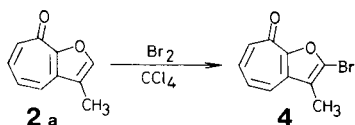


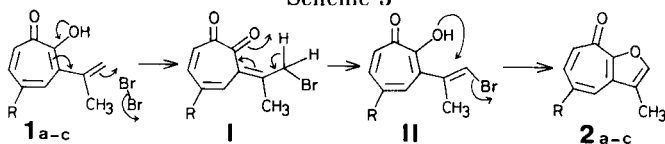
Scheme 2



The reaction of 3-isopropenyltropolone (**1a**) with an equimolar amount of bromine in acetic acid gave 5,7-dibromo-3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**3a**) in 24% yield. The treatment with two molar equivalents of bromine afforded the compound **3a** in 53% yield. Similarly, 5-alkyl-substituted tropolones **1b,c** were cyclized with two molar equivalents of bromine to give the corresponding compound **3b,c** in 44 and 72% yields, respectively.

In these reactions, the formation of **2a-c** seemed to proceed through intermediates **II** (Scheme 3). The reaction would be initiated by electrophilic attack of bromine at the ω -position of the isopropenyl group to form intermediates **II** via **I**. This reaction is facilitated by the participation of a neighboring hydroxyl group. The intermediates **II** were cyclized to the products **2a-c** by the nucleophilic attack of the hydroxyl oxygen atom to the ω -carbon atom bearing bromine atom by dehydrobromination. Such a process has been reported in the cyclization of 2-hydroxy- β -bromostyrenes to benzofuran derivatives [7,8]. The compounds **3a-c** would be formed by bromination of **1a-c** and the successive cyclization as similar as the formation of **2a-c**. This is supported by the fact that the treatment of 3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**2a**) with bromine did not give 7-bromo- or 5,7-dibromo-3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**3a**) but gave 2-bromo-3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**4**).

Scheme 3



Reactions of 3-Isopropenyltropolones **1a-c** with NBS.

A mixture of 3-isopropenyltropolone (**1a**) and an equimolar amount of NBS in carbon tetrachloride was stirred for 1 hour at room temperature to afford 5,7-dibromo-3-(2-bromo-1-methylethenyl)tropolone (**5a**) in 31% yield. Bromination with two molar equivalents of bromine gave **5a** in 60% yield. From the orientation in electrophilic substitution at the tropolone nucleus, it was expected that the bromo substituents should be present at 5-, 7-, and/or ω -position. The structure was confirmed on the basis of its spectral data and elemental analysis. The ir spectrum showed the tropolone hydroxyl and carbonyl absorptions at 3185 and 1600 cm^{-1} , respectively. This is also supported by coloration with iron(III) chloride solution. In the ^1H nmr spectrum, two doublet peaks ($J = 1.6$ Hz) at δ 7.67 and 8.32 showed that two bromine atoms are substituted

at the 5- and 7-positions. Another bromine atom is present on the side chain. This is supported by observation of a multiplet of the olefinic proton at δ 6.37. Further, the methyl signal at δ 2.11 (d, $J = 1.8$ Hz) showed that the olefinic proton is orientated in *Z*-form.

Bromination of 3-isopropenyl-5-methyltropolone (**1b**) also gave 7-bromo-3-(2-bromo-1-methylethenyl)-5-methyltropolone (**5b**) in 55% yield. However, 3-isopropenyl-5-isopropyltropolone (**1c**) afforded the corresponding substitution product **5c** (11%) and additionally cyclized 7-bromo-5-isopropyl-3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**3c**) (35%). In the reaction of the compound **1c**, the formation of the cyclization product **3c** might be attributed to releasing steric hindrance of the more bulky isopropyl group at the 5-position.

Cyclization of 3-(2-Bromo-1-methylethenyl)tropolones **5a-c**.

