Reactions of 3-Isopropyl-, 3-Isopropenyl-, and 3-Acetyltropolone Methyl Ethers with Guanidines. Synthesis of 9*H*-Cyclohepta[d]pyrimidin-9-ones and Cycloheptimidazoles

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3-Isopropyl- and 3-isopropenyltropolone methyl ethers reacted with guanidine, 1-methylguanidine, and 1,1-dimethylguanidine to afford the corresponding 4-isopropyl- and 4-isopropenylcycloheptimidazoles **4a-f**, respectively. The reactions of 3-acetyl-2-methoxytropones **2c-e** with guanidines afforded 4-methyl-9*H*-cyclohepta[*d*]pyrimidin-9-ones **8a-i**, while the reactions of 7-acetyl-2-methoxytropones **3c,d** produced 4-acetylcycloheptimidazoles **4g-l**. From these reactions, several minor products were also isolated.

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It is well known that 2-methoxytropones reacted with guanidine to yield cycloheptimidazoles (1,3-diazaazulenes). Previously, we found a new type of reaction in the reactions of 3-acetyltropolone methyl ethers with guanidine and benzamidine [1]. Namely, although 7-acetyl-2-methoxytropone gave 4-acetylcycloheptimidazoles, 3-acetyl-2-methoxytropone reacted with guanidine to give 4-methyl-9*H*-cyclohepta[*d*]pyrimidin-9-ones.

Herein, in order to ascertain the generalities of the formation of 9*H*-cyclohepta[*d*]pyrimidin-9-ones, the reactions of methyl ethers of several 3-acetyltropolones bearing an alkyl-substituent at the 5-position with guanidine, 1-methylguanidine, and 1,1-dimethylguanidine were carried out. The reactions of 3-isopropyl- and 3-isopropenyltropolone methyl ethers with these guanidines are also described.

Results and Discussion.

Preparation of Methyl Ethers.

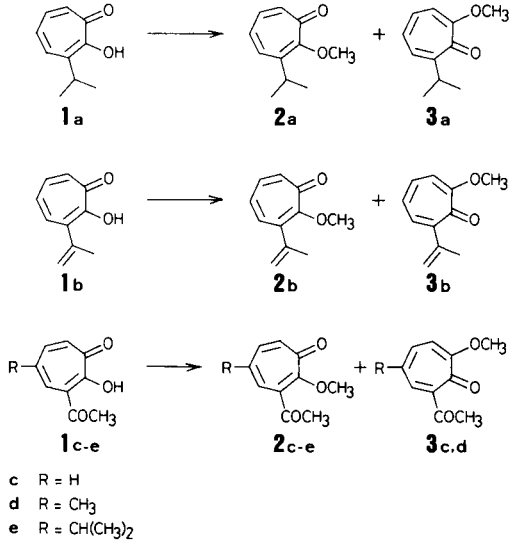
3-Isopropyl- (**1a**) and 3-isopropenyltropolone (**1b**) are called α-thujaplicin and α-dolabrin, respectively, and are present as tropolonic constituents in nature. Although two isomeric methyl ethers, **2a** and **3a**, of the former are also known [2,3], 3-isopropenyltropolone methyl ethers were prepared in the present work as 3-isopropenyl- (**2b**) and 7-isopropenyl-2-methoxytropone (**3b**).

In addition to 3-acetyltropolone methyl ethers **2c** and **3c** [4], 3-acetyl-5-methyltropolone (**1d**) [5] was etherified with diazomethane to afford two isomeric methyl ethers **2d** and **3d**. However, the etherification of 3-acetyl-5-isopropyltropolone (**1e**) [5] gave only 3-acetyl-5-isopropyl-2-methoxytropone (**2e**).

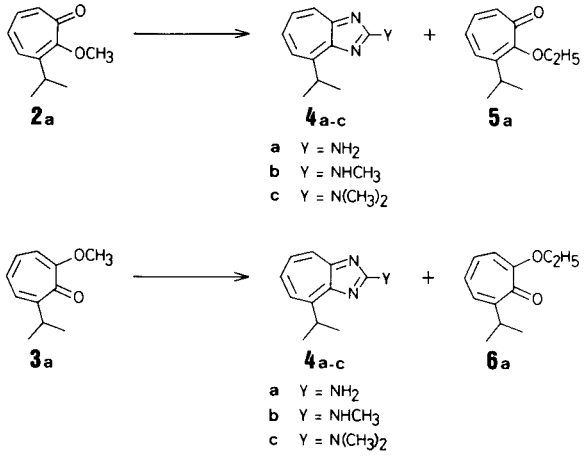
Reactions of 3-Isopropyl- and 3-Isopropenyltropolone Methyl Ethers with Guanidines.

