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Reactions of 3-(2-Methyl-1,3-dioxolan-2-yl)tropolone Methyl Ethers with Hydrazines, Thiourea, Guanidine, and Amidines

Kimiaki IMAFUKU,* Yosuke KIKUCHI,† and Bing-Zhu YIN††
Department of Chemistry, Faculty of Science, Kumamoto University, Kurokami, Kumamoto 860
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3-(2-Methyl-1,3-dioxolan-2-yl)tropolone, prepared from 3-acetyltropolone, was methylated with diazomethane to afford 2-methoxy-3-(2-methyl-1,3-dioxolan-2-yl)tropone (**3a**) and 2-methoxy-7-(2-methyl-1,3-dioxolan-2-yl)tropone (**3b**). The methyl ether **3a** reacted with hydrazine to afford 2-hydrazono-3-(2-methyl-1,3-dioxolan-2-yl)-3,5-cycloheptadien-1-one and 3-methyl-1,8-dihydrocycloheptapyrazol-8-one. The reaction with methylhydrazine afforded 3-(2-methyl-1,3-dioxolan-2-yl)-2-methylhydrazono-3,5-cycloheptadien-1-one and 1,3- and 2,3-dimethyl-dihydrocycloheptapyrazol-8-ones. Another methyl ether **3b** reacted with hydrazine to afford 2-hydrazino-7-(2-methyl-1,3-dioxolan-2-yl)tropone, while the reaction with methylhydrazine gave 2-(2-methyl-1,3-dioxolan-2-yl)-7-(2-methylhydrazino)tropone, 2-(2-methyl-1,3-dioxolan-2-yl)-7-(1-methylhydrazino)tropone, and 1,3-dimethyl-8-methylhydrazono-1,8-dihydrocycloheptapyrazole. On the other hand, the methyl ether **3a** reacted with guanidine, acetamidine, and benzamidine to give 4-(2-methyl-1,3-dioxolan-2-yl)-2-amino-, 2-methyl-, and 2-phenylcycloheptimidazole, respectively. The reaction of the methyl ether **3b** also gave the same products. The reaction of **3b** with thiourea afforded 2-mercapto-4-(2-methyl-1,3-dioxolan-2-yl)cycloheptimidazole but **3a** resulted in the rearrangement to ethyl 2-(2-methyl-1,3-dioxolan-2-yl)benzoate.

We found that 3-acetyltropolone is useful as starting material for the synthesis of heterocycle-fused troponoid compounds, because it has β-diketone structure.[1] On the other hand, the acetyl group not only enhances the reactivity of the tropolone nucleus but also becomes the reaction center for nucleophilic reactions. For example, 3-acetyltropolone and its methyl ether reacted with hydrazines to give 1,8-dihydrocycloheptapyrazol-8-one derivatives.[2-4] We also reported reactions of 3-acetyltropolone methyl ethers, 2-acetyl-7-methoxytropone and 3-acetyl-2-methoxytropone, with guanidine and amidines.[5] In these reactions, we found that the former produced the usual cycloheptimidazole derivatives but the latter produced 9*H*-cyclohepta[*d*]pyrimidine derivatives.

In the present work, 3-acetyltropolone (**1**) reacted with ethylene glycol in the presence of *p*-toluenesulfonic acid to afford 3-(2-methyl-1,3-dioxolan-2-yl)tropolone (**2**), which was methylated with diazomethane to give two isomeric methyl ethers, 2-methoxy-3-(2-methyl-1,3-dioxolan-2-yl)tropone (**3a**) and 2-methoxy-7-(2-methyl-1,3-dioxolan-2-yl)tropone (**3b**). All of the other isomers, 2-methoxy-4-, -5-, and -6-(2-methyl-1,3-dioxolan-2-yl)tropones, have been reported.[6]

Furthermore, we describe reactions of 2-methoxy-3-(2-methyl-1,3-dioxolan-2-yl)tropone and 2-methoxy-7-(2-methyl-1,3-dioxolan-2-yl)tropone (**3a** and **3b**) with hydrazines, urea, thiourea, guanidine, and amidines.

Results and Discussion

Synthesis of 3-(2-Methyl-1,3-dioxolan-2-yl)tropolone (2) and Its Methyl Ethers (3a and 3b). 3-Acetyltropolone (**1**)[2] reacted with ethylene glycol in dry benzene in the presence of *p*-toluenesulfonic acid to give 3-(2-methyl-1,3-dioxolan-2-yl)tropolone (**2**) as colorless prisms. Ketalization was confirmed by spectral data, such as a disappearance of the acetyl carbonyl absorption in the IR spectrum and the appearance of an ethylenedioxy resonance as an A_2B_2 pattern in the ^{1}H NMR spectrum.

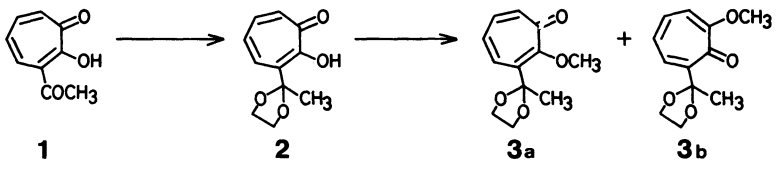
Methylation of **2** with diazomethane gave two isomeric methyl ethers as crystals which were determined to be 2-methoxy-3-(2-methyl-1,3-dioxolan-2-yl)tropone (**3a**) (mp 80—81 °C) and 2-methoxy-7-(2-methyl-1,3-dioxolan-2-yl)tropone (**3b**) (mp 121—122 °C) by their spectral data.