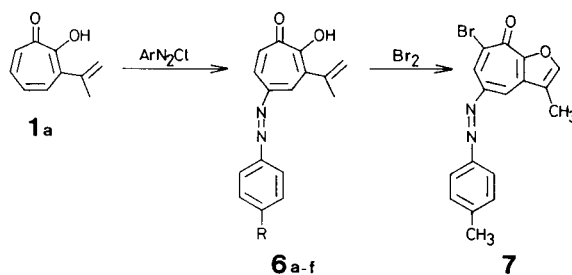
A solution of 3-(2-bromo-1-methylethenyl)tropolone (**5a**) in carbon tetrachloride was refluxed for 3 hours in the presence of potassium carbonate to afford the cyclized compound **3a** in 87% yield. The compounds **5b,c** also gave the corresponding compounds **3b,c** in 82 and 76% yields, respectively.

Azo-coupling Reactions and Nitration of 3-Isopropenyltropolone (**1a**).

In addition to the bromination reactions, a few electrophilic substitution reactions were carried out. Azo-coupling reactions of 3-isopropenyltropolone (**1a**) with several arenediazonium ions gave the corresponding 5-aryloxy-3-isopropenyltropolones **6a-f**. The treatment of the compound **6b** with bromine afforded the cyclized 7-bromo-3-methyl-5-(4-methylphenylazo)-8*H*-cyclohepta[*b*]furan-8-one (**7**) in 49% yield. These structures were determined on the basis of their spectral data and elemental analyses.

Nitration of 3-isopropenyltropolone (**1a**) gave complex resinous material but no product was isolated.

Scheme 4



a	R = H	d	R = Cl
b	R = CH ₃	e	R = Br
c	R = OCH ₃	f	R = NO ₂

EXPERIMENTAL

Measurements.

The melting points were determined with a Yanagimoto MP-S3 apparatus and are uncorrected. The ir spectra were taken on a JASCO A-102 and a Perkin-Elmer 1730 spectrophotometer. The ¹H nmr spectra were measured with a JEOL JNM-PMX60SI spectrometer.

Reaction of 3-Isopropenyltropolones **1a-c** with Bromine in Carbon Tetrachloride.

General Procedure.

To a stirred solution of 3-isopropenyltropolones **1a-c** (2 mmoles) in carbon tetrachloride (5 ml) was added bromine (640 mg, 4 mmoles) in carbon tetrachloride (1 ml) at water-cooled temperature. After stirring for 1 hour, the mixture was poured into water (100 ml) and extracted with chloroform. The extract was washed with a sodium hydrogensulfite solution and water, and dried over sodium sulfate. The evaporated residue was chromatographed on two Wakogel B-10 plates (30 x 30 cm) with ethyl acetate and recrystallized from ethanol to give 3-methyl-8*H*-cyclohepta[*b*]furan-8-ones **2a-c** and their bromo-substituted derivatives **3a-c**.

3-Methyl-8*H*-cyclohepta[*b*]furan-8-one (**2a**).

This compound was obtained as pale orange-yellow prisms, mp 95-97° (lit [5], 95-96°).

3,5-Dimethyl-8*H*-cyclohepta[*b*]furan-8-one (**2b**).

This compound was obtained as pale yellow prisms, mp 160-161°; ir (chloroform): ν max 1625 cm⁻¹ (C=O); ¹H nmr (deuteriochloroform): δ 2.23 (3H, s, 3-CH₃), 2.44 (3H, s, 5-CH₃), 7.21 (3H, s, H-4, 6, 7), 7.64 (1H, s, H-2).

Anal. Calcd. for C₁₁H₁₀O₂: C, 75.84; H, 5.79. Found: C, 75.59; H, 5.81.

5-Isopropyl-3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**2c**).

This compound was obtained as pale yellow prisms, mp 67-69°; ir (chloroform): ν max 1625 cm⁻¹ (C=O); ¹H nmr (deuteriochloroform) δ 1.29 [6H, d, J = 7.0 Hz, 5-C(CH₃)₂], 2.25 (3H, s, 3-CH₃), 2.93 (1H, sept, J = 7.0 Hz, 5-CH), 7.26 (3H, s, H-4, 6, 7), 7.65 (1H, brs, H-2).

Anal. Calcd. for C₁₃H₁₄O₂: C, 77.20; H, 6.98. Found: C, 77.09; H, 7.11.

5,7-Dibromo-3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**3a**).

