  Bull. Chem. Soc. Jpn., 58, 515—520 (1985)

The Synthesis of the Chloro and Dichloro Derivatives of 2,10-Dihydroxydicyclohepta[*b,d*]furan-3,9-diones

Tomoyuki KUSABA, Akira MORI,† and Hitoshi TAKESHITA*,†

Graduate School of Engineering Sciences, 39, Kyushu University, Kasuga-koen, Kasuga, Fukuoka 816

†*Research Institute of Industrial Science, 86, Kyushu University, Kasuga-koen, Kasuga, Fukuoka 816*

(Received September 3, 1984)

4,8-Dichloro- and 5,7-dichloro-2,10-dihydroxydicyclohepta[*b,d*]furan-3,9-diones were synthesized. Although the latter could be obtained by condensation of 4-chloro-*p*-tropoquinone and its hydroquinone, the former required the hydrolysis of condensate of 3-chloro-*p*-tropoquinone and 7-chloro-5-hydroxy-2-methoxytropone. This mixed condensation led to several unsymmetrically substituted derivatives in improved yields.

In 1968, Norin and Baggaley[1] reported a structural study on a dimeric troponoid constituent from a conifer, *Juniperus utahensis Lemm.*, utahin (**1a**).[2] They suggested its identity with the oxidative condensation product obtained *via* several routes from hinokitiol (4-isopropyltropolone)[3,4] but was reluctant to draw a final conclusion as to its structure. A similar condensate (**1b**) has been obtained from 4-methyltropolone by Haworth *et al.*[5] Recently, we have reported the synthesis of the parent compound, 2,10-dihydroxydicyclohepta[*b,d*]furan-3,9-dione[6] (**2**), from 5-hydroxytropolone (**3**) and *p*-tropoquinone (**4**),[7] as well as the unambiguous synthesis of **1a**.[8]

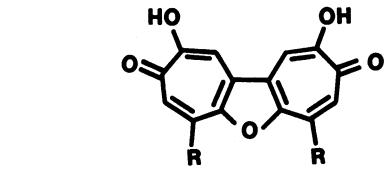
In this paper, we wish to describe the synthesis of 4,8-, 5,7-, and 1,8-dichloro derivatives as well as the controlled mixed condensation of the tropoquinones with 5-hydroxy-2-methoxytropones.

First two chloro-*p*-tropoquinones have been prepared as follows: 4-Chloro-*p*-tropoquinone (**5**) was easily prepared by means of DDQ (2,3-dichloro-5,6-dicycano-*p*-benzoquinone)-oxidation of 4-chloro-5-hydroxytropolone (**6**) which was derived from *p*-tropoquinone (**4**)[9] with hydrochloric acid.[10] On the other hand, 3-chloro-*p*-tropoquinone (**7**) was prepared from 5-acetoxytrpolone (**8**) *via* 5-acetoxy-2-methoxytropone (**9**), 4-acetoxy-2-chloro-7-methoxytropone (**10**), and 3-chloro-5-hydroxytropolone (**11**) by sequential reactions with diazomethane, *N*-chlorosuccinimide (NCS),[11] hydrochloric acid in acetic acid, and the DDQ-dehydrogenation.

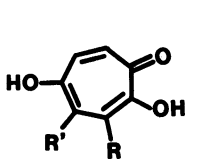
Following our previous methods, preparation of the 5,7-dichloro derivative (**12**) was carried out in two ways; the first was the partial reduction of **5** with acetic acid to yield **12** in 32% yield. The major reaction path in this case was, however, the reduction of **5** to its hydroquinone, **6**. The second was the coupling of **5** and **6** in tetrahydrofuran (THF) to give **12** in 22% yield. Again the reduction of **5** to **6** was the preferred process; this has led us to conclude that THF is also suitable for the reduction of tropoquinones to 5-hydroxytropolones.

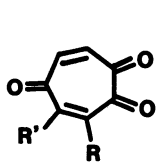
Moreover, attempts to prepare 4,8-dichloro derivative (**13**) or 1,8-dichloro derivative (**14**) by the two methods failed; again, the reduction of **7** to **11** was exclusive. Therefore, we have modified the substrate to the 2-methoxytropone derivative based on the following grounds.

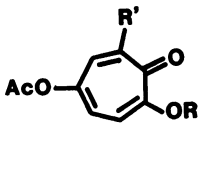
Since 3-bromotropolone (**A**) has been known to exist mainly as the tautomeric form of 3-bromo-2-hydroxytropone (**Aa**),[12] the predominant tautomer of 3-chloro-5-hydroxytropolone (**11**) must be a similar 3-chloro-2,5-dihydroxytropone (**11a**). From the view on this bond fixation, the condensation of **11** must be facilitated at C-4 over C-6. On the other hand, a steric hindrance from the adjacent chlorine atom must disfavor the condensation at C-4. Consequently, the attempted