Reactions with Hydrazine. It is well known that reactive troponoids, such as 2-methoxy-, 2-tosyloxy-, and 2-chlorotropones, react with hydrazine to afford 2-hydrazinotropones.[7] Previously, it was reported that 2-methoxy-4-, -5-, and -6-(2-methyl-1,3-dioxolan-2-yl)tropones reacted with hydrazine to afford, respectively, 2-hydrazino-4-, -5-, and -6-(2-methyl-1,3-dioxolan-2-yl)tropones.[6]

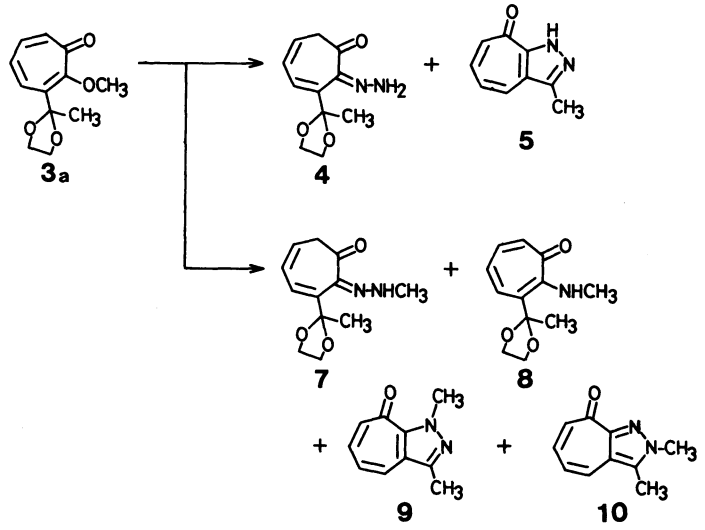
A solution of 2-methoxy-3-(2-methyl-1,3-dioxolan-2-yl)tropone (**3a**) and hydrazine hydrate in methanol was refluxed for 1 h to afford 2-hydrazono-3-(2-methyl-1,3-dioxolan-2-yl)-3,5-cycloheptadien-1-one (**4**) and 3-methyl-1,8-dihydrocycloheptapyrazol-8-one (**5**)[2] in 19 and 36% yields, respectively. The former is a tautomer of 2-hydrazino-3-(2-methyl-1,3-dioxolan-2-yl)tropone. Its structure was determined by its spectral data. The ^{1}H NMR spectrum shows peaks at δ 1.84 (3H, s) for CH_3, 3.01 (2H, d, J=6 Hz) for 7-CH_2, 3.5—4.2 (4H, m) for OCH_2CH_2O, 5.71 (1H, dt, J=9.5 and

† Present address: Fujirebio Inc., Komiya-cho, Hachioji, Tokyo 192.

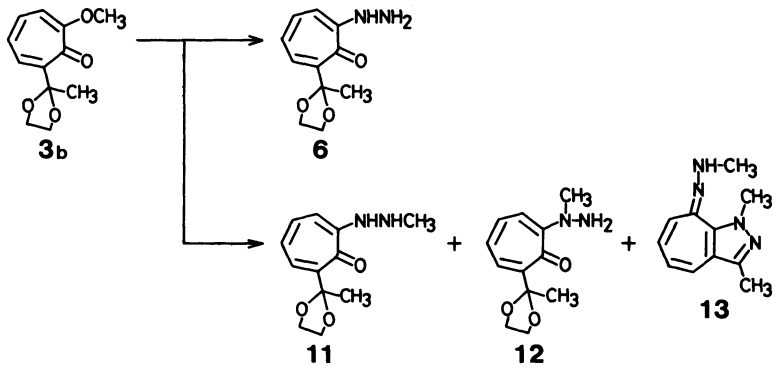
†† Permanent address: Department of Chemistry, Yanbian University, Yanji, Jilin-sheng, China.



Scheme 1.



Scheme 2.



Scheme 3.

6 Hz) for H-6, 6.21 (1H, dd, J=9.5 and 5.5 Hz) for H-5, 6.67 (1H, d, J=5.5 Hz) for H-4, and 10.5 (2H, br) for NH_2. The UV spectrum is different from those of 2-hydrazino-4-, -5-, and -6-(2-methyl-1,3-dioxolan-2-yl)tropones.[6] It is thought that the tropone ring cannot maintain a planar hydrazino-substituted structure by steric hindrance of the vicinal bulky 2-methyl-1,3-dioxolan-2-yl group at the 3-position and, thus, tautomerized to a non-planar hydrazono-substituted structure.

The 2-methyl-1,3-dioxolan-2-yl group in compound **4** was hydrolyzed with 2 M (1 M=1 mol dm^{-3}) hydrochloric acid and did not give 3-acetyl-2-hydrazinotropone but, rather, its cyclized product **5** in 89% yield.

Another methyl ether **3b** in methanol was refluxed for 6 h with hydrazine hydrate to give 2-hydrazino-7-(2-methyl-1,3-dioxolan-2-yl)tropone (**6**) in 74% yield; it was determined by its elemental analysis and spectral data. The UV spectrum is similar to those of its isomers, 2-hydrazino-4-, -5-, and -6-(2-methyl-1,3-dioxolan-2-yl)tropones. Thus, all of the isomers have been obtained except for 2-hydrazino-3-(2-methyl-1,3-dioxolan-2-yl)tropone, which exsists in tautomeric form, 2-hydrazono-3-(2-methyl-1,3-dioxolan-2-yl)-3,5-cycloheptadien-1-one (**4**).