This compound was obtained as greenish yellow needles, mp 228-229°; ir (chloroform): ν max 1627 cm⁻¹ (C=O); ¹H nmr (deuteriochloroform): δ 2.23 (3H, s, CH₃), 7.67 (1H, s, H-2), 7.74 (1H, d, J = 1.6 Hz, H-6), 8.47 (1H, d, J = 1.6 Hz, H-4).

Anal. Calcd. for C₁₀H₆O₂Br₂: C, 37.77; H, 1.90. Found: C, 38.02; H, 1.95.

7-Bromo-3,5-dimethyl-8*H*-cyclohepta[*b*]furan-8-one (**3b**).

This compound was obtained as greenish yellow needles, mp 172-174°; ir (chloroform): ν max 1630 cm⁻¹ (C=O); ¹H nmr (deuteriochloroform): δ 2.23 (3H, s, 3-CH₃), 2.46 (3H, s, 5-CH₃), 7.21 (1H, d, J = 1.6 Hz, H-6), 7.62 (1H, s, H-2), 8.14 (1H, d, J = 1.6 Hz, H-4).

Anal. Calcd. for C₁₁H₉O₂Br: C, 52.20; H, 3.58. Found: C, 52.26; H, 3.47.

7-Bromo-5-isopropyl-3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**3c**).

This compound was obtained as pale yellow prisms, mp 147-149°; ir (chloroform): ν max 1625 cm⁻¹ (C=O); ¹H nmr (deuteriochloroform): δ 1.28 [6H, d, J = 7.0 Hz, 5-C(CH₃)₂], 2.23 (3H, s, 3-CH₃), 2.95 (1H, sept, J = 7.0 Hz, 5-CH), 7.26 (1H, d, J = 1.6 Hz, H-6), 7.65 (1H, s, H-2), 8.19 (1H, d, J = 1.6 Hz, H-4).

Anal. Calcd. for C₁₃H₁₃O₂Br: C, 55.53; H, 4.66. Found: C, 55.83; H, 4.39.

Bromination of 3-Methyl-8*H*-cyclohepta[*b*]furan-8-one (**2a**) with Bromine.

To a stirred solution of 3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**2a**) (160 mg, 1.0 mmole) in carbon tetrachloride (5 ml) was added bromine (160 mg, 1.0 mmoles) in carbon tetrachloride (1 ml). After stirring for 1 hour, the mixture was poured into water, extracted with chloroform, washed with sodium hydrogensulfite solution and water, and dried over sodium sulfate. The evaporated residue was chromatographed on a Wakogel B-10 plate (30 x 30 cm) with ethyl acetate to give 2-bromo-3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**4**) as colorless micro-crystals, yield 61 mg (26%), mp 172-173°; ir (chloroform): ν max 1625 cm⁻¹ (C=O); ¹H nmr (deuteriochloroform): δ 2.18 (3H, s, CH₃), 6.8-7.5 (4H, m).

Anal. Calcd. for C₁₀H₇O₂Br: C, 50.24; H, 2.95. Found: C, 49.83; H, 3.06.

Reaction of 3-Isopropenyltropolones **1a-c** with Bromine in Acetic acid.

General Procedure.

To a stirred solution of 3-isopropenyltropolones **1a-c** (10 mmoles) in acetic acid (30 ml) containing sodium acetate (1.2 g, 15 mmoles) was added bromine (3.2 g, 20 mmoles) in acetic acid (3 ml) at water-cooled temperature. After stirring for 1 hour, a yellowish orange precipitate was collected and dissolved in chloroform. The solution was washed with a sodium hydrogen-carbonate solution, sodium hydrogensulfite solution, and water, and dried over sodium sulfate. The evaporated residue was recrystallized from ethanol to afford bromo-substituted-3-methyl-8*H*-cyclohepta[*b*]furan-8-ones **3a-c**.

Reaction of 3-Isopropenyltropolones **1a-c** with NBS.

General Procedure.

A mixture of 3-isopropenyltropolones **1a-c** (5 mmoles) and NBS (1.78 g, 10 mmoles) in carbon tetrachloride (16 ml) was refluxed for 30 minutes on a water bath. After removal of a precipitate, the filtrate was washed with a sodium hydrogensulfite solution and water and dried over sodium sulfate. The evaporated residue was recrystallized from ethanol to give 3-(2-bromo-1-methylethenyl)tropolone [**5a** (1.20 g, 60%), **5b** (920 mg, 55%)] from **1a,b** and 7-bromo-5-isopropyl-3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**3c**) (490 mg, 35%) and 3-(2-bromo-1-methylethenyl)-5-isopropyltropolone (**5c**) (195 mg, 11%)] from **1c**, respectively.

