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Synthesis of 4, 6-Dicyano-2, 5-dimethoxytropone

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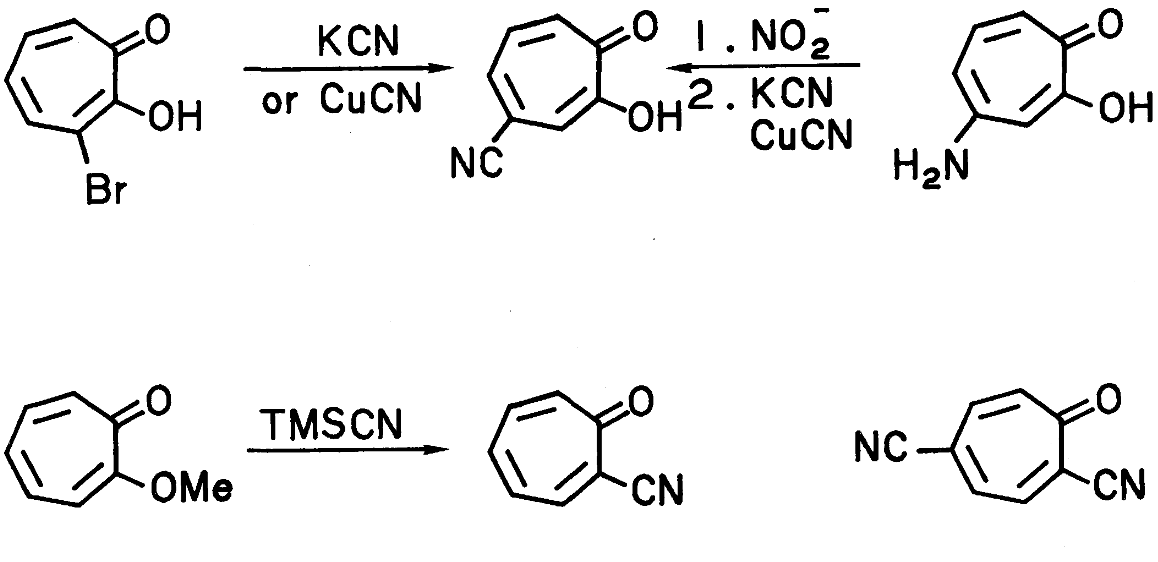
4,6-Dicyano-2,5-dimethoxytropone, a potential dicyano-*p*-tropoquinone precursor, was prepared from 4,6-bis(formyloxymethyl)-2,5-dimethoxytropone. The other cyanotropones prepared by the reaction of 2,5-dimethoxytropone with trimethylsilyl cyanide were 2-cyano-5-methoxy- and 5-cyano-2-methoxytropones.

Previously, cyanotropolones were prepared by the substitution of 3-bromotropolone with potassium cyanide[1] or copper(I) cyanide[2] and by the Sandmeyer reaction of 4- and 5-aminotropolones,[3] but the yields were not always satisfactory. Recently, Saito has prepared 2-cyanotropone from trimethylsilyl cyanide and 2-methoxytropone under mild conditions.[4] In this paper, we will describe the synthesis of several cyanotropones, such as 2-cyano-5-methoxy- (**1**) and 5-cyano-2-methoxytropones (**2**) as well as 4,6-dicyano-2,5-dimethoxytropone (**3**), possible precursors for cyano-*p*-tropoquinones.