1a R = ^{i}Pr
1b R = Me
2 R = H

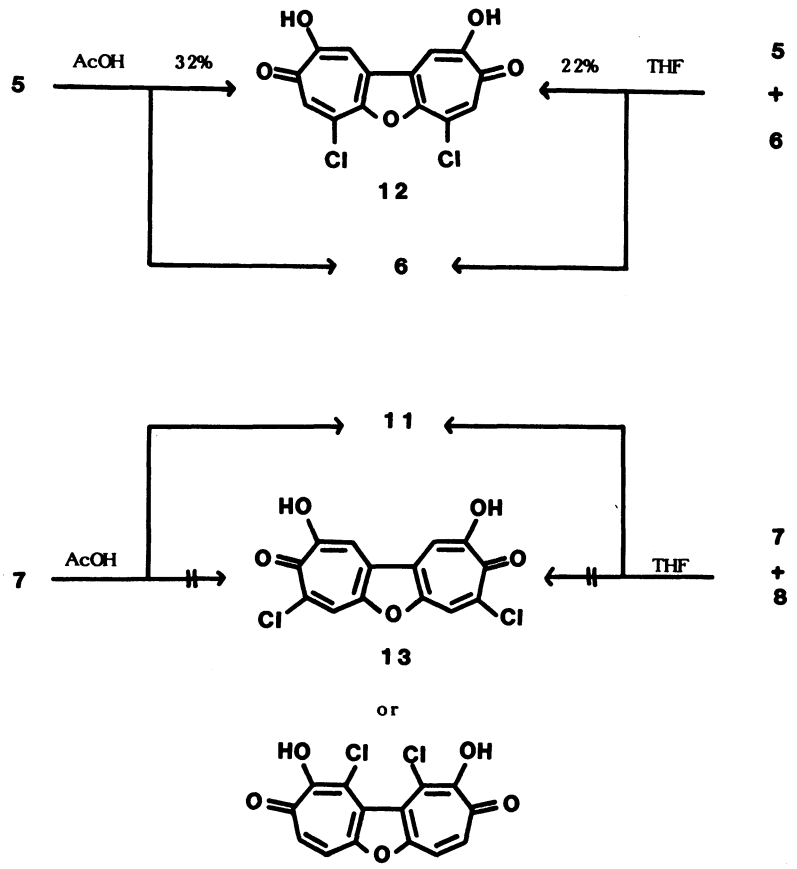






3 R = R' = H **4** R = R' = H **8** R = R' = H
6 R = H, R' = Cl **5** R = H, R' = Cl **9** R = Me, R' = H
11 R = Cl, R' = H **7** R = Cl, R' = H **10** R = Me, R' = Cl

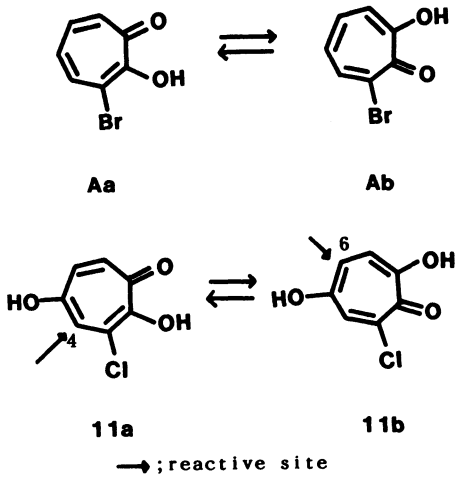
Scheme 1.



Scheme 2.

condensation of **11** with the quinone, **7**, which also possesses an adjacent chlorine atom at the reactive site, C-4, should merely have resulted in the reduction of **7** to **11**.