Reactions with Methylhydrazine. A solution of the methyl ether **3a** and methylhydrazine in methanol was refluxed for 8 h to afford 3-(2-methyl-1,3-dioxolan-2-yl)-2-methylhydrazono-3,5-cycloheptadien-1-

one (**7**), 2-methylamino-3-(2-methyl-1,3-dioxolan-2-yl)tropone (**8**), 1,3-dimethyl-1,8-dihydrocycloheptapyrazol-8-one (**9**)[3] and 2,3-dimethyl-2,8-dihydrocycloheptapyrazol-8-one (**10**)[3] in 7, 9, 3, and 13% yields, respectively. Product **7** was isolated as a tautomer of 3-(2-methyl-1,3-dioxolan-2-yl)-2-(2-methylhydrazino)tropone. Its structure was determined by its spectral data. The UV spectrum is similar to that of compound **4**. The ^{1}H NMR spectrum also shows a similar pattern. The methylene protons at the 7-position was observed at δ 2.91 as a doublet peak (J=7 Hz). Compound **7** was heated with 2 M hydrochloric acid on a water bath to afford the cyclized product **10** in 91% yield. Compound **8** was also confirmed spectroscopically. Methyl ether **3a** reacted with methylamine to give the same product **8** in 10% yield.

A mixture of methyl ether **3b** and methylhydrazine in methanol was refluxed for 24 h to afford 2-(2-methyl-1,3-dioxolan-2-yl)-7-(2-methylhydrazino)tropone (**11**), 2-(2-methyl-1,3-dioxolan-2-yl)-7-(1-methylhydrazino)tropone (**12**), and 1,3-dimethyl-8-methylhydrazono-1,8-dihydrocycloheptapyrazole (**13**)[3] in 31, 29, and 8% yields, respectively. Compound **11** was determined by its spectral data. The UV spectrum is similar to that of compound **6**. The structure of the compound **12** was also confirmed by its spectral data. The ^{1}H NMR spectrum shows peaks at δ 1.90 (3H, s) for C-CH_3, 3.32 (3H, s) for N-CH_3, 3.5—4.2 (4H, m) for OCH_2CH_2O, 4.2 (2H, br) for NH_2, 6.2—7.2 (3H, m) for H-4,5,6, and 7.43 (1H, dd, J=9 and 2 Hz) for H-3. Previously, we reported that similar-type compounds could be obtained by the reactions of 2-tosyloxy- and 2-chlorotropones with methylhydrazine.[8]

Reactions with Urea and Thiourea. It is well known that 2-methoxytropones react with guanidine and thiourea to afford cycloheptimidazole derivatives.[9,10] However, reactions with urea do not give cycloheptimidazole, except for the case of 4-(*p*-nitrostyryl)tropolone methyl ethers.[11] Reactions of both methyl ethers of 3-acetyltropolone with urea gave 2-acetylbenzoic acid as a rearrangement product.

A mixture of the methyl ether **3a** and urea in absolute ethanol was refluxed for 1 h in the presence of sodium ethoxide to afford the rearrangement product, ethyl 2-(2-methyl-1,3-dioxolan-2-yl)benzoate (**14**), in 83% yield. Its IR spectrum shows an ester carbonyl absorption at 1720 cm^{-1}. The ethyl group in the ester and the ethylenedioxy group were confirmed by the ^{1}H NMR spectrum.

The reaction of **3b** with urea in the presence of sodium ethoxide gave 3-(2-methyl-1,3-dioxolan-2-yl)tropolone (**2**) as a hydrolysis product and 2-ethoxy-7-(2-methyl-1,3-dioxolan-2-yl)tropone (**15**) as the alkoxy-exchanged product in 45 and 47% yields, respectively. For the latter, the introduction of an ethoxyl group into the 2-position was confirmed by the ^{1}H NMR spectrum. The UV spectrum is very similar to that of the methyl ether **3b**.

The methyl ether **3a** was heated in the presence of sodium ethoxide to give **14** in 82% yield. In a similar manner, **3b** gave **2** and **15** in 22 and 61% yields, respectively. The use of potassium hydroxide instead of sodium ethoxide gave also similar results. Namely, **3a** gave **14** in 72% yield, while **3b** gave **2** and **15** in 21 and 44% yields, respectively. Thus, these results show that urea does not participate in the reactions. This type of rearrangement with alkali or alkoxide is well known.[12,13]

A solution of **3a** and thiourea was refluxed for 2 h in the presence of sodium ethoxide gave a rearrangement product **14** in 80% yield. On the other hand, the

Table 1. Reactions of 3-(2-Methyl-1,3-dioxolan-2-yl)tropolone Methyl Ethers (**3a** and **3b**)