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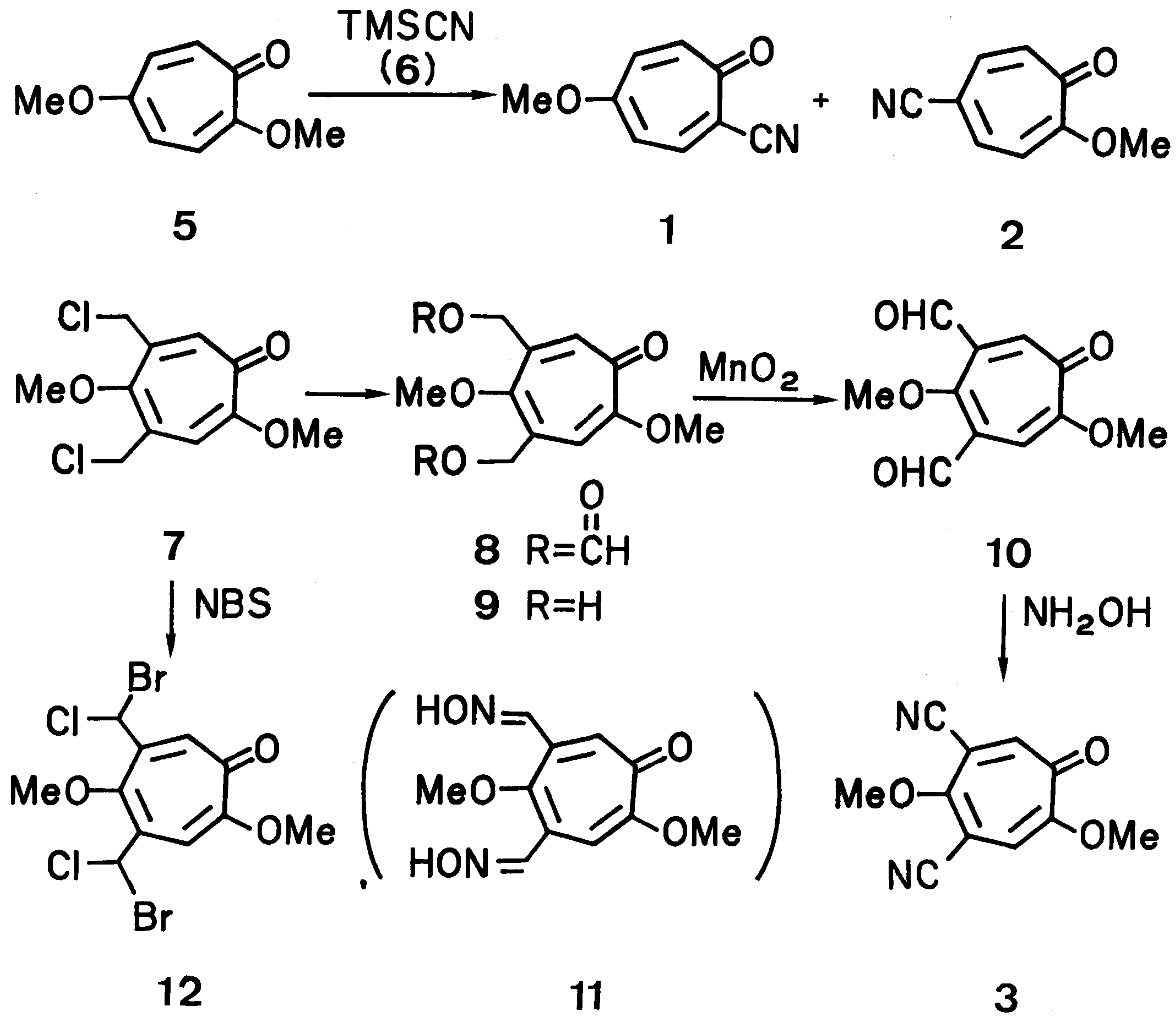
First of all, in a hope of preparing 2,5-dicyanotropone (**4**), we attempted the reaction of 2,5-dimethoxytropone (**5**) with trimethylsilyl cyanide (**6**) under Saito's conditions,[4] two monocyanotropones (**1** and **2**) were obtained in 28% and 22% yields. Since less-polar product, **2**, exhibited two pairs of *AB*-type signals and a methoxy signal being long-range-coupled to the broad doublet signal at 7.03, which was the highest signal among the ring protons, the structure of **2** is shown to be 5-cyano-2-methoxytropone. On the other hand, the ^{1}H NMR spectrum of **1** exhibited a methoxy signal which long-range-coupled to an aromatic proton signal at 6.55; its structure must be 2-cyano-5-methoxytropone. The results were parallel to the Saito's mechanism;[4] the attack of **6** occurred at the carbon bearing the substituent. Since it failed to give dicyanotropone directly, we attempted to convert 4,6-bis-(chloromethyl)-2,5-dimethoxytropone (**7**)[5] to the dicyano derivative.