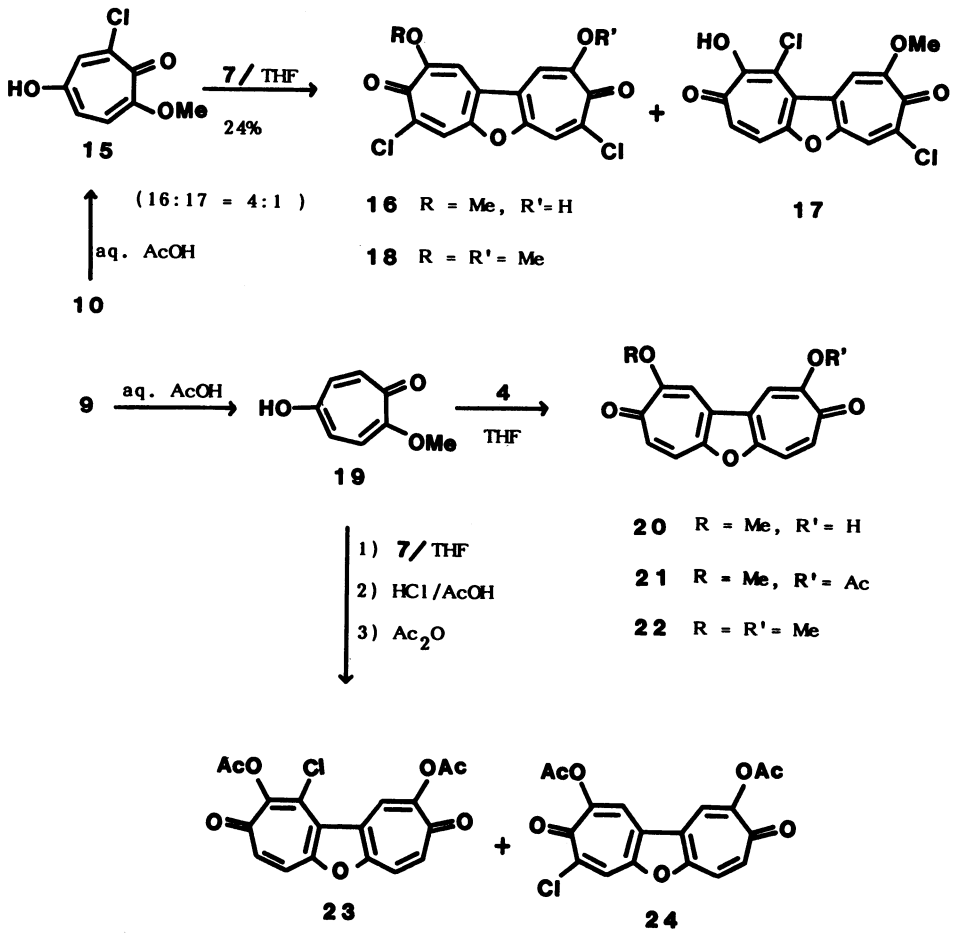
Thus, in view of the bond alternation, the fixed C=C bond system of **11** in the 2-chloro-7-hydroxy form would facilitate the condensation. This can be simply done by making a monomethyl ether. A mild condensation of 2-chloro-4-hydroxy-7-methoxytropone (**15**), which could be prepared from **10** by a 33%-aqueous acetic acid-hydrolysis, with **7** at 15—25 °C furnished two condensates in 24% yield with a 4:1 ratio; they are 4,8-dichloro-2-methoxy derivative (**16**) and 1,8-dichloro-10-methoxy derivative (**17**). From the mixture, the major product, **16**, was isolated after methylation to 4,8-dichloro-2,10-dimethoxy derivative (**18**) by sublimation. The hydrochloric acid-hydrolysis of **18** or **16** in acetic acid afforded **13**. Thus, the use of the 5-hydroxy-2-methoxytropones has not only provided an entry for mixed types of condensates, but also improved the yields for the single species condensates; *e.g.*, when 5-hydroxy-2-methoxytropone (**19**), which could be prepared easily from **9**, was mixed with **4** in THF at 15—25 °C for 15 min, the condensate isolated in 45% yield was the 2-methoxy derivative (**20**). This compound **20** was characterized as 2-acetoxy-10-methoxy derivative (**21**), and 2,10-dimethoxy derivative (**22**).



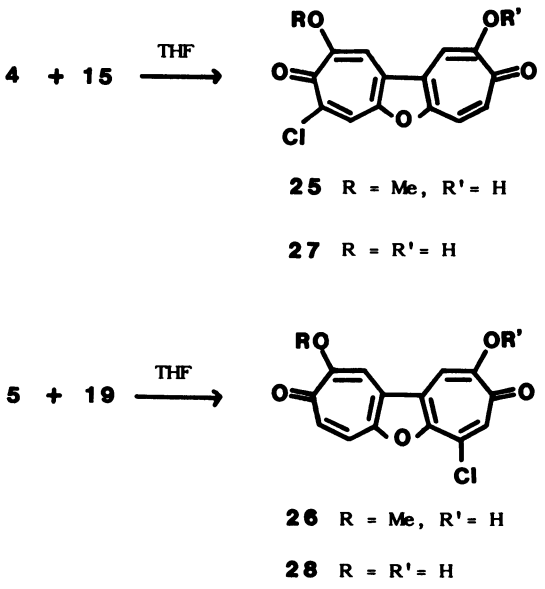
Scheme 3.

Similarly, the condensation products of **7** and **19**, isolated by consecutive treatments with hydrochloric acid in acetic acid and with acetic anhydride, were 2,10-diacetoxy-1-chloro derivative (**23**) and 2,10-diacetoxy-4-chloro derivative (**24**). Further, the condensations of **4** with **15** and **5** with **19** gave 4-chloro-2-methoxy derivative (**25**) and 7-chloro-2-methoxy derivative (**26**) in regiospecific fashion, respectively. The hydrolysis of **25** and **26** yielded 4-chloro (**27**) and 5-chloro (**28**) derivatives.

In conclusion, appropriate combinations of the



Scheme 4.



Scheme 5.

two components, *p*-tropoquinones and 5-hydroxy-2-methoxytropones, are capable of leading to various kinds of the dicyclohepta[*b*,*d*]furandione derivatives in improved yields, some of which are indeed quantitative after subtracting the amounts of recovered troponoids. Various aspects of the chemistry of these condensed furan derivatives are under investigation.

Experimental

Elemental analyses were performed with a Hitachi 026 Model CHN Analyzer by Miss M. Yamaguchi and S. Hirashima, at this Institute. The mps were measured by a Yanagimoto Micro-mp Apparatus, and were uncorrected. The IR spectra were taken either in CCl_4 solutions or as KBr disks with a Jasco Model A 102 spectrometer. The NMR spectra were measured, in $CDCl_3$ solution unless otherwise stated, by a JEOL FX100 Model Spectrometer, and the chemical shifts were expressed in the δ unit from the internal TMS. The mass spectra were measured on a JEOL OlSG Model Apparatus.