A solution of 3-isopropyl-2-methoxytropone (**2a**) and two molar equivalents of guanidine, 1-methylguanidine, and 1,1-dimethylguanidine in ethanol was refluxed for 2 hours in the presence of sodium ethoxide gave 2-amino-, 2-methylamino-, and 2-dimethylamino-4-isopropylcycloheptimidazoles **4a-c** in very low yields [**4a** (9%), **4b** (4%), and **4c** (8%)] along with the alkoxy-exchanged product, 2-ethoxy-3-isopropyltropone (**5a**) in 29-39% yields. Isomeric 7-isopropyl-2-methoxytropone (**3a**) reacted with guanidines to

Scheme 1



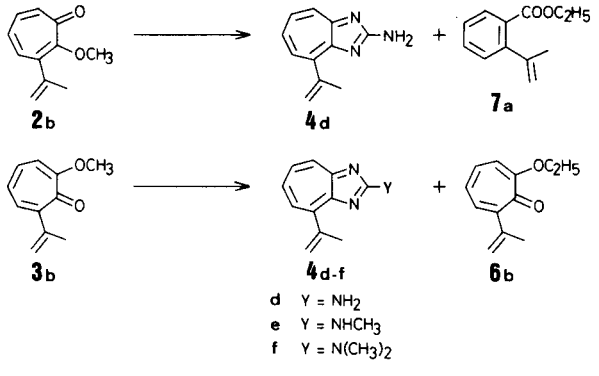
Scheme 2



give the corresponding cycloheptimidazoles [**4a** (47%), **4b** (11%), and **4c** (14%)] together with the alkoxy-exchanged 2-ethoxy-7-isopropyltropone (**6a**) in 21-54% yields.

The reaction of 3-isopropenyl-2-methoxytropone (**2b**) with guanidine to afford 2-amino-4-isopropenylcycloheptimidazole (**4d**) in very low yield (5%) along with the rearranged product, ethyl 2-isopropenylbenzoate (**7a**) (47%), while the reactions with 1-methyl- and 1,1-dimethylguanidine gave only the rearranged compound **7a** as a sole product in 67 and 57% yields, respectively. On the other hand, the rections of isomeric 7-isopropenyl-2-methoxytropone (**3b**) with guanidines gave 2-amino-, 2-methylamino-, and 2-dimethylamino-4-isopropenylcycloheptimidazole [**4d** (45%), **4e** (19%), and **4f** (30%)] together with the alkoxy-exchanged 2-ethoxy-7-isopropenyltropone (**6b**) in 18-57% yields.

Scheme 3

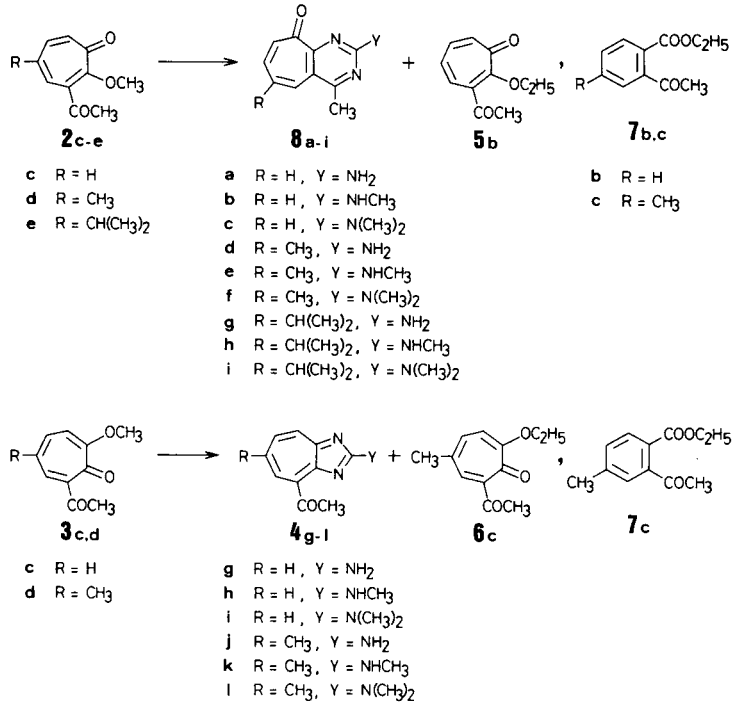


These results indicate that the methyl ether **2b** was attacked by the ethoxide species at the carbonyl carbon atom and rearranged to ethyl benzoate because the reactive C-2 carbon atom of the methyl ether **2b** is sterically hindered from the attack of nucleophiles.

Reactions of 3-Acetyltropolone Methyl Ethers with Guanidines.

Previously, we reported that 3-acetyl-2-methoxytropone (**2c**) reacted with guanidine to afford 2-amino-4-methyl-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8a**) [1]. A solution the methyl ether **2e** and 1-methylguanidine in ethanol was refluxed for 2 hours in the presence of potassium carbonate to give 4-methyl-2-methylamino-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8b**) in 33% yield along with the alkoxy-exchanged product **5b** (44%), while the reaction with 1,1-dimethylguanidine gave 2-dimethylamino-4-methyl-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8e**) in 58% yield together with the rearranged product **7b** (20%). Similarly, the reactions of 3-acetyl-5-methyl-2-methoxytropone (**2d**) with guanidines gave the corresponding 2-amino-substituted 4,6-dimethyl-9*H*-cyclohepta[*d*]pyrimidin-9-ones [**8d** (29%), **8e** (17%), and **8f** (31%)] together with the rearranged product, ethyl 2-acetyl-4-methylbenzoate (**7c**), in 25-63% yields. The reactions of 3-acetyl-5-isopropyl-2-methoxytropone (**2e**) with gauanidines also gave the corresponding 2-amino-substituted 6-isopropyl-4-methyl-9*H*-cyclohepta[*d*]pyrimidin-9-ones [**8h** (37%), **8i** (29%), and **8j** (44%)].

