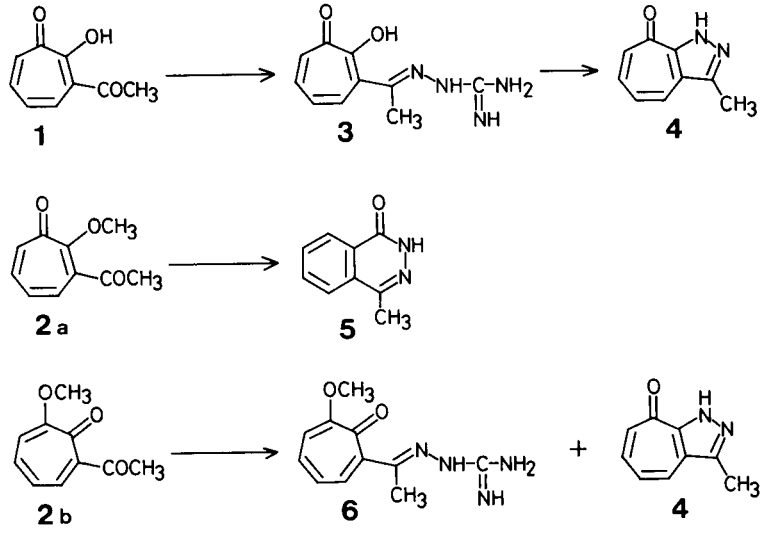
3-Acetyltropolone (**1**) and its methyl ethers (**2a** and **2b**) are very useful as starting materials for synthesis of heterocycle-condensed troponoid compounds. Previously, we reported the reactions of **1**, **2a**, and **2b** with hydrazines (1-3), semicarbazide and thiosemicarbazide (4), hydroxylamine (5), *o*-phenylenediamine (6) and amidines (7). In connection with these studies, we now wish to report the reactions with aminoguanidine. The presence of a chain of three nitrogen and one carbon atoms in the aminoguanidine makes this compound a versatile reagent for a variety of cyclization reactions (8).

Results and Discussion.

Refluxing of a methanol solution of 3-acetyltropolone (**1**) and an equimolar amount of aminoguanidine carbonate in the presence of potassium hydroxide gave 3-acetyltropolone guanylhydrazone (**3**) (mp 234-235°) in 72% yield. Its structure was confirmed by its elemental analysis and spectral data. The ir spectrum shows no acetyl carbonyl group near 1700 cm^{-1}. The nmr spectrum shows peaks at δ 2.00 for the methyl group and 7.3-7.9 ppm for the seven-membered ring protons. The compound (**3**) was heated in acetic acid to give 3-methyl-1,8-dihydrocycloheptapyrazol-8-one (**4**) (1) by hydrolytic removal of the guanyl group. Previously, similar cyclizations were observed in the reactions of **1** with semicarbazide and thiosemicarbazide (4).

The reaction of 3-acetyl-2-methoxytropone (**2a**) with aminoguanidine in the same condition gave a rearrangement product, 4-methyl-1(2*H*)-phthalazinone (**5**). The product (**5**) was identified by comparison of its mp and spectral data with those of an authentic semple (9). It is well

Scheme



known that a similar rearrangement takes place in the reactions of troponoids.

On the other hand, the reaction of 7-acetyl-2-methoxytropone (**2b**) with aminoguanidine was carried out in the presence of potassium hydroxide to give tarry material, which afforded no pure product. The reaction was tried under acidic condition to afford three products. A main product was determined to be 7-acetyl-2-methoxytropone guanylhydrazone (**6**) (mp 124-125°) by its elemental analysis and spectral data. The nmr spectrum shows peaks at δ 2.00 for the methyl group, 3.89 for the methoxyl group, and 6.7-7.3 (3H) and 7.4-7.8 ppm (1H) for the seven-membered ring protons. One of minor products was **4** (9%). As another product, a trace amount of yellow crystals (**7**) (mp 173-174°) was isolated. However, the yield was not enough to determine its structure. The compound (**6**) was cyclized to **4** by heating in acetic acid.

EXPERIMENTAL

The melting points were determined with a Yanagimoto MP-S2 melting point apparatus and are uncorrected. The ir spectra were taken on a JASCO IRA-1 spectrophotometer. The nmr spectra were recorded with a Hitachi R-24 spectrometer (60 MHz).

Reaction of 3-Acetyltropolone (**1**) with Aminoguanidine.

To a solution of 3-acetylropolone (**1**) (328 mg, 2 mmoles) in methanol (20 ml) were added aminoguanidine carbonate (272 mg, 2 mmoles) and potassium hydroxide (112 mg, 2 mmoles). The mixture was refluxed for 3 hours on a water bath and allowed to stand overnight at room temperature. A precipitate was collected by filtration, washed with water, and recrystallized from 50% ethanol to give 3-acetyltropolone guanylhydrazone (**3**) as yellow plates, yield, 230 mg (72%); mp 234-235°; ir (potassium bromide): ν max 3430, 1610 cm^{-1}; nmr (trifluoroacetic acid): δ 2.00 (s, 3H , CH_3), 7.3-7.9 ppm (m, 4H, H-4,5,6,7).