*Preparation of 4-Chloro-*p*-tropoquinone (5).* To an acetone solution (10 cm^3) of **6**[9] (260 mg), was added an acetone solution (5 cm^3)of DDQ (375 mg) at 15—25 °C. After 10 min, the acetone was removed *in vacuo*, and the residue was washed with benzene. The benzene washings were combined, concentrated, and chromatographed on a silica-gel column with benzene to yield pale yellow needles, mp 91—93 °C (decomp), **5**, 198 mg (77%) [Found: C, 49.32; H, 1.84%. Calcd for $C_7H_3O_3Cl$: C, 49.29; H, 1.78%. MS *m/z*, 170 and 172 (M^+). ^1H NMR δ=6.83 (1H, d, J=13 Hz), 6.97 (1H, d, J=13 Hz), and 7.30 (1H, s). ^{13}C-NMR δ=133.3, 133.7, 137.6, 147.2, 179.6, 182.5, and 183.4. IR ν 3050, 1655, 1630, 1600, 1235, 920, and 855 cm^{-1}].

Preparation of 5-Acetoxytropolone (8). To an AcOH solution (20 cm^3) of **3** (2.50 g), Ac_2O (2 cm^3) was added at 100 °C for 1 h, and the mixture was refluxed for 1.5 h. The reaction mixture was distilled *in vacuo*, and the residue

washed with $CHCl_3$ to recover the insoluble **3**, 1.28 g (51%). From the filtrate, colorless crystals, **8**, 1.60 g (100%), mp 107—108 °C (lit,[13] 110—111 °C) [^1H NMR δ=2.29 (3H, s), 7.08 (2H, dd, J=11, 1.5 Hz), 7.16 (2H, dd, J=11, 1.5 Hz), and 8.37 (1H, br. s). ^{13}C NMR δ=20.9, 122.6 (2C), 131.6 (2C), 149.3, 169.4 (2C), and 170.7], were isolated after recrystallizations from EtOAc–hexane (1:2).

Preparation of 5-Acetoxy-2-methoxytropone (9). A $CHCl_3$ solution (10 cm^3) of **8** (1.6 g) was treated with an Et_2O solution of CH_2N_2 at 0 °C to give **9**, 1.6 g (94%), colorless crystals, mp 85—86 °C [Found: C, 61.97;, H, 5.25%. Calcd for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19%. ^1H NMR δ=2.29 (3H, s), 3.93 (3H, s), 6.65 (1H, d, J=11 Hz), 6.80 (1H, ddd, J=11, 2, 1 Hz), 7.01 (1H, dd, J=13, 2 Hz), and 7.16 (1H, dd, J=13, 1 Hz). ^{13}C NMR δ=20.8, 56.4, 110.5, 123.6, 133.8, 135.9, 148.9, 164.0, 169.3, and 179.3. MS m/z, 194 (M^+). IR ν 3000, 1760, 1570, 1200, 1145, and 910 cm^{-1}].

Preparation of 4-Acetoxy-2-chloro-7-methoxytropone (10) from 9 and NCS. A benzene solution (30 cm^3) of **9** (1.00 g) and NCS (830 mg) was refluxed for 24 h with stirring. The mixture was heated *in vacuo* to remove the solvent. Pale yellow crystalline residue was washed with benzene, and the washings chromatographed on a silica-gel column; the eluent obtained from EtOAc–hexane (2:1) was **10**, 560 mg (77%), pale yellow needles, mp 112—113 °C [Found: C, 52.53; H, 3.87%. Calcd for $C_{10}H_9O_4Cl$: C, 52.53; H, 3.98%. ^1H NMR δ=2.29 (3H, s), 3.94 (3H, s), 6.72 (1H, d, J=11 Hz), 6.86 (1H, dd, J=11, 2 Hz), and 7.67 (1H, d, J=2 Hz). ^1H NMR δ=20.8, 56.8, 111.1, 124.3, 133.5, 143.0, 145.9, 162.2, 169.2, and 172.5. MS m/z, 228 and 230 (M^+). IR ν 3030, 2950, 1760, 1625, 1610, 1595, 1220, 1160, 1125, and 990 cm^{-1}], and subsequently, the recovered **9**, 380 mg (38%), was obtained.

Preparation of 3-Chloro-5-hydroxytropolone (11). A glacial AcOH solution (5 cm^3) of **10** (210 mg) and conc HCl (1 cm^3) was refluxed for 4 h. The mixture was heated *in vacuo* to remove the solvent, and the residue washed with EtOAc and recrystallized from MeOH–EtOAc to give **11**, colorless needles, mp 221—222 °C (decomp), 149 mg (94%) [Found: C, 48.62; H, 2.92%. Calcd for $C_7H_5O_3Cl$: C, 48.72; H, 2.93%. ^1H NMR (CD_3OD) δ=7.00 (1H, dd, J=12, 3 Hz), 7.30 (1H, d, J=12 Hz), and 7.65(1H, d, J=3 Hz). ^{13}C NMR (CD_3OD) δ=123.5, 123.9, 129.7, 140.2, 157.9, 163.6, and 167.8. MS m/z, 172 and 174 (M^+). IR ν 3200—2400, 1585, 970, 960, 930, 850, and 760 cm^{-1}].