Scheme 4



On the other hand, it was reported that the reaction of 7-acetyl-2-methoxytropone (**3c**) with guanidine gave 4-acetyl-2-aminocycloheptimidazole (**4g**) in 85% yield [1]. Thus, 3-acetyl-2-methoxytropone (**3c**) reacted with 1-methyl- and 1,1-dimethylguanidine to afford 4-acetyl-2-methylamino- and -2-dimethylaminocycloheptimidazoles **4h,i** in high yields (91 and 95%), respectively. The reactions of 3-acetyl-2-methoxy-5-methyltropone (**3d**) with guanidines also gave the corresponding 2-amino-substituted 4-acetyl-6-methylcycloheptimidazoles in good yields [**4j** (71%), **4k** (28%), and **4l** (87%)] together with the alkoxy-exchanged tropone **6c** and the rearranged compound **7c**.

The difference between the reactions of the 3-acetyl-2-methoxytropones **2c-e** and the 7-acetyl-2-methoxytropones **3c,d** may be explicable as follows. In the reactions of the methyl ethers **3c,d**, guanidines attack at the carbon atom bearing the methoxy group to afford the cycloheptimidazoles **4g-l**. On the other hand, as the methoxy group of the methyl ethers **2c-e** is sterically hindered, guanidines attack at the acetyl group and cyclization then occurs at the carbon atom bearing the methoxy group to afford the 9*H*-cyclohepta[*d*]pyrimidin-9-ones **8a-i**. Thus, the latter reactions are useful for synthesis of pyrimidine-fused troponoid compounds.

EXPERIMENTAL

Measurements.

The melting points were determined with a Yanagimoto MP-S2 apparatus and are uncorrected. The ir spectra were taken on a JASCO A-102 spectrophotometer. The ^{1}H nmr spectra were recorded with a JEOL JNM-PMX60SI spectrometer. The mass spectral data were obtained with a JEOL JMS-01-SG2 spectrometer.

Preparation of The Methyl Ethers.

a) Etherification of 3-Isopropenyltropolone (**1b**).

To a solution of 3-isopropenyltropolone (**1b**) (3.2 g, 20 mmoles) in chloroform (50 ml) was added an excess of a ethereal diazomethane solution. The mixture was allowed to stand overnight. After removal of the solvent, the residue was chromatographed on a column (Kieselgel 60, 150 g) with ethyl acetate. The first fraction gave 3-isopropenyl-2-methoxytropone (**2b**), yield 1.8 g (51%), amber oil; ir (chloroform): ν max 1626 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.05 [3H, br s, 3-C(CH$_3$)], 3.91 (3H, s, OCH$_3$), 4.91 [1H, m, 3-C(=CH$_E$)], 5.1-5.3 [1H, m, 3-C(=CH$_Z$)], 6.8-7.3 (4H, m). Found: m/z 176.0842 (M$^+$). Calcd. for $C_{11}H_{12}O_2$: M, 176.0838.

The second fraction gave 7-isopropenyl-2-methoxytropone (**3b**), yield 0.9 g (26%), pale yellow needles (from ethanol), mp 32°; ir (chloroform): ν max 1593 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 2.01 [3H, br s, 7-C(CH$_3$)], 3.93 (3H, s, OCH$_3$), 5.11 [2H, m, 7-C(=CH$_2$)], 6.6-7.2 (3H, m), 7.3-7.6 (1H, m).

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.87. Found: C, 74.69; H, 6.89.

b) Etherification of 3-Acetyl-5-methyltropolone (**1d**).

To a solution of 3-acetyl-5-methyltropolone (**1d**) (4.2 g, 20 mmoles) in chloroform (50 ml) was added an excess of a ethereal diazomethane solution. After allowing it to stand overnight, the evaporated residue was chromatographed on a column (Kieselgel 60, 150 g) with ethyl acetate. The first fraction gave 3-acetyl-2-methoxy-5-methyltropone (**2d**), yield 1.45 g (32%), pale yellow needles (from ethanol), mp 64-65°; ir (chloroform): ν max 1709 (COCH$_3$), 1580 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 2.35 (3H, s, CH$_3$), 2.47 (3H, s, COCH$_3$), 3.93 (3H, s, OCH$_3$), 6.6-6.8 (1H, m, H-4), 7.0-7.3 (2H, m, H-6,7); ms: m/z 192 (M$^+$).

Anal. Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.30. Found: C, 68.69; H, 6.41.

The second fraction gave 7-acetyl-2-methoxy-5-methyltropone (**3d**), yield 820 mg (19%), pale yellow needles (from hexane), mp 95-96°; ir (chloroform): ν max 1692 (COCH$_3$), 1593 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 2.20 (3H, s, 5-CH$_3$), 2.43 (3H, s, COCH$_3$), 3.87 (3H, s, OCH$_3$), 6.4-7.3 (2H, m, H-3,4), 7.50 (1H, d, J = 2.0 Hz, H-6); ms: m/z 192 (M$^+$).

Anal. Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.30. Found: C, 68.81; H, 6.21.

c) Etherification of 3-Acetyl-5-isopropyltropolone (**1e**).