When a hexamethylphosphoric triamide solution of **7** and sodium formate was heated at 50 °C for 2 h, 4,6-bis(formyloxymethyl)-2,5-dimethoxytropone (**8**) was obtained in 89% yield. An acid hydrolysis of **8** gave a bis(hydroxymethyl) derivative (**9**) in 81% yield. The manganese (IV) oxide oxidation of **9** afforded a bisaldehyde (**10**) in 40% yield. Treatment of **10** with hydroxylamine gave a dicyano derivative (**3**) in 6% but no dioxime (**11**); the yield of **3**, however, could not be improved inspite of intensive survey of reaction conditions. This poor yield might be due to the nucleophilic attack of hydroxylamine into C-7 position, whose electron density decreased by the introduction of two cyano groups. Similar reaction has occurred when a 2-benzoyltropone derivative was treated with 1,2-diaminobenzene to give a benzodiazepinone derivative instead of 1,2-diazaazulene derivative.[6] Alternatively, by refluxing benzene solution of **7** with *N*-bromosuccinimide and 2,2′-azobis(isobutyronitrile), an unstable dibromodichloro derivative (**12**) was obtained in 25% yield.

The further transformation of **3** to *p*-tropoquinone derivatives is under going and will be published elsewhere.

Experimental

The elemental analyses were performed by Miss S. Hirashima, of This Institute. The NMR spectra were measured by a JEOL FX 100 Spectrometer in $CDCl_3$ solution, unless otherwise specified, and the chemical shifts expressed were in δ unit. The mass spectra were measured with a JEOL OlSG-2 Spectrometer. The IR spectra were taken as KBr disks or as a liquid film inserted between NaCl plates using a Jasco IR-A 102 Spectrometer. The UV spectra were measured by a Hitachi U-3200 Spectrophotometer.

Reaction of 6 and 2,5-Dimethoxytropone (5). An anhydrous CH_2Cl_2 solution (1 cm^3) of **5** (211 mg) and **6** (253 mg) was stirred at room temperature for 5.5 d in the presence of ZnI_2 (14 mg). The volatile materials were evaporated in vacuo and the residue was chromatographed on a silica-gel column to give **2** [yellow crystals, mp 154-156 °C, 35.3 mg ; 22%. Found : *m/z*, 161.0482: Calcd for $C_9H_7NO_2$: 161.0476. ^1H NMR $\delta(CD_3OD) = 3.99$ (3H, s), 7.03 (1H, d, $J = 10.5$ Hz), 7.13 (1H, dd, $J = 12.5, 0.7$ Hz), 7.46 (1H, dd, $J = 12.5, 1.6$ Hz), and 7.70 (1H, ddd, $J = 10.5, 1.6, 0.7$ Hz). ^{13}C NMR $\delta(CF_3COOD) = 59.7$, 113.2, 116.5, 119.1, 136.8, 144.1, 146.4, 171.4, and 183.0. IR ν : 2220, 1620, and 1580 cm^{-1}. UV λ^{MeOH}_{max} : 222 nm ($\varepsilon = 13000$), 249 (14000), 318 (7500, sh), 330 (8800), 353 (6600, sh), and 370 (4700, sh)] and **1** [yellow needles, mp > 300 °C , 45.8 mg ; 28%. Found : 161.0475. ^1H NMR $\delta(CD_3OD) = 3.91$ (3H, s) 6.55 (1H, ddd, $J = 10.4, 2.5, 1.2$ Hz), 7.08 (1H, dd, $J = 13.3, 1.2$ Hz), 7.25 (1H, dd, $J = 13.3, 2.5$ Hz), and 7.87 (1H, d, $J = 10.4$ Hz). ^{13}C NMR $\delta(CF_3COOD) = 59.2$, 114.5, 116.1, 117.5, 141.4, 143.2, 152. 8, 176.6, and 187.1. IRν : 2230, 1640, 1595, and 1570 cm^{-1}. UV λ^{MeOH}_{max} : 218 nm ($\varepsilon = 13000$, sh), 243 (13000), 247 (13000, sh), 328 (9200), 353 (8400), 369 (7200, sh), and 388 (3800, sh)] .

Reaction of 7 with HCOONa. An HMPA solution (2 cm^3) of **7** (29 mg) and HCOONa (17.5 mg) was stirred at 50 °C for 2 h under N_2 atmosphere. The reaction mixture was diluted with water and extracted with AcOEt. The extract was washed with water, dried on $MgSO_4$, and heated in vacuo to leave 8 [pale yellow needles, mp 96-98 °C , 27.6 mg ; 89%. Found : C, 55.15 ; H, 5.05%. Calcd for $C_{13}H_{14}O_7$: C, 55.32 ; H, 5.00%. ^{1}H NMR δ = 3.76 (3H, s) 3.90 (3H, d, J = 0.5 Hz), 5.18 (2H, t, J = 1 Hz), 5.25 (2H, d, J = 1 Hz), 6.73 (1H, s), 7.33 (1H, br s), 8.14 (1H, t, J = 1 Hz), and 8.15 (1H, t, J = 1 Hz). ^{13}C NMR δ = 56.4, 62.5, 63.0, 63.1, 112.9, 130.2, 135.5, 141.4, 155.6, 160.2, 160.7, 162.0, and 178.8. IR ν : 1705, 1625, 1605, and 1580cm^{-1}. UV λ_{max}^{MeOH} : 243 nm (ε = 24000), 312 (6300, sh), 326 (7200), 353 (6400, sh), and 368 (5200, sh)] .