Preparation of 3-Chloro-p-tropoquinone (7). Under the similar conditions to those in the preparation of **5** from **6**, **11** (48 mg) was converted to **7**, 38 mg (80%). Recrystallizations from benzene gave pale yellow crystals, mp 73—74 °C (decomp) [Found: C, 49.51; H, 1.75%. ^1H NMR δ=6.84 (2H, d, J=1 Hz) and 7.30 (1H, t, J=1 Hz). ^{13}C NMR δ=133.8, 137.2, 138.5, 143.4, 180.2, 184.5, and 184.8. MS m/z, 170 and 172 (M^+). IR ν 3030, 1695, 1660, 1320, 1170, 925, 880, 860, and 850 cm^{-1}].

Formation of 5,7-Dichloro Derivative (12) by Partial Reduction of 5. An AcOH (3 cm^3) solution of **5** (104 mg) was refluxed for 1.5 h with stirring. The solvent was removed *in vacuo*, and the residue washed with MeOH. The residue thus obtained was sublimed on a cold finger to give **12**, yellow needles, mp>300 °C, 8 mg (32%) [Found: C, 51.79; H, 2.08%. Cacld for $C_{14}H_6O_5Cl_2$: C, 51.72; H, 1.86%. ^1H NMR (CF_3COOD) δ=8.24 (2H, s) and 8.32 (2H, s). MS m/z, 324 and 326 (M^+). IR ν 3250, 3050, 1620, 1590, 1540, 1510, and 1400 cm^{-1}]. From the MeOH soluble fractions, 79 mg (75%) of **6** was obtained.

Condensation of 5 with 6. To a THF solution (10 cm^3) of **6** (252 mg), a THF solution (5 cm^3) of **5** (249 mg) was added at once. The mixture was kept at 15—25 °C under N_2 atmosphere for 16 h with stirring. After the removal of the solvent *in vacuo*, the residue was washed with a small amount of MeOH. Insoluble solid material was collected by filtration to give **12**, 33 mg (22%). From the MeOH washings, 348 mg (69%) of **6** was obtained.

Attempted Formation of 4,8-Dichloro Derivative (13) or 1,8-Dichloro Derivative (14). *a)*: A THF solution (4 cm^3) of **7** (43 mg) and **11** (43 mg) was kept at room temperature for 2 d. The solvent was removed *in vacuo*, and the residue crystallized from MeOH to give 76 mg (100%) of **11**. No other compound was identified.

b): An AcOH solution (2 cm^3) of **7** (38 mg) was refluxed for 2 h, and the solvent removed *in vacuo*; the pale yellow crystals obtained by recrystallizations from MeOH were **11**, 39 mg (100%).

Preparation of 2-Chloro-4-hydroxy-7-methoxytropone (15). An aqueous AcOH solution (33%, 3 cm^3) of **10** (200 mg) was heated at 100 °C for 10 h with stirring. The mixture was then evaporated *in vacuo* and the residue washed with EtOAc, and recrystallized from MeOH to give **15**, 155 mg (95%), mp 170—173 °C (decomp) [Found: C, 51.37; H, 3.82%. Calcd for $C_8H_7O_3Cl$: C, 51.49; H, 3.79%. ^1H NMR (CD_3OD) δ=3.88 (3H, s), 6.77 (1H, dd, J=11, 2.5 Hz), 7.15 (1H, d, J=11 Hz), and 7.85 (1H, d, J=2.5 Hz). ^{13}C NMR (CD_3OD) δ=57.2, 116.3, 118.7, 133.2, 146.2, 157.8, 159.9, and 172.9. MS m/z, 186 and 188 (M^+). IR ν 3050—2500, 1615, 1590, 1540, 1480, 1475, 1450, 1440, 1355, 1250, 1220, 1000, 835, and 755 cm^{-1}].

The Condensation of 7 with 15 to 4,8-Dichloro-10-methoxy Derivative (16) and 1,8-Dichloro-10-methoxy Derivative (17). To a THF suspension (30 cm^3) of **15** (830 mg), a THF solution (20 cm^3) of **7** (1.00 g) was added at once under N_2 atmosphere. The mixture was kept at 15—25 °C for 16 h. The solvent was removed *in vacuo*, and the residue washed with MeOH. The insoluble mass was passed through a Celite column with $CHCl_3$ to yield a 4:1-mixture of **16** and **17**, 380 mg (24%). Droplet-counter-current distribution fractionation of the mixture with $CHCl_3$–AcOH–H_2O (2:2:1) led to a separation of **16**, yellow crystals, mp 274—277 °C (decomp) [Found: C, 53.07; H, 2.33%. Calcd for $C_{15}H_8O_5Cl_2$: C, 53.12; H, 2.38%. MS m/z, 338, 340, and 342 (M^+). ^1H NMR δ=4.08 (3H, s), 7.16 (1H, s), 7.75 (1H, s), 8.27 (1H, s), and 8.40 (1H, s). IR ν 3500—3300, 3250, 3040, 1615, 1570, 1510, 900, and 860 cm^{-1}], and **17**, yellow crystals, mp 225—227 °C (decomp) [Found: M. W., 337.9750. Calcd for $C_{15}H_8O_5{}^{35}Cl_2$: M. W., 337.9749. ^1H NMR δ=4.04 (3H, s), 7.39 (1H, d, J=12 Hz), 7.85 (1H, d, J=12 Hz), 8.24 (1H, s), and 8.69 (1H, s). IR ν 3150, 1615, 890, and 850 cm^{-1}]. From the MeOH washings, the troponoids, **11** and **15**, 1.4 g (1:1), were recovered.