Substrate	Reagent	Base	Reaction time / h	Product/Yield/%			
3a	NH_2NH_2[a]	—	1	**4** (19)	**5** (36)		
3b	NH_2NH_2[a]	—	6	**6** (74)			
3a	CH_3NHNH_2	—	8	**7** (7)	**8** (9)	**9** (3)	**10** (13)
3b	CH_3NHNH_2	—	24	**11** (31)	**12** (29)	**13** (8)	
3a	$(H_2N)_2C{=}O$	NaOEt	1		**14** (83)		
3b	$(H_2N)_2C{=}O$	NaOEt	0.5		**15** (47)	**2** (45)	
3a	$(H_2N)_2C{=}S$	NaOEt	1		**14** (80)		
3b	$(H_2N)_2C{=}S$	NaOEt	2	**16** (81)			
3a	$(H_2N)_2C{=}NH$[b]	KOH	2	**17** (5)	**14** (64)		
3a	$(H_2N)_2C{=}NH$[c]	—	24	**17** (21)	**14** (37)		
3b	$(H_2N)_2C{=}NH$[b]	KOH	2	**17** (62)	**15** (21)		
3b	$(H_2N)_2C{=}NH$[c]	—	24	**17** (74)			
3a	$CH_3C(=NH)NH_2$[b]	NaOEt	2	**18** (4)	**14** (78)		
3b	$CH_3C(=NH)NH_2$[b]	NaOEt	3	**18** (30)	**15** (11)		
3a	$PhC(=NH)NH_2$[b]	NaOEt	2	**19** (14)	**14** (45)		
3b	$PhC(=NH)NH_2$[b]	NaOEt	8	**19** (69)	**15** (4)		

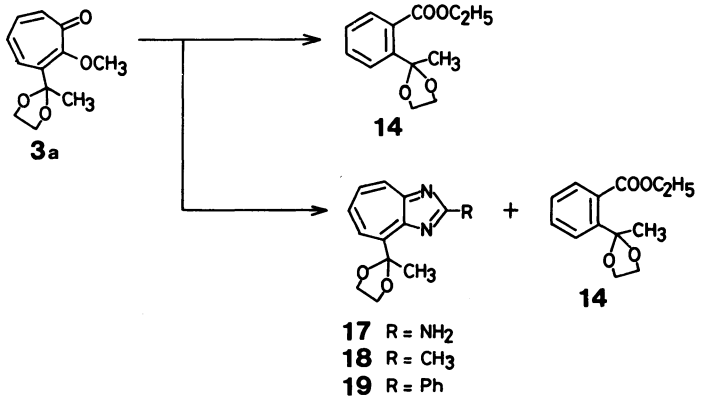
a) Hydrate. b) Hydrochloride. c) Carbonate.

reaction of **3b** afforded 2-mercapto-4-(2-methyl-1,3-dioxolan-2-yl)cycloheptimidazole (**16**) as reddish-orange prisms in 81% yield. Its UV spectrum [235 (log ε 4.26), 256 (4.53), 313 (3.88), and 450 nm (4.26)] is very similar to those of isomers, 5-(2-methyl-1,3-dioxolan-2-yl)- [227 (log ε 4.26), 253 (4.55), 310 (3.78), and 440 nm (4.23)] and 6-(2-methyl-1,3-dioxolan-2-yl)-2-mercaptocycloheptimidazole [230 (log ε 4.64), 305 (3.84), 440 nm (4.37)].[14]

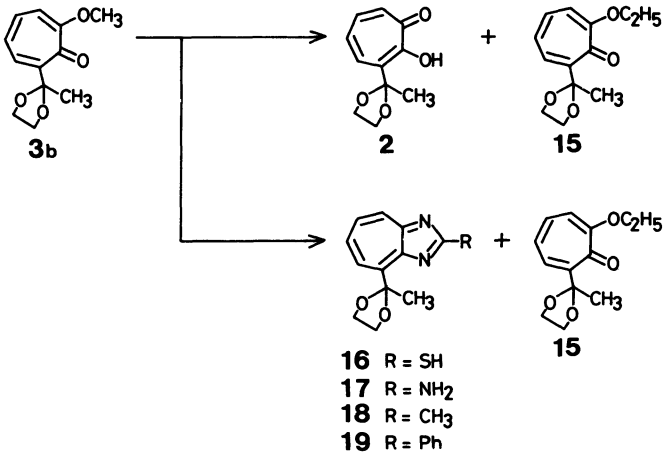
Reactions with Guanidine. A mixture of the methyl ether **3a** and guanidine hydrochloride in absolute ethanol was refluxed for 2 h in the presence of potassium hydroxide to give 2-amino-4-(2-methyl-1,3-dioxolan-2-yl)cycloheptimidazole (**17**) as yellow prisms in 5% yield, in addition to the rearrangement product **14** in 64% yield. The UV spectrum of the former is very similar to those of isomeric 2-amino-5- and -6-(2-methyl-1,3-dioxolan-2-yl)cycloheptimidazoles.[14] The ^{1}H NMR spectrum shows peaks at δ 2.07 (3H, s) for CH_3, 3.7—4.3 (4H, m) for OCH_2CH_2O, 7.2—7.8 (2H, m) for H-6 and -7, 7.60 (2H, br) for NH_2, 7.97 (1H, dm, J=9 Hz) for H-5, and 8.30 (1H, dd, J=10 and 2.5 Hz) for H-8. On the other hand, the reaction of **3a** with guanidine carbonate improved the yield of **17** to 21%. The cycloheptimidazole **17** was hydrolyzed to afford 4-acetyl-2-aminocycloheptimidazole (**20**)[5] in 83% yield.

The reaction of **3b** with guanidine hydrochloride gave cycloheptimidazole **17** and the alkoxy-exchanged product **15** in 62 and 21% yields, respectively.