To a solution of 3-acetyl-5-isopropyltropolone (**1e**) (4.2 g, 20 mmoles) in chloroform (20 ml) was added an excess of a diazomethane ethereal solution. After allowing to stand overnight, the evaporation residue was chromatographed on a column (Kieselgel 60, 150 g) with ethyl acetate-chloroform (1:4). The first fraction gave 3-acetyl-5-isopropyl-2-methoxytropone (**2e**), yield 2.2 g (50%), amber oil; ir (chloroform): ν max 1708 (COCH$_3$), 1580 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 1.23 [6H, d, J = 7 Hz, 5-C(CH$_3$) x 2], 2.30 (1H, sept, J = 7 Hz, 5-CH), 2.50 (3H, s, COCH$_3$), 3.97 (3H, s, OCH$_3$), 6.67 (1H, br s, H-4), 7.20 (2H, br s, H-6,7); ms: m/z 220 (M$^+$). Found: m/z 220.1103 (M$^+$). Calcd. for $C_{13}H_{16}O_3$: M, 220.1099.

Reactions of 3-Isopropyl-2-methoxytropone (**2a**) with Guanidines.

a) Reaction with Guanidine.

A solution of the methyl ether **2a** (178 mg, 1.0 mmole) and guanidine hydrochloride (191 mg, 2.0 mmoles) in sodium ethoxide solution, prepared from sodium (58 mg, 2.5 mmoles) and absolute ethanol (10 ml), was refluxed for 2 hours. After removal of the solvent, the residue was triturated with water, neutralized with 30% acetic acid, and extracted with chloroform. The evaporation residue from the extract was chromatographed on a Wakogel B-10 plate (30 x 30 cm) with ethyl acetate. The lower fraction gave 2-amino-4-isopropylcycloheptimidazole (**4a**), yield 16 mg (9%), yellow prisms (from ethanol), mp 180-182°; ir (chloroform): ν max 3435 cm^{-1} (NH); ^{1}H nmr (deuteriochloroform): δ 1.39 [6H, d, J = 7 Hz, 4-C(CH$_3$) x 2], 4.32 (1H, sept, J = 7 Hz, 4-CH), 6.75 (2H, br, NH$_2$), 7.3-8.3 (4H, m).

Anal. Calcd. for $C_{11}H_{13}N_3$: C, 70.56; H, 7.00; N, 22.44. Found: C, 70.31; H, 7.12; N, 22.41.

The upper fraction gave 2-ethoxy-3-isopropenyltropone (**5a**), yield 67 mg (34%), amber oil; ir (chloroform): ν max 1580 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 1.19 [6H, d, J = 7 Hz, 3-C(CH$_3$) x 2], 1.36 (3H, t, J = 7 Hz, OC-CH$_3$), 3.75 (1H, sept, J = 7 Hz, 3-CH), 4.15 (2H, q, J = 7 Hz, CH$_2$), 6.6-7.2 (4H, m). Found: m/z 192.1148 (M$^+$). Calcd. for $C_{12}H_{16}O_2$: M, 192.1151.

b) Reaction with 1-Methylguanidine.

A solution of the methyl ether **2a** (178 mg, 1.0 mmole) and 1-methylguanidine hydrochloride (220 mg, 2.0 mmoles) in the sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 2 hours and worked up, as described above, to give 2-ethoxy-3-isopropyltropone (**5a**), yield 76 mg (39%), and 4-isopropyl-2-methylaminocycloheptimidazole (**4b**), yield 8 mg (4%), yellow oil; ir (chloroform) ν max 3470 cm^{-1} (NH); ^1H nmr (deuteriochloroform): δ 1.39 [6H, d, J = 7 Hz, 4-C(CH_3) x 2], 3.27 (3H, d, J = 5 Hz, N-CH_3), 4.32 (1H, sept, J = 7 Hz, 4-CH), 6.77 (1H, br, NH), 7.3-7.9 (3H, m, H-5,6,7), 8.0-8.2 (1H, m, H-8). Found: m/z 201.1266 (M^+). Calcd. for $C_{12}H_{15}N_3$: M, 201.1267.

c) Reaction with 1,1-Dimethylguanidine.

A solution of the methyl ether **2a** (178 mg, 1.0 mmole) and 1,1-dimethylguanidine hydrochloride (248 mg, 2.0 mmoles) in sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 2 hours and worked up, as described above, to give 2-ethoxy-3-isopropyltropone (**5a**), yield 58 mg (29%), and 2-dimethylamino-4-isopropylcycloheptimidazole (**4c**), yield 17 mg (8%), yellow oil; ^1H nmr (deuteriochloroform): δ 1.38 [6H, d, J = 7 Hz, 4-C(CH_3) x 2], 3.40 (6H, s, N-CH_3 x 2), 4.37 (1H, sept, J = 7 Hz, 4-CH), 7.1-7.8 (3H, m, H-5,6,7), 7.9-8.1 (1H, m, H-8). Found: m/z 215.1436 (M^+). Calcd. for $C_{13}H_{17}N_3$: M, 215.1423.

Reactions of 7-Isopropyl-2-methoxytropone (**3a**) with Guanidines.

a) Reaction with Guanidine.