Methylation of 16 to 18. To a $CHCl_3$ solution (50 cm^3) of **16** (345 mg) was treated with ethereal CH_2N_2 to form precipitates, 223 mg, which were collected and sublimed at 300 °C to obtain 219 mg (55%) of colorless crystals, mp> 300 °C, **18** [Found: C, 54.30; H, 2.90%. Calcd for $C_{16}H_{10}O_5Cl_2$: C, 54.41; H, 2.86%. ^1H NMR δ=4.08 (6H, s), 7.12 (2H, s), and 8.25 (2H, s). MS m/z, 352, 354, 356 (M^+). IR ν 3025, 2940, 1615, 1580, and 990 cm^{-1}].

Hydrolysis of 16 to 13. An AcOH solution (4 cm^3) containing conc HCl (1 cm^3) of **16** (41 mg) was heated at 90 °C for 24 h. After evaporation of the mixture, the residue was washed with MeOH and sublimed on a cold finger to yield

yellow needles, **13**, mp>300 °C, 33 mg (85%) [Found: C, 51.90; H, 2.16%. Calcd for $C_{14}H_6O_5Cl_2$: C, 51.72; H, 1.86%. ^{1}H NMR (CF_3COOD) δ=8.38 (2H, s) and 8.75 (2H, s). MS *m/z*, 324, 326, 328 (M^+). IR ν 3250, 3040, 1620, 1590, 1570, 1500, and 1450 cm^{-1}].

Preparation of 5-Hydroxy-2-methoxytropone (19). A 50%-aqueous AcOH solution (10 cm^3) of **9** (600 mg) was heated at 90 °C for 16 h. The mixture was evaporated to dryness, and the residue washed by AcOEt. The crystalline residue was sublimed on a cold finger to yield **19**, pale yellow needles, mp 154—155 °C, 423 mg (91%) [Found: C, 62.99; H, 5.25%. Calcd for $C_8H_8O_3$: C, 63.15; H, 5.30%. ^{1}H NMR (CD_3OD) δ=3.86 (3H, s), 6.74 (1H, dd, *J*=11, 2 Hz), 7.11 (1H, d, *J*=11 Hz), and 7.24 (2H, d, *J*=2 Hz). ^{13}C NMR (CD_3OD) δ=56.6, 116.4, 119.1, 134.1, 138.1, 160.6, 161.9, and 178.5. IR ν 3100—2400, 1595, 1535, 980, 858, 840, and 780 cm^{-1}].

Condensation and Acetylation of 19 with 4 to 2-Acetoxy-10-methoxy Derivative (21). To a THF suspension (10 cm^3) of **19** (210 mg), a THF solution (10 cm^3) of **4** (190 mg) was added at 15—25 °C. After 16 h with stirring, the mixture was heated *in vacuo* to remove the solvent, and, without further purifications, was acetylated by Ac_2O (5 cm^3), and kept at 100 °C until the mixture became homogeneous. After cooling the mixture, the solvent was removed *in vacuo*, and the residual mass washed with EtOAc, and crystallized from $CHCl_3$ to give 275 mg (100%) of **21**, mp 237—239 °C [Found: C, 65.11; H, 3.80%. Calcd for $C_{17}H_{12}O_6$: C, 65.38; H, 3.87%. ^{1}H NMR δ=2.40 (3H, s), 4.01 (3H, s), 6.94 (1H, s), 7.16 (1H, d, *J*=12 Hz), 7.22 (1H, d, *J*=12 Hz), 7.54 (1H, d, *J*=12 Hz), 7.61 (1H, d, *J*=12 Hz), and 7.68 (1H, s). ^{13}C NMR δ=20.7, 56.6, 102.0, 119.3, 122.5, 123.8, 124.5, 125.4, 134.2, 136.4, 151.5, 153.6, 154.1, 161.3, 168.7, 178.1, and 179.8]. EtOAc-soluble fractions gave a mixture of 2,5-diacetoxytropone and **9**, 209 mg.

Hydrolysis of 21 to 10-Methoxy Derivative (20). A 50%-aqueous AcOH solution (10 cm^3) of **21** (275 mg) was heated at 100 °C with stirring for 16 h. After the solvent was evaporated, the residue was sublimed on a cold finger to give **20**, 220 mg (93%), mp>300 °C [Found: C, 66.54; H, 3.87%. Calcd for $C_{15}H_{10}O_5$: C, 66.67; H, 3.73%. ^{1}H NMR (CF_3COOD) δ=4.63 (3H, s), 8.09 (1H, d, *J*=12.5 Hz), 8.44 (1H, d, *J*=12.5 Hz), 8.53 (1H, d, *J*=11.7 Hz), 8.58 (1H, s), 8.97 (1H, d, *J*=11.7 Hz), and 9.03 (1H, s). MS *m/z*, 270 (M^+). UV ($CHCl_3$) λ_{max}: 263 nm (ε=29600), 272 (36200), 299 (18000), 321 (15200), 380 (20500), 396 (30800), and 411 (28500). IR ν 3250, 3050, 1610, 1565, 1520, 1460, 1410, 1250, 1200, 1155, 1110, and 980 cm^{-1}].