Reactions with Amidines. A mixture of methyl ether **3a** and acetamidine hydrochloride in absolute ethanol was refluxed for 2 h in the presence of sodium ethoxide to afford 2-methyl-4-(2-methyl-1,3-dioxolan-2-yl)cycloheptimidazole (**18**) as yellow prisms and the rearrangement product **14** in 4 and 78% yields, respectively. The ^{1}H NMR spectrum of the former shows two singlet peaks at δ 2.44 for the 2-CH_3 and 2.95 for the acetal CH_3 and three multiplet peaks at δ 3.7—4.4 for the OCH_2CH_2O, 7.75—8.15 for H-6 and -7, and 8.3—8.8 for H-5 and -8 protons. In the UV spectrum, four absorption bands were observed at 228 (log ε 4.42), 260 (4.62), 323 (4.01), and 399 nm (3.14). The reaction of the methyl ether **3b** with acetamidine afforded the same cycloheptimidazole **18** and the alkoxy-exchanged product **15** in 30 and 11% yields, respectively. The cycloheptimidazole **18** was decomposed by heating with dilute hydrochloric acid and



Scheme 4.



Scheme 5.

did not give the hydrolysis product, 4-acetyl-2-methylcycloheptimidazole.

With benzamidine, the reaction of **3a** gave 4-(2-methyl-1,3-dioxolan-2-yl)-2-phenylcycloheptimidazole (**19**) as yellow needles and the rearrangement product **14** in 14 and 45% yields, respectively. The UV spectrum of the former exhibits the absorption bands at 259 (log ε 4.53), 277 sh (4.46), 356 sh (4.39), 366 (4.40), and 415 nm sh (3.25). Compound **19** was hydrolyzed with dilute hydrochloric acid to afford 4-acetyl-2-phenylcycloheptimidazole (**21**)[5] in 65% yield.

Methyl ether **3b** also reacted with benzamidine to give the cycloheptimidazole **19** and the alkoxy-exchanged product **15** in 69 and 4% yields, respectively.

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, and the UV spectra on a Hitachi EPS-3T spectrophotometer. The ^{1}H NMR spectra were recorded with a Hitachi-Perkin-Elmer R-24 spectrometer (60 MHz). The high-resolution mass spectra were obtained with a JEOL DX-300 apparatus.

3-(2-Methyl-1,3-dioxolan-2-yl)tropolone (2). A mixture of 3-acetyltropolone (**1**) (3.76 g, 20 mmol) and ethylene glycol (40 ml) in dry benzene (120 ml) was refluxed under stirring in the presence of *p*-toluenesulfonic acid (0.4 g). As water produced in the reaction was removed by azeotropic distillation with benzene, dry benzene (1000 ml) was gradually added into the reaction mixture. After refluxing for 10 h, the reaction mixture was diluted with water and extracted with benzene. The benzene extract was washed with water. The evaporation residue from the extract yielded 3-(2-methyl-1,3-dioxolan-2-yl)tropolone (**2**) (3.4 g, 71%) as colorless prisms (from benzene–hexane): Mp 86—87 °C; IR ($CHCl_3$) 1600 cm^{-1} (C=O); UV (CH_3OH) 247 (log ε 4.38), 253 sh (4.30), 310 sh (3.78), 324 (3.88), 362 (3.84), 376 (3.82), 404 nm sh (3.00); ^{1}H NMR ($CDCl_3$) δ=1.85 (3H, s, CH_3), 3.7—4.3 (4H, m, OCH_2CH_2O), 6.8—7.5 (3H, m), 8.00 (1H, dm, J=9 Hz, H-7), 9.50 (1H, br, OH). Found: C, 63.61; H, 5.84%. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81%.

Methylation of 3-(2-Methyl-1,3-dixolan-2-yl)tropolone (2). To a solution of **2** (5.2 g, 25 mmol) in chloroform (50 ml), an ethereal solution of diazomethane was added dropwise until the resulting mixture gave no colorlation with an iron(III) chloride solution. After removing the solvent, the residue was chromatographed on a Wakogel C-100 column (600 g) using ethyl acetate as an eluant. The evaporation residue from the former fractions was twice rechromatographed on four Wakogel B-10 plates (30×30 cm) with chloroform to give 2-methoxy-3-(2-methyl-1,3-dioxolan-2-yl)tropone (**3a**) (1.9 g, 34%) as pale yellow crystals (from benzene–hexane): Mp 80—81 °C; IR ($CHCl_3$) 1580 cm^{-1} (C=O); UV (CH_3OH) 239 (log ε 4.21), 330 nm (3.82); ^{1}H NMR ($CDCl_3$) δ=1.71 (3H, s, CH_3), 3.75—4.1 (4H, m, OCH_2CH_2O), 3.89 (3H, s, OCH_3), 6.6—7.3 (3H, m), 7.50 (1H, dm, J=10 Hz, H-7). Found: C, 64.75; H, 6.53%. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.53%. The evaporation residue from the latter fractions gave 2-methoxy-7-(2-methyl-1,3-dioxolan-2-yl)tropone (**3b**) (2.9 g, 52%) as colorless prisms (from benzene–hexane): Mp 121—122 °C; IR ($CHCl_3$) 1600 cm^{-1} (C=O); UV (CH_3OH) 243 (log ε 4.18), 308 sh (3.70), 322 (3.74), 345 sh (3.69), 355 nm (3.68); ^{1}H NMR ($CDCl_3$) δ=1.88 (3H, s, CH_3), 3.8—4.1 (4H, m, OCH_2CH_2O), 3.88 (3H, s, OCH_3), 6.4—7.45 (3H, m), 7.75 (1H, d, J=10 Hz, H-3). Found: C, 65.05; H, 6.30%. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35%.

General Procedure for the Reactions of the Methyl Ethers (3a and 3b) with Hydrazines. A solution of the methyl ether **3a** or **3b** (444 mg, 2 mmol) and the reagent (4 mmol) in methanol (20 ml) was refluxed. After removing the solvent, the residue was triturated with water and extracted with chloroform. The products were separated by chromatography on Wakogel B-10 plates (30×30 cm) with ethyl acetate. These results are summarized in Table 1.