A solution of the methyl ether **3a** (178 mg, 1.0 mmole) and guanidine hydrochloride (192 mg, 2.0 mmoles) in sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 3 hours and worked up, as described above. The lower fraction in the preparative thin-layer chromatography gave 2-amino-4-isopropylcycloheptimidazole (**4a**), yield 90 mg (47%). The upper fraction gave 2-ethoxy-7-isopropyltropone (**6a**), yield 42 mg (21%), amber oil; ir (chloroform): ν max 1592 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 1.19 [6H, d, J = 7 Hz, 7-C(CH_3) x 2], 1.51 (3H, t, J = 7 Hz, OC-CH_3), 3.65 (1H, sept, J = 7 Hz, 7-CH), 4.21 (2H, q, J = 7 Hz, CH_2), 6.5-7.4 (4H, m). Found: m/z 192.1141 (M^+). Calcd. for $C_{12}H_{16}O_2$: M, 192.1150.

b) Reaction with 1-Methylguanidine.

A solution of the methyl ether **3a** (178 mg, 1.0 mmole) and 1-methylguanidine hydrochloride (220 mg, 2.0 mmoles) in sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 3 hours and worked up, as described above, to give 2-ethoxy-7-isopropyltropone (**6a**), yield 83 mg (41%), and 4-isopropyl-2-methylaminocycloheptimidazole (**4b**), yield 23 mg (11%).

c) Reaction with 1,1-Dimethylguanidine.

A solution of the methyl ether **3a** (178 mg, 1.0 mmole) and 1,1-dimethylguanidine hydrochloride (247 mg, 2.0 mmoles) in sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 3 hours and worked up, as described above, to give 2-ethoxy-7-isopropyltropone (**6a**), yield 107 mg (53%), and 2-dimethylamino-4-isopropylcycloheptimidazole (**4c**), yield 32 mg (14%).

Reactions of 3-Isopropenyl-2-methoxytropone (**2b**) with Guanidines.

a) Reaction with Guanidine.

A solution of the methyl ether **2b** (176 mg, 1.0 mmole) and guanidine hydrochloride (191 mg, 2.0 mmoles) in sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 2 hours and chromatographed, as described above. The lower fraction gave 2-amino-4-isopropenylcycloheptimidazole (**4d**), yield 9 mg (5%), yellow prisms (from ethanol), mp 210-211°; ir (chloroform): ν max 3442 cm^{-1} (NH); ^1H nmr (deuteriochloroform): δ 2.33 [3H, br s, 4-C(CH_3) x 2], 4.91 [1H, m, 4-C(=CH_E)], 5.3-5.5 [1H, m, 4-C(=CH_Z)], 6.92 (2H, br, NH_2), 7.4-8.2 (4H, m).

Anal. Calcd. for $C_{11}H_{11}N_3$: C, 71.33; H, 5.99; N, 22.69. Found: C, 71.09; H, 6.02; N, 22.68.

The upper fraction gave ethyl 2-isopropenylbenzoate (**7a**), yield 89 mg (47%), amber oil; ir (chloroform): ν max 1720 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 1.35 (3H, t, J = 7 Hz, OC-CH_3), 2.11 [3H, br s, 2-C(CH_3)], 4.38 (2H, q, J = 7 Hz, OCH_2), 4.91 [1H, m, 2-C(=CH_E)], 5.1-5.3 [1H, m, 2-C(=CH_Z)], 7.2-7.5 (3H, m, H-3,4,5), 7.8-8.0 (1H, m, H-6). Found: m/z 190.1003 (M^+). Calcd. for $C_{12}H_{14}O_2$: M, 190.0995.

b) Reaction with 1-Methylguanidine.

A solution of the methyl ether **2b** (176 mg, 1.0 mmole) and 1-methylguanidine hydrochloride (220 mg, 2.0 mmoles) in sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 2 hours and worked up, as described above, to give ethyl 2-isopropenylbenzoate (**7a**), yield 130 mg (67%).

c) Reaction with 1,1-Dimethylguanidine.

A solution of the methyl ether **2b** (175 mg, 1.0 mmole) and 1,1-dimethylguanidine hydrochloride (246 mg, 2.20 mmoles) in sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 2 hours and worked up, as described above, to give ethyl 2-isopropenylbenzoate (**7a**), yield 114 mg (57%).

Reaction of 7-Isopropenyl-2-methoxytropone (**3b**) with Guanidines.

a) Reaction with Guanidine.

A solution of the methyl ether **3b** (176 mg, 1.0 mmole) and guanidine hydrochloride (190 mg, 2.0 mmoles) in sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 2 hours and chromatographed, as described above. The lower fraction gave 2-amino-4-isopropenylcycloheptimidazole (**4a**), yield 87 mg (45%). The upper fraction gave 2-ethoxy-7-isopropenyltropone (**6b**), yield 36 mg (18%), pale yellow oil; ir (chloroform): ν max 1593 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 1.49 (3H, t, J = 7 Hz, OC-CH_3), 2.04 [3H, br s, 7-C(CH_3)], 4.42 (2H, q, J = 7 Hz, OCH_2), 5.03 [2H, m, 7-C(=CH_2)], 6.5-7.2 (3H, m), 7.2-7.5 (1H, m). Found: m/z 190.0998 (M^+). Calcd. for $C_{12}H_{14}O_2$: M, 190.0995.

b) Reaction with 1-Methylguanidine.