Methylation of 20 to 2,10-Dimethoxy Derivative (22). A $CHCl_3$ solution (3 cm^3) of **20** (50 mg) was treated with CH_2N_2 in Et_2O at 0—5 °C. Sublimation on a cold finger of the mixture yielded **20**, yellow crystals, mp 227—230 °C, 22 mg (57%) [Found: M. W., 284.0685. Calcd for $C_{16}H_{12}O_5$: M. W., 284.0684. ^{1}H NMR δ=4.08 (6H, s), 7.05 (2H, s), 7.21 (2H, d, *J*=13 Hz), and 7.62 (2H, d, *J*=13 Hz). ^{13}C NMR δ=56.5 (2C,) 103.0 (2C), 123.8 (2C), 124.9 (2C), 134.1 (2C), 151.7 (2C), 161.0 (2C), and 179.9 (2C). IR ν 1610, 1560, and 1520 cm^{-1}].

Condensation of 19 with 7 and Subsequent Transformation to 2,10-Diacetoxy-1-chloro Derivative (23) and 2,10-Diacetoxy-4-chloro Derivative (24). To a THF suspension (2 cm^3) of **19** (95 mg), a THF solution (4 cm^3) of **7** (106 mg) was added at 15—25 °C under N_2 atmosphere. The solvent was removed *in vacuo*, the resultant residue washed with MeOH, and the reddish yellow crystalline solid directly hydrolyzed in AcOH (7 cm^3) with conc HCl (1.5 cm^3) at 100 °C for 16 h. After evaporation of the solvent *in vacuo*, the residue, 74 mg, was acetylated with Ac_2O (7 cm^3) at 100 °C for 16 h. After removal of Ac_2O *in vacuo*, the residue was chromatographed on a silica-gel column to give at first, yellow crystals, **24**, mp 225—226 °C, 43 mg (50%) [Found: C, 57.47; H, 3.33%. Calcd for $C_{18}H_{11}O_7Cl$: C, 57.69; H, 2.96%. ^{1}H NMR δ=2.38 (3H, s), 2.40 (3H, s), 7.27 (1H, d, *J*=13 Hz), 7.60 (1H, s), 7.68 (1H, d, *J*=13 Hz), 7.69 (1H, s), and 8.30 (1H, s). ^{13}C NMR δ=20.5 (2C), 118.4, 118.8, 122.3, 122.7, 125.2, 137.3, 144.2, 151.6, 152.1, 154.3, 154.7, 168.3 (2C), 171.9, and 178.1. IR ν 3050, 2940, 1765, 1615, 1580, 1540, 1375, 1350, 1190, 1115, 1050, 930, and 855 cm^{-1}], and subsequently, other yellow needles, mp 158—159 °C, **23**, 2 mg (2%) [Found: C, 57.75; H, 3.13%. Calcd for $C_{18}H_{11}O_7Cl$: C, 57.69; H, 2.96%. ^{1}H NMR δ=2.38 (3H, s), 2.43 (3H, s), 7.17 (1H, d, *J*=12.5 Hz), 7.25 (1H, d, *J*=12.7 Hz), 7.64 (1H, d, *J*=12.5 Hz), 7.66 (1H, d, *J*=12.7 Hz), and 8.76 (1H, s). ^{13}C NMR δ=20.4, 20.6, 121.2, 121.4, 123.6, 125.2, 125.4, 133.1, 135.8, 136.9, 151.6, 152.9, 153.0, 154.7, 167.1, 168.4, 176.1, and 178.1. MS *m/z*, 374 and 376 (M^+). IR ν 3050, 2950, 1770, 1620, 1585, and 1179 cm^{-1}].

From the MeOH soluble fractions of the condensation reaction mixture, **11** and **9**, 98 mg (44%) were obtained.

Condensation of 15 with 4. Formation of 4-Chloro-2-methoxy Derivative (25): To a THF solution (2 cm^3) of **15** (164 mg), a THF solution (4 cm^3) of **4** (120 mg) was added at once under N_2 atmosphere. After stirring for 48 h the solvent was removed, and the residue washed with MeOH. The residue was collected by filtration and washed again with MeOH to give yellow crystals, mp>300 °C, **25**, 113 mg (35%) [Found: C, 59.00: H, 3.13%. Calcd for $C_{15}H_9O_5Cl$: C, 59.13; H, 2.98%. ^{1}H NMR (CF_3COOD) δ=4.44 (3H, s), 8.18 (1H, d, *J*=12 Hz), 8.38 (1H, s), 8.51 (1H, d, *J*=12 Hz), 8.87 (1H, s), and 8.95 (1H, s). MS *m/z*, 304 and 306 (M^+). UV ($CHCl_3$) λ_{max}:268 nm (ε=31600), 276 (37600), 299 (20000), 405 (32900), and 422 (32900). IR ν 3300, 3050, 1610, 1570, 1520, 1470, 1405, 1240, 1170, and 980 cm^{-1}].