2-Hydrazono-3-(2-methyl-1,3-dioxolan-2-yl)-3,5-cycloheptadien-1-one (4): Yellow crystals (from benzene–hexane); mp 120 °C (decomp); IR ($CHCl_3$) 3440 (NH), 3370 (NH), 1600 cm^{-1} (C=O); UV (CH_3OH) 281 (log ε 3.65), 335 nm (3.72); ^{1}H NMR ($CDCl_3$) δ=1.84 (3H, s, CH_3), 3.01 (2H, d, J=6 Hz, 7-CH_2), 3.5—4.2 (4H, m, OCH_2CH_2O), 5.71 (1H, dt, J=9.5, 6 Hz, H-6), 6.21 (1H, dd, J=9.5, 5.5 Hz, H-5), 6.67 (1H, d, J=5.5 Hz, H-4), 10.5 (2H, br, NH_2). Found: m/z 222.0971. Calcd for $C_{11}H_{14}N_2O_3$: M, 222.1004.

3-Methyl-1,8-dihydrocycloheptapyrazol-8-one (5): Orange plates; mp 183—184 °C (lit,[2] 183—184 °C).

2-Hydrazino-7-(2-methyl-1,3-dioxolan-2-yl)tropone (6): Orange needles (from benzene–hexane); mp 161 °C (decomp); IR ($CHCl_3$) 3300 (NH), 3240 (NH), 1600 cm^{-1} (C=O); UV (CH_3OH) 232 (log ε 4.39), 343 (4.11), 410 nm (4.09); ^{1}H NMR ($CDCl_3$) δ=1.90 (3H, s, CH_3), 3.5—4.5 (4H, m, OCH_2CH_2O), 6.60 (1H, ddd, J=12, 9, 3 Hz, H-4), 7.0—7.4 (2H, m, H-5,6), 7.81 (1H, d, J=9 Hz, H-3), 8.8 (1H, br, NH). Found: C, 59.43; H, 6.52; N, 12.41%. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.60%.

3-(2-Methyl-1,3-dioxolan-2-yl)-2-methylhydrazono-3,5-cycloheptadien-1-one (7): Yellow oil; IR ($CHCl_3$) 3450 (NH), 1640 cm^{-1} (C=O); UV (CH_3OH) 216 (log ε 4.23), 287 (3.86), 350 nm (4.02); ^{1}H NMR ($CDCl_3$) δ=1.82 (3H, s, C-CH_3), 2.91 (2H, d, J=7 Hz, 7-CH_2), 3.33 (3H, s, N-CH_3), 3.5—4.2 (4H, m, OCH_2CH_2O), 5.69 (1H, dt, J=9.5, 6 Hz, H-6), 6.18 (1H, dd, J=9.5, 5.5 Hz, H-5), 6.55 (1H, d, J=5.5 Hz, H-4), 12.95 (1H, br, NH). Found: m/z 236.1071. Calcd for $C_{12}H_{16}N_2O_3$: M, 236.1161.

2-Methylamino-3-(2-methyl-1,3-dioxolan-2-yl)tropone (8): Pale yellow needles (from benzene–hexane); mp 125—126 °C; IR ($CHCl_3$) 3300 (NH), 1600 cm^{-1} (C=O); UV (CH_3OH) 212 (log ε 3.88), 256 (4.37), 342 (4.04), 412 nm (3.96); ^{1}H NMR ($CDCl_3$) δ=1.06 (3H, s, C-CH_3), 2.97 (3H, d, J=6 Hz, N-CH_3), 3.5—4.2 (4H, m, OCH_2CH_2O), 6.3—7.6 (5H, m, H-4,5,6+NH). Found: m/z 221.1013. Calcd for $C_{12}H_{15}N_2O_3$: M, 221.1052.

1,3-Dimethyl-1,8-dihydrocycloheptapyrazol-8-one (9): Pale yellow needles; mp 100—101 °C (lit,[3] 96—98 °C).

2,3-Dimethyl-2,8-dihydrocycloheptapyrazol-8-one (10): Pale yellow needles; mp 178—180 °C (lit,[3] 178—179 °C).

2-(2-Methyl-1,3-dioxolan-2-yl)-7-(2-methylhydrazino)tropone (11): Yellow needles (from benzene–hexane); mp 151 °C (decomp); IR ($CHCl_3$) 3260 (NH), 1590 cm^{-1} (C=O); UV (CH_3OH) 247 (log ε 4.13), 344 (4.27), 412 nm (4.05); ^{1}H NMR ($CDCl_3$) δ=1.80 (3H, s, C-CH_3), 2.62 (3H, s,

N-CH_3), 3.5—4.2 (4H, m, OCH_2CH_2O), 4.09 (1H, br, NH), 6.55 (1H, ddd, J=12, 9, 3 Hz, H-4), 6.9—7.3 (2H, m, H-5,6), 7.71 (1H, d, J=9 Hz, H-3), 8.6 (1H, br, NH). Found: m/z 236.1063. Calcd for $C_{12}H_{16}N_2O_3$: M, 236.1161.