A solution of the methyl ether **3b** (176 mg, 1.0 mmole) and 1-methylguanidine hydrochloride (221 mg, 2.0 mmoles) in sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 2 hours and worked up, as described above, to give 2-ethoxy-7-isopropenyltropone (**6b**), yield 96 mg (50%), and 4-isopropenyl-2-methylaminocycloheptimidazole (**4e**), yield 39 mg (19%), yellow oil; ir (chloroform): ν max 3475 cm^{-1} (NH); ^1H nmr (deuteriochloroform): δ 2.34 [3H, br s, 4-C(CH_3)], 3.27 (3H, d, J = 5 Hz, N-CH_3), 5.25 [1H, m, 4-C(=CH_E)], 5.3-5.4 [1H, m, 4-C(=CH_Z)], 7.1 (1H, br, NH), 7.2-7.8 (3H, m, H-5,6,7), 7.9-8.2 (1H, m, H-8). Found: m/z 199.1108 (M^+). Calcd. for $C_{12}H_{13}N_3$: M, 199.1110.

c) Reaction with 1,1-Dimethylguanidine.

A solution of the methyl ether **3b** (176 mg, 1.0 mmole) and 1,1-dimethylguanidine hydrochloride (246 mg, 2.0 mmoles) in sodium ethoxide solution (2.5 mmoles/10 ml) was refluxed for 2 hours and worked up, as described above, to give 2-ethoxy-7-isopropenyltropone (**6b**), yield 117 mg (57%), and 2-dimethylamino-4-isopropenylcycloheptimidazole (**4f**), yield 69 mg (30%), yellow oil; ^{1}H nmr (deuteriochloroform): δ 2.39 [3H, br s, 4-C(CH_3)], 3.39 (6H, s, N-CH_3 x 2), 5.2-5.4 [2H, m, 4-C(=CH_2)], 7.0-7.8 (3H, m, H-5,6,7), 7.9-8.1 (1H, m, H-8). Found: m/z 213.1285 (M^+). Calcd. for $C_{13}H_{15}N_3$: M, 213.1267.

Reactions of 3-Acety-2-methoxytropone (**2c**) with Guanidines.

a) Reaction with 1-Methylguanidine.

A solution of the methyl ether **2c** (178 mg, 1.0 mmole) and 1-methylguanidine hydrochloride (220 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 2 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles). After removal of the solvent, the residue was triturated with water and extracted with chloroform. The evaporation residue from the extract was chromatographed on a Wakogel B-10 plate (30 x 30 cm) with ethyl acetate. The lower fraction gave 4-methyl-2-methylamino-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8b**), yield 66 mg (33%), yellow prisms (from benzene-hexane), mp 182-183°; ir (chloroform): ν max 3464 (NH), 1587 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 2.76 (3H, s, 4-CH_3), 3.12 (3H, d, J = 5 Hz, N-CH_3), 6.20 (1H, br s, NH), 6.2-7.7 (4H, m); ms: m/z (%) 201 (M^+, 100), 173 (M^+-CO, 22), 144 (40).

Anal. Calcd. for $C_{11}H_{11}N_3O$: C, 65.65; H, 5.51; N, 20.88. Found: C, 65.63; H, 5.68; N, 21.01.

The upper fraction gave 3-acetyl-2-ethoxytropone (**5b**), yield 84 mg (44%), pale yellow oil; ir (chloroform): ν max 1709 ($COCH_3$), 1584 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 1.31 (3H, t, J = 7 Hz, OC-CH_3), 2.49 (3H, s, $COCH_3$), 4.31 (2H, q, J = 7 Hz, CH_2), 6.7-7.3 (4H, m). Found: m/z 192.0791 (M^+). Calcd. for $C_{11}H_{12}O_3$: M, 192.0786.

b) Reaction with 1,1-Dimethylguanidine.

A solutilon of the methyl ether **2c** (178 mg, 1.0 mmole) and 1,1-dimethylguanidine hydrochloride (272 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 2 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above, to give 2-dimethylamino-4-methyl-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8c**), yield 125 mg (58%), yellow prisms (from benzene-hexane), mp 112-113°; ir (chloroform): ν max 1585 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 2.73 (3H, s, 4-CH_3), 3.33 (6H, s, N-CH_3 x 2), 6.3-7.6 (4H, m); ms: m/z 215 (M^+).

Anal. Calcd. for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found: C, 67.06; H, 5.98; N, 19.48.

The upper fraction gave ethyl 2-acetylbenzoate (**7b**), yield 38 mg (20%).

Reactions of 3-Acetyl-5-methyl-2-methoxytropone (**2d**) with Guanidines.

a) Reaction with Guanidine.

A solution of the methyl ether **2d** (192 mg, 1.0 mmole) and guanidine carbonate (180 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 2 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above, to give 2-amino-4,6-dimethyl-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8d**), yield 58 mg (29%), pale yellow micro-crystals (from benzene), mp 181-182°; ir (chloroform): ν max 3428 (NH), 1607 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 2.43 (3H, s, 6-CH_3), 2.63 (3H, s, 4-CH_3), 6.20 (2H, br s, NH_2), 7.28 (2H, br s, H-7,8), 7.57 (1H, br s, H-5); ms: m/z (%) 201 (M^+, 100), 173 (M^+-CO, 84).

Anal. Calcd. for $C_{11}H_{11}N_3O$: C, 65.65; H, 5.51; N, 20.88. Found: C, 65.37; H, 5.74; N, 20.71.