Acid Hydrolysis of 8. A 50% aqueous AcOH solution (2 cm^3) of **8** (29.2 mg) in the presence of concd HCl (0.1 cm^3) was stirred at room temperature for 1.5 h. The mixture was then heated in vacuo to leave **9** [light brown needles, mp 75-77 °C, 18.9 mg ; 81%. Found : C, 58.22 ; H, 6.24%. Calcd for $C_{11}H_{14}O_5$: C, 58.40 ; H, 6.24%. ^{1}H NMR δ(CD_3OD) = 3.71 (3H, br s), 3.98 (3H, s), 4.66 (2H d, J = 1 Hz), 4.72 (2H, s), 7.53 (1H, s), and 7.69 (1H, s). ^{13}C NMR δ(CD_3OD) = 57.0, 61.5, 62.1, 62.7, 116.5, 132.9, 141.5, 152.6, 157.2, 163.2, and 179.6. IR ν : 3400-3200 and 1575 cm^{-1}. UVλ_{max}^{MeOH} : 244 nm (ε = 23000), 325 (7200, sh), 337 (7500), 350 (7100, sh), and 362 (5600, sh)] .

The MnO_2-Oxidation of 9. An acetone solution (3 cm^3) of **9** (26.8 mg) was refluxed for 7 h with MnO_2 (130 mg). The mixture was passed through a Celite column and the filtrate was chromatographed on a silica-gel column to give **10** [yellow crystals, mp 139-141 °C, 8.9 mg ; 40%. Found : C, 59.19 ; H, 4.63%. Calcd for $C_{11}H_{10}O_5$: C, 59.46 ; H, 4.54%. ^{1}H NMR δ = 3.96 (3H, s), 3.98 (3H, d, J = 0.5 Hz), 7.29 (1H, dd, J = 1, 0.5 Hz), 7.72 (1H, d, J = 0.6 Hz), 10.32 (1H, d, J = 1 Hz), and 10.45 (1H, d, J = 0.6 Hz). ^{13}C NMR δ = 56.7, 66.2, 107.4, 129.7, 137.4, 141.0, 162.6, 163.9, 179.4, 189.2, and 189.8. IR ν : 2970, 2840, 1710, 1675, 1605, 1600, and 1575 cm^{-1}. UVλ_{max}^{MeOH} : 232 nm (ε = 16000, sh), 249 (19000), 328 (7100), 371 (7200), and 415 (3500, sh)] .

The Reaction of 10 with NH_2OH. An MeOH solution (8 cm^3) of **10** (93 mg), NH_2OH• HCl (118 mg), and AcONa (138 mg) was refluxed for 4 h. After removal of the solvent in vacuo, the residue was diluted with water and extracted with BuOH. The silica-gel column chromatography of the extract gave **3** [yellow crystals, mp 242-247 °C, 4.8 mg ; 6%. Found : m/z, 216.0551. Calcd for $C_{11}H_8O_3N_2$: 216.0534. ^{1}H NMR δ(CD_3OD) = 3.83 (3H, s), 3.90 (3H, s), 7.46 (1H, s), and 8.33 (1H, s). IR ν : 2230 cm^{-1}] .

The Reaction of 7 with NBS. An anhydrous benzene solution (2 cm^3) of **7** (50.3 mg), NBS (76.2 mg), and AIBN (10 mg) was refluxed for 31 h. The reaction mixture was chromatographed on a silica-gel column to give **12** [reddish yellow oil, 20 mg ; 25%. Found : m/z, 418 : 420 : 422 : 424 = 100 : 346 : 330 : 94.2. ^{1}H NMR δ = 3.88 (3H, s), 4.03 (3H, br s), 7.00 (1H, d, J = 0.6 Hz), 7.12 (1H, br s), 7.27 (1H, d, J = 0.6 Hz), and 7.90 (1H, s)] .

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