2-(2-Methyl-1,3-dioxolan-2-yl)-7-(1-methylhydrazino)tropone (12): Yellow plates (from benzene–hexane); mp 149 °C (decomp); IR ($CHCl_3$) 3500 (NH), 3300 (NH), 1600 cm^{-1} (C=O); UV (CH_3OH) 216 (log ε 4.13), 260 (4.17), 355 (4.08), 422 nm (3.86); ^1H NMR ($CDCl_3$) δ=1.90 (3H, s, *C*-CH_3), 3.22 (3H, s, *N*-CH_3), 3.5—4.2 (4H, m, OCH_2CH_2O), 4.2 (2H, br, NH_2), 6.2—7.2 (3H, m, H-4,5,6), 7.43 (1H, dd, J=9, 2 Hz, H-3). Found: m/z 236.1058. Calcd for $C_{12}H_{16}N_2O_3$: M, 236.1161.

1,3-Dimethyl-8-methylhydrazono-1,8-dihydrocycloheptapyrazole (13): Reddish orange needles; mp 113—114 °C (lit,[3] 112—113 °C).

Hydrolysis of the Hydrazone (4) with Hydrochloric Acid. The hydrazone **4** (111 mg, 0.5 mmol) in 2 M hydrochloric acid (5 ml) was heated for 1 h on a water bath. The mixture was diluted with water and extracted with chloroform. The extract was washed with water and dried over sodium sulfate. The evaporation of the solvent gave the cycloheptapyrazol-8-one **5** (71 mg, 89%).

Hydrolysis of the Hydrazone (6) with Hydrochloric Acid. The hydrazone **6** (118 mg, 0.5 mmol) in 2 M hydrochloric acid (5 ml) was heated for 1 h on a water bath. The mixture was worked up, as mentioned above, to give the cycloheptapyrazol-8-one **10** (80 mg, 92%).

Reaction of the Methyl Ether (3a) with Methylamine. A mixture of **3a** (122 mg, 0.5 mmol) and 40% methylamine solution (2 ml) in methanol (5 ml) was allowed to stand for 4 d at room temperature. After removing the solvent, the residue was dissolved in chloroform, washed with water, and dried over sodium sulfate. The evaporation residue from the chloroform solution was chromatographed on a Wakogel B-10 plate (30×30 cm) with ethyl acetate to afford the methylaminotropone **8** (12 mg, 10%).

General Procedure for the Reactions of the Methyl Ethers (3a and 3b) with Urea, Thiourea, Guanidine, and Amidines. A solution of the methyl ether **3a** or **3b** (222 mg, 1 mmol) in absolute ethanol (5 ml) was added a solution of the reagent (2 mmol) and the base (2 mmol) (indicated in Table 1) in absolute ethanol (5 ml). After removing the solvent, the residue was triturated with water, made slightly acidic with 10% acetic acid, and extracted with chloroform. The products were separated by chromatography on Wakogel B-10 plates (30×30 cm) with chloroform or ethyl acetate. These results are summarized in Table 1.

Ethyl 2-(2-Methyl-1,3-dioxolan-2-yl)benzoate (14): Colorless prisms (from cyclohexane); mp 49—50 °C; IR ($CHCl_3$) 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=1.36 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.78 (3H, s, CH_3), 3.4—4.2 (4H, m, OCH_2CH_2O), 4.30 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 7.2—7.7 (4H, m). Found: C, 66.02; H, 6.83%. Calcd for $C_{13}H_{16}O_4$: C, 66.08; H, 6.65%.

2-Ethoxy-7-(2-methyl-1,3-dioxolan-2-yl)tropone (15): Colorless prisms (from benzene–hexane); mp 108—109 °C; IR ($CHCl_3$) 1620 cm^{-1} (C=O); UV (CH_3OH) 244 (log ε 4.23), 323 (3.92), 353 nm (3.86); ^1H NMR ($CDCl_3$) δ=1.50 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.89 (3H, s, CH_3), 3.6—4.2 (4H, m, OCH_2CH_2O), 4.06 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 6.5—7.25 (3H, m), 7.75 (1H, dd, J=7, 2 Hz, H-3). Found: C, 66.20; H, 6.89%. Calcd for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83%.

2-Mercapto-4-(2-methyl-1,3-dioxolan-2-yl)cycloheptimidazole (16): Reddish orange prisms (from benzene–hexane); mp 228—229 °C; UV (CH_3OH) 235 (log ε 4.26), 256 (4.53), 274 sh (4.13), 313 (3.88), 450 nm (4.26); ^1H NMR ($CDCl_3$) δ=1.75 (3H, s, CH_3), 3.7—4.4 (4H, m, OCH_2CH_2O), 7.3—8.2 (4H, m), 10.85 (1H, br, SH). Found: C, 58.32; H, 4.88; N, 10.99%. Calcd for $C_{12}H_{12}N_2O_2S$: C, 58.06; H, 4.84; N, 11.29%.

2-Amino-4-(2-methyl-1,3-dioxolan-2-yl)cycloheptimidazole (17): Yellow prisms (from ethanol); mp 208—209 °C; UV (CH_3OH) 240 sh (log ε 4.29), 263 (4.52), 290 sh (4.01), 360 nm (4.24); ^1H NMR ($CDCl_3$) δ=2.07 (3H, s, CH_3), 3.7—4.3 (4H, m, OCH_2CH_2O), 7.2—7.8 (2H, m, H-6,7), 7.60 (2H, br, NH_2), 7.97 (1H, dm, J=9 Hz, H-5), 8.30 (1H, dd, J=10, 2.5 Hz, H-8). Found: C, 62.05; H, 5.93; N, 18.32%. Calcd for $C_{12}H_{13}N_3O_2$: C, 62.32; H, 5.67; N, 18.23%.