The upper fraction gave ethyl 2-acetyl-4-methylbenzoate (**7c**), yield 68 mg (33%), amber oil; ir (chloroform): ν max 1765 (COOR), 1704 cm^{-1} ($COCH_3$); ^{1}H nmr (deuteriochloroform): δ 1.13 (3H, t, J = 7 Hz, OC-CH_3), 1.80 (3H, s, 4-CH_3), 2.51 (3H, s, $COCH_3$), 4.34 (2H, q, J = 7 Hz, CH_2), 7.0-7.9 (3H, m). Found: m/z 206.0935 (M^+). Calcd. for $C_{12}H_{14}O_3$: M, 206.0944.

b) Reaction with 1-Methylguanidine.

A solution of the methyl ether **2d** (192 mg, 1.0 mmoles) and 1-methylguanidine hydrochloride (220 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 2 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above, to give 4,6-dimethyl-2-methylamino-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8e**), yield 37 mg (17%), yellow prisms (from benzene), mp 145-146°; ir (chloroform): ν max 3468 (NH), 1586 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 2.32 (3H, s, 6-CH_3), 2.75 (3H, s, 4-CH_3), 3.11 (3H, d, J = 5 Hz, N-CH_3), 5.8 (1H, br, NH), 6.7-7.5 (3H, m); ms: m/z (%) 215 (M^+, 100), 187 (M^+-CO, 26), 158 (43).

Anal. Calcd. for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found: C, 67.12; H, 5.94; N, 19.71.

The upper fraction gave ethyl 2-acetyl-4-methylbenzoate (**7c**), yield 130 mg (63%).

c) Reaction with 1,1-Dimethylguanidine.

A solution of the methyl ether **2d** (192 mg, 1.0 mmole) and 1,1-dimethylguanidine hydrochloride (272 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 2 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above, to give 4,6-dimethyl-2-dimethylamino-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8f**), yield 71 mg (31%), yellow micro-crystals (from benzene), mp 105-106°; ir (chloroform): ν max 1583 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 2.32 (3H, s, 6-CH_3), 2.74 (3H, s, 4-CH_3), 3.33 (6H, s, N-CH_3 x 2), 6.8-7.0 (1H, m, H-5), 7.29 (2H, br s, H-7,8); ms: m/z (%) 229 (M^+, 100), 214 (M^+-CH_3), 200 (44).

Anal. Calcd. for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found: C, 67.91; H, 6.36; N, 18.29.

The upper fraction gave ethyl 2-acetyl-4-methylbenzoate (**7c**), yield 52 mg (25%).

Reactions of 3-Acetyl-5-isopropyl-2-methoxytropone (**2e**) with Guanidines.

a) Reaction with Guanidine.

A solution of the methyl ether **2e** (220 mg, 1.0 mmole) and guanidine carbonate (180 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 2 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above, to give 2-amino-6-isopropyl-4-methyl-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8g**), yield 85 mg (37%), yellow oil; ir (chloroform): ν max 3428 (NH), 1605 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ 1.26 [6H, d, J = 7 Hz, 6-C(CH_3) x 2], 2.70 (3H, s, 4-CH_3), 4.96 (1H, sept, J = 7 Hz, 6-CH), 6.22 (2H, br, NH_2), 6.8-7.9 (3H, m); ms: m/z (%) 229 (M^+, 100), 201 (M^+-CO, 22). Found: m/z 229.1193

(M^+). Calcd. for $C_{13}H_{15}N_3O$: M, 229.1216.

Anal. Calcd. for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found: C, 67.86; H, 6.65; N, 18.40.

b) Reaction with 1-Methylguanidine.

A solution of the methyl ether **2e** (220 mg, 1.0 mmole) and 1-methylguanidine hydrochloride (220 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 2 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above, to give 6-isopropyl-4-methyl-2-methylamino-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8h**), yield 71 mg (29%), yellow oil; ir (chloroform): ν 3460 (NH), 1583 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 1.24 [6H, d, J = 7 Hz, 6-C(CH_3) x 2], 2.75 (3H, s, 4-CH_3), 3.07 (3H, d, J = 5 Hz, N-CH_3), 4.95 (1H, sept, J = 7 Hz, 6-CH), 6.0 (1H, br s, NH), 6.8-7.1 (1H, m, H-5), 7.26 (2H, br s, H-7,8); ms: m/z (%) 243 (M^+, 100), 215 (M^+-CO, 36). Found: m/z 243.1357 (M^+). Calcd. for $C_{14}H_{17}N_3O$: M, 243.1372.

c) Reaction with 1,1-Dimethylguanidine.

A solution of the methyl ether **2e** (220 mg, 1.0 mmole) and 1,1-dimethylguanidine hydrochloride (272 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 2 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above to give 2-dimethylamino-6-isopropyl-4-methyl-9*H*-cyclohepta[*d*]pyrimidin-9-one (**8i**), yield 113 mg (44%), yellow oil; ir (chloroform): ν max 1581 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 1.24 [6H, d, J = 7 Hz, 6-C(CH_3) x 2], 2.75 (3H, s, 4-CH_3), 3.32 (6H, s, N-CH_3 x 2), 4.96 (1H, sept, J = 7 Hz, 6-CH), 6.8-7.4 (3H, m); ms: m/z (%) 257 (M^+, 100), 229 (M^+-CO, 41). Found: m/z 257.1551 (M^+). Calcd. for $C_{15}H_{19}N_3O$: M, 257.1529.