Anal. Calcd. for $C_{10}H_{14}N_4O_2$: C, 54.54; H, 5.49; N, 25.44. Found: C, 54.51; H, 5.48; N, 25.20.

Cyclization of 3-Acetyltropolone Guanylhydrazone (**3**).

A solution of **3** (90 mg) in acetic acid (5 ml) was heated for 3 hours on a water bath. After cooling, the mixture was neutralized with sodium hydrogencarbonate solution and extracted with chloroform. The evaporation residue from the extract was chromatographed on a Wakogel B-10 plate (30 × 30 cm^2) with ethyl acetate to give 3-methyl-1,8-dihydrocycloheptapyrazol-8-one (**4**) (1), yield, 50 mg (77%).

Reaction of 3-Acetyl-2-methoxytropone (**2a**) with Aminoquanidine.

To a solution of 3-acetyl-2-methoxytropone (**2a**) (178 mg, 1 mmole) in methanol (10 ml) were added aminoguanidine carbonate (136 mg, 1 mmole) and potassium hydroxide (56 mg, 1 mmole). The mixture was refluxed for 2 hours on a water bath. After removal of the solvent, the residue was diluted with water, neutralized with 0.1 *M* hydrochloric acid, and extracted with chloroform. The evaporation residue from the extract was recrystallized from benzene-petroleum ether to give 4-methyl-1-(2*H*)-phthalazinone (**5**), yield, 60 mg (38%), mp 231-232° [lit (9) 222°].

Reaction of 7-Acetyl-2-methoxytropone (**2b**) with Aminoguanidine.

A solution of 7-acetyl-2-methoxytropone (**2b**) (356 mg, 2 mmoles) and aminoguanidine carbonate (272 mg, 2 mmoles) in water (20 ml) containing acetic acid (2 ml) was heated for 3 hours on a water bath. After cooling, the reaction mixture was slightly alkalized with sodium hydrogencarbonate solution to give a precipitate, which was collected by filtration and recrystallized from water to afford 7-acetyl-2-methoxytropone guanylhydrazone (**6**) as yellow plates, yield, 260 mg (56%); mp 124-125°; ir (potassium bromide): ν 3280, 1586 cm^{-1}; nmr (DMSO-d_6): δ 2.00 (s, 3H, CH_3), 3.89 (s, 3H, OCH_3), 6.7-7.3 (m, 3H, H-4,5,6), 7.4-7.8 ppm (m, 1H, H-3); nmr (trifluoroacetic acid): δ 2.02 (s, 3H), 4.08 (s, 3H), 7.8-8.5 ppm (m, 4H).

Anal. Calcd. for $C_{11}H_{14}N_4O_2 \cdot H_2O$: C, 52.42; H, 6.30; N, 22.19. Found: C, 52.63; H, 5.96; N, 21.49.

The filtrate was extracted with chloroform, concentrated, and chromatographed on a Wakogel B-10 plate (30 × 30 cm^2) with ethyl acetate to give **4** (30 mg, 9%) and **7** (trace), the latter compound **7** as yellow crystals, mp 173-174°.

Cyclization of 7-Acetyl-2-methoxytropone Guanylhydrazone (**6**).

A solution of **6** (80 mg) in acetic acid (5 ml) was heated for 2 hours on a water bath. After cooling, the mixture was neutralized with sodium hydrogencarbonate solution and extracted with chloroform to give **4** (35 mg, 64%).

Acknowledgement.

This work was supported in part by a Grant-in-Aid for Scientific Research No. 56540308 from the Ministry of Education, Science and Culture, Japan.

REFERENCES AND NOTES

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

(2) A. Yamane, K. Imafuku, and H. Matsumura, *ibid.*, **53**, 1461 (1980).

(3) K. Imafuku, A. Yamane, and H. Matsumura, *J. Heterocyclic Chem.*, **17**, 1293 (1980).

(4) Z.-T. Jin, K. Imafuku, and H. Matsumura, *Yuki Gosei Kagaku Kyokai Shi*, **39**, 862 (1981).

(5) Y. Sudoh, Z.-T. Jin, K. Imafuku, and H. Matsumura, *J. Heterocyclic Chem.*, **19**, (1982), in press.

(6) K. Imafuku, A. Yamane, and H. Matsumura, *ibid.*, **18**, 335 (1981).

(7) Z.-T. Jin, K. Imafuku, and H. Matsumura, *J. Chem. Soc., Perkin Trans., I*, 1037 (1982).

(8) F. Kurzer and L. E. A. Godrey, *Angew. Chem., Int. Ed. Engl.*, **2**, 459 (1963).

(9) S. Gabriel and A. Neumann, *Ber.*, **26**, 705 (1893).