2-Methyl-4-(2-methyl-1,3-dioxolan-2-yl)cycloheptimidazole (18): Yellow prisms (from cyclohexane); mp 119—120 °C; UV (CH_3OH) 228 (log ε 4.42), 260 (4.62), 307 sh (3.93), 323 (4.01), 399 nm (3.14); ^1H NMR ($CDCl_3$) δ=2.14 (3H, s, CH_3), 2.95 (3H, s, 2-CH_3), 3.7—4.4 (4H, m, OCH_2CH_2O), 7.75—8.15 (2H, m, H-6,7), 8.3—8.8 (2H, m, H-5,8). Found: C, 67.78; H, 6.19; N, 12.10%. Calcd for $C_{13}H_{14}N_4O_2$: C, 67.81; H, 6.19; N, 12.17%.

4-(2-Methyl-1,3-dioxolan-2-yl)-2-phenylcycloheptimidazole (19): Yellow needles (from cyclohexane); mp 155—156 °C; UV (CH_3OH) 259 (log ε 4.53), 277 sh (4.46), 356 sh (4.39), 366 (4.40), 415 nm sh (3.25); ^1H NMR ($CDCl_3$) δ=2.28 (3H, s, CH_3), 3.6—4.2 (4H, m, OCH_2CH_2O), 7.2—7.6 (3H, m, H-3′,4′,5′), 7.65—8.0 (2H, m, H-6,7), 8.3—8.5 (1H, m, H-5), 8.55—8.9 (3H, m, H-2′,6′,8). Found: C, 74.05; H, 5.63; N, 9.52%. Calcd for $C_{18}H_{16}N_4O_2$: C, 73.95; H, 5.52; N, 9.58%.

Rearrangement of the Methyl Ether (3a) with Sodium Ethoxide or Potassium Hydroxide. (a) To a sodium ethoxide solution, prepared from sodium (28 mg, 1.2 mmol) and absolute ethanol (6 ml), was added **3a** (113 mg, 0.6 mmol). The mixture was refluxed for 30 min to give **14** (116 mg, 82%).

(b) A mixture of **3a** (266 mg, 1.2 mmol) and potassium hydroxide (67 mg, 1.2 mmol) in absolute ethanol (10 ml) was refluxed for 1 h to give **14** (204 mg, 72%).

Reaction of the Methyl Ether (3b) with Sodium Ethoxide or Potassium Hydroxide. (a) Methyl ether **3b** (222 mg, 1 mmol) in sodium ethoxide solution, prepared from sodium (46 mg, 2 mmol) and absolute ethanol (10 ml), was refluxed for 30 min to give **2** (45 mg, 22%) and **15** (145 mg, 62%).

(b) A mixture of **3b** (222 mg, 1 mmol) and potassium hydroxide (56 mg, 1 mmol) in absolute ethanol (10 ml) was refluxed for 1 h to give **2** (44 mg, 21%) and **15** (105 mg, 44%).

Hydrolysis of the Cycloheptimidazole (17). Compound **17** (231 mg, 1 mmol) in 2 M hydrochloric acid (20 ml) was heated on a water bath for 20 min. The mixture was diluted with water, neutralized with a saturated sodium hydrogencarbonate solution, and extracted with chloroform. The evaporation residue from the extract was chromatographed on a Wakogel B-10 plate (30×30 cm) with ethyl acetate to give 4-acetyl-2-aminocycloheptimidazole (**20**) (155 mg, 83%) as yellow needles (from ethanol): mp 218—219 °C (lit,[5] 213—214 °C).

Hydrolysis of the Cycloheptimidazole (19): Compound **19** (81 mg, 0.28 m mol) in 1 M hydrochloric acid (4 ml) was heated on a water bath for 20 min. The mixture was worked

up, as mentioned above, to give 4-acetyl-2-phenylcycloheptimidazole (**21**) (43 mg, 65%) as yellow needles (from cyclohexane): mp 148—149 °C (lit,[5] 142—143 °C).

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References

1) K. Imafuku and Z.-T. Jin, *Yanbian Daxue Xuebao,* **1983**, 35.

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

3) A. Yamane, K. Imafuku, and H. Matsumura, *Bull. Chem. Soc. Jpn.*, **53**, 1461 (1980).

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

5) Z.-T. Jin, K. Imafuku, and H. Matsumura, *J. Chem. Soc., Perkin Trans., 1,* **1982**, 1037.

6) I. Murata, *Bull. Chem. Soc. Jpn.*, **34**, 577 (1961).

7) T. Nozoe, K. Takase, and H. Matsumura, "Dai Yuki Kagaku," ed by M. Kotake, Asakura Shoten, Tokyo (1960), Vol. 13, p. 343.

8) K. Imafuku, K. Kamachi, Y. Matsuda, and H. Matsumura, *Bull. Chem. Soc. Jpn.*, **52**, 2447 (1979).

9) T. Nozoe and K. Kikuchi, "Dai Yuki Kagaku," ed by M. Kotake, Asakura Shoten, Tokyo (1960), Vol. 13, p. 579.

10) F. Pietra, *Chem. Rev.*, **73**, 293 (1973).

11) H. Matsumura and S. Kitahara, presented at the 9th National Meeting of the Chemical Society of Japan, Kyoto, 1956.

12) T. Nozoe, "Non-benzenoid Aromatic Compounds," ed by D. Ginsburg, Interscience, New york (1959), p. 410.

13) T. Nozoe, K. Takase, and H. Matsumura, "Dai Yuki Kagaku," ed by M. Kotake, Asakura Shoten, Tokyo (1960), Vol. 13, p. 186.

14) I. Murata, *Bull. Chem. Soc. Jpn.*, **34**, 580 (1961).