Reactions of 7-Acetyl-2-methoxytropone (**3c**) with Guanidines.

a) Reaction with 1-Methylguanidine.

A solution of the methyl ether **3c** (178 mg, 1.0 mmole) and 1-methylguanidine hydrochloride (220 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 3 hours and worked up, as described above, to give 4-acetyl-2-methylaminocycloheptimidazole (**4h**), yield 183 mg (91%), yellow micro-crystals (from benzene-hexane), mp 173-174; ir (chloroform): ν max 3688 (NH), 1687 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.93 (3H, s, $COCH_3$), 3.32 (3H, d, J = 5 Hz, N-CH_3), 6.8 (1H, br s, NH), 7.1-8.3 (4H, m); ms: m/z (%) 201 (M^+, 100), 186 (M^+-CH_3, 24), 173 (43), 159 (38).

Anal. Calcd. for $C_{11}H_{11}N_3O$: C, 65.66; H, 5.51; N, 20.88. Found: C, 65.71; H, 5.48; N, 20.62.

b) Reaction with 1,1-Dimethylguanidine.

A solution of the methyl ether **3c** (178 mg, 1.0 mmole) and 1,1-dimethylguanidine hydrochloride (272 mg, 2.0 moles) in absolute ethanol (20 ml) was refluxed for 3 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above, to give 4-acetyl-2-dimethylaminocycloheptimidazole (**4i**), yield 204 mg (95%), yellow needles (from benzene-hexane), mp 115-116°; ir (chloroform): ν max 1682 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.94 (3H, s, $COCH_3$), 3.39 (6H, s, N-CH_3 x 2), 7.0-8.1 (4H, m); ms: m/z (%) 215 (M^+, 100), 200 (M^+-CH_3, 30), 187 (38).

Anal. Calcd. for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found: C, 66.81; H, 5.97; N, 19.26.

Reactions of 7-Acetyl-5-methyl-2-methoxytropone (**3d**) with Guanidines.

a) Reaction with Guanidine.

A solution of the methyl ether **3d** (192 mg, 1.0 mmole) and guanidine carbonate (180 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 3 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above. The third fraction gave 4-acetyl-2-amino-6-methylcycloheptimidazole (**4j**), yield 143 mg (71%), yellow needles (from benzene-hexane), mp 254-255°; ir (chloroform): ν max 3436 (NH), 1693 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.68 (3H, s, 6-CH_3), 2.88 (3H, s, $COCH_3$), 5.90 (2H, br s, NH_2), 7.64 (2H, br s, H-7,8), 7.95 (1H, s, H-5); ms: m/z (%) 201 (M^+, 100), 186 (M^+-CH_3, 31), 173 (27).

Anal. Calcd. for $C_{11}H_{11}N_3O$: C, 65.65; H, 5.51; N, 20.88. Found: C, 65.66; H, 5.41; N, 20.61.

The first fraction gave ethyl 2-acetyl-4-methylbenzoate (**7c**), yield 14 mg (7%). The second fraction gave 7-acetyl-2-ethoxytropone (**6c**, yield 33 mg (16%).

b) Reaction with 1-Methylguanidine.

A solution of the methyl ether **3d** (192 mg, 1.0 mmole) and 1-methylguanidine hydrochloride (220 mg, 2.0 mmoles) in absolute ethanol (20 ml) was refluxed for 3 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above. The third fraction gave 4-acetyl-6-methyl-2-methylaminocycloheptimidazole (**4k**), yield 60 mg (28%), yellowish orange prisms (from benzene-hexane), mp 228-229°; ir (chloroform): ν max 3684 (NH), 1700 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.66 (3H, s, 6-CH_3), 2.93 (3H, s, $COCH_3$), 3.29 (3H, d, J = 5 Hz, N-CH_3), 6.75 (1H, br s, NH), 7.5-8.2 (3H, m); ms: m/z (%) 215 (M^+, 100), 200 (M^+-CH_3, 38), 187 (26).

Anal. Calcd. for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found: C, 67.05; H, 6.22; N, 19.24.

The first fraction gave ethyl 2-acetyl-4-methylbenzoate (**7c**), yield 10 mg (5%). The second fraction gave 7-acetyl-2-ethoxytropone (**6c**), yield 66 mg (32%).

c) Reaction with 1,1-Dimethylguanidine.

A solution of the methyl ether **3d** (192 mg, 1.0 mmole) and 1,1-dimethylguanidine hydrochloride (272 mg, 2.0 mmoles) in the absolute ethanol (20 ml) was refluxed for 3 hours in the presence of potassium carbonate (138 mg, 2.0 mmoles) and worked up, as described above, to give 4-acetyl-2-dimethylamino-6-methylcycloheptimidazole (**4l**), yield 200 mg (87%), yellow needles (from benzene-hexane), mp 97-98°; ir (chloroform): ν max 1684 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.57 (3H, s, 6-CH_3), 2.95 (3H, s, $COCH_3$), 3.38 (6H, s, N-CH_3 x 2), 7.51 (1H, d, J = 11 Hz, H-7), 7.53 (1H, d, J = 11 Hz, H-8), 7.7-8.2 (1H, m, H-5); ms: m/z (%) 229 (M^+, 100), 214 (M^+-CH_3, 79), 200 (64).

Anal. Calcd. for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found: C, 67.93; H, 6.59; N, 18.12.

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