Hydrolysis of 25 to 27. An AcOH solution (3 cm^3) of **25** (50 mg) and conc HCl (1 cm^3) was heated at 100 °C for 24 h. After removal of solvent *in vacuo*, the residue was sublimed on a cold finger to give yellow crystals, mp>300 °C, **27**, 44 mg (95%) [Found: C, 57.82; H, 2.70%. Calcd for $C_{14}H_7O_5Cl$: C, 57.85; H, 2.43%. ^{1}H NMR (CF_3COOD) δ=8.30 (1H, d, *J*=11.7 Hz), 8.40 (1H, s), 8.61 (1H, d, *J*=11.7 Hz), 8.81 (1H, s), and 8.83 (1H, s). UV ($CHCl_3$) λ_{max}:271 nm (ε=33100), 278 (39200), 302 (18100), 330 (13500), 394 (20700), 412 (31600), and 427 (27600). IR ν 3250, 3050, 1630, 1600, 1565, 1550, 1460, 1250, 1170, 1120, 880, 850, and 840 cm^{-1}].

Acetylation of 27 to 24. An Ac_2O solution (3 cm^3) of **27** (26 mg) was heated at 100 °C for 20 h to form yellow crystals, mp 225—226 °C, 28 mg (78%), which was identical with **24**.

Condensation of 19 with 5. To a THF suspension (10 cm^3) of **19** (69 mg), a THF solution (4 cm^3) of **5** (77 mg) was added at 15—25 °C. After 16 h, the mixture was heated *in vacuo* to remove the solvent, the residue was washed with MeOH to recover **19**, 40 mg (57%), and **6**, 42 mg (55%), and the residue sublimed *in vacuo* to give yellow crystals, mp 292—294 °C (decomp), 58 mg (100%), **26** [Found: C, 58.84; H, 2.97%. Calcd for $C_{15}H_9O_5Cl$: C, 59.13; H, 2.98%. ^{1}H NMR (CF_3COOD) δ=4.61 (3H, s), 8.28 (1H, s), 8.52 (1H, d, *J*=12 Hz), 8.65 (1H, s), 8.96 (1H, s), and 8.99 (1H, d, *J*=12 Hz). MS *m/z*, 304 and 306 (M^+). IR ν 3250, 3030, 1605, 1570, 1545, and 1510 cm^{-1}].

Hydrolysis of 26 to 5-Chloro Derivative (28). An AcOH

solution (3 cm^3) of **26** (17 mg) and conc HCl(1.5 cm^3) was heated at 100 °C for 4 h. Then, the mixture was evaporated *in vacuo*, and the residue trituated with MeOH, and sublimed on a cold finger to give **28**, 15 mg (83%) [Found: C, 57.82; H, 2.70%. Calcd for $C_{14}H_7O_5Cl$: C, 57.85; H, 2.43%. ^1H NMR (CF_3COOD) δ=8.16 (1H, d, J=12 Hz), 8.30 (1H, s), 8.44 (1H, s), 8.54 (1H, d, J=12 Hz), and 8.60 (1H, s). IR ν 3250, 3050, 1620, 1560, 1540, and 1519 cm^{-1}].

References

1) K. H. Baggaley and T. Norin, *J. Chem. Soc., Chem. Commun.*, **1968**, 233.

2) J. Runeberg, *Acta Chem. Scand.*, **14**, 797 (1960).

3) T. Nozoe, S. Ebine, S. Itô, and A. Konishi, *Proc. Jpn. Acad.*, **27**, 10 (1951).

4) T. Nozoe, S. Seto, S. Itô, M. Sato, and T. Katono, *Proc. Jpn. Acad.*, **28**, 488 (1952).

5) P. Akroyd, R. D. Haworth, and P. R. Jefferies, *J. Chem. Soc.*, **1954**, 286.

6) To avoid repetitions of lengthy names for these tricyclic compounds, they are expressed with the term, "derivative," unless otherwise specified for substituents on the C-2 and C-10, this is equivalent to 2,10-dihydroxydicyclohepta[*b,d*]-furan-3,9-dione.

7) H. Takeshita, T. Kusaba, and A. Mori, *Chem. Lett.*, **1982**, 701.

8) H. Takeshita, T. Kusaba, and A. Mori, *Chem. Lett.*, **1983**, 1371.

9) S. Itô, Y. Shoji, H. Takeshita, M. Hirama, and K. Takahashi, *Tetrahedron Lett.*, **1975**, 1075.

10) S. Itô and M. Hirama, *Tetrahedron Lett.*, **1976**, 2339.

11) This is an extended version of the Takase-Yasunami's NBS-bromination of 2-methoxytropone to 2,4-dibromo-7-methoxytropone. See K. Takase, M. Yasunami, and Y. Sasagawa, *Chem. Lett.*, **1980**, 205.

12) H. Sugiyama, S. Itô, and T. Nozoe, *Tetrahedron Lett.*, **1965**, 179.

13) T. Nozoe, S. Seto, S. Itô, M. Sato, and T. Katono, *Sci. Repts. Tohoku Univ. Ser. I*, **37**, 191 (1953).