5,7-Dibromo-3-(2-bromo-1-methylethenyl)tropolone (**5a**).

This compound was obtained as yellow needles, mp 164-165°; ir (potassium bromide): ν max 3185 (OH), 1610 cm⁻¹ (C=O); ¹H nmr (deuteriochloroform): δ 2.11 [3H, s, 3-C(CH₃)₂], 6.37 (1H, m, =CH₂), 7.67 (1H, d, J = 1.6 Hz, H-4), 8.32 (1H, d, J = 1.6 Hz, H-6).

Anal. Calcd. for C₁₀H₇O₂Br₃: C, 30.11; H, 1.77. Found: C, 30.24; H, 1.82.

7-Bromo-5-methyl-3-(2-bromo-1-methylethenyl)tropolone (**5b**).

This compound was obtained as yellow micro-needles, mp 104-106°; ir (chloroform): ν max 3140 (OH), 1610 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.12 [3H, d, $J = 1.8$ Hz, 3-C(CH₃)], 2.43 (3H, s, 5-CH₃), 6.29 (1H, m, =CH_Z), 7.23 (1H, brd, $J = 2.0$ Hz, H-4), 7.29 (1H, brd, $J = 2.0$ Hz, H-6).

Anal. Calcd. for C₁₁H₁₀O₂Br₂: C, 39.55; H, 3.02. Found: C, 39.85; H, 3.00.

7-Bromo-5-isopropyl-3-(2-bromo-1-methylethenyl)tropolone (**5c**).

This compound was obtained as yellow needles, mp 139-140°; ir (chloroform): ν max 3140 (OH), 1605 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 1.27 [6H, d, $J = 7.0$ Hz, 5-C(CH₃)₂], 2.13 (3H, brs, 3-C(CH₃)₂), 2.82 (1H, sept, $J = 7.0$ Hz, 5-CH), 6.31 (1H, m, =CH_Z), 7.27 (1H, d, $J = 1.8$ Hz, H-4), 7.90 (1H, brd, $J = 1.8$ Hz, H-6).

Anal. Calcd. for C₁₃H₁₄O₂Br₂: C, 43.21; H, 3.90. Found: C, 43.21; H, 4.02.

Cyclization of 3-(2-Bromo-1-methylethenyl)tropolones **5a-c**.

General Procedure.

A solution of 3-(2-bromo-1-methylethenyl)tropolones **5a-c** (0.1 mmole) in carbon tetrachloride (5 ml) was refluxed for 3 hours in the presence of potassium carbonate (14 mg, 0.1 mmole). After filtration of the carbonate, the filtrate was evaporated to dryness and recrystallized from ethanol to give the 8*H*-cyclohepta[*b*]furan-8-one [**3a** (28 mg, 87%), **3b** (21 mg, 82%), **3c** (21 mg, 76%)].

Diazo-coupling Reaction of 3-Isopropenyltropolone (**1a**).

General Procedure.

To a solution of 3-isopropenyltropolone (**1a**) (810 mg, 5 mmoles) in pyridine (10 ml) was added dropwise the arenediazonium chloride solution, prepared from the substituted aniline (5.5 mmoles), with stirring under cooling with an ice-cooled bath. After stirring for 2 hours at the same temperature, the precipitate was collected and recrystallized from benzene to give 5-arylazo-3-isopropenyltropolones **6a-f**.

3-Isopropenyl-5-phenylazotropolone (**6a**).

This compound was obtained as orange needles; yield 530 mg (40%), mp 142-143°; ir (potassium bromide): ν max 3175 (OH), 1605 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.21 (3H, s, CH₃), 5.15 (1H, m, =CH_E), 5.30 (1H, m, =CH_Z), 7.2-8.3 (6H, m).

Anal. Calcd. for C₁₆H₁₄N₂O₂: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.18; H, 5.31; N, 10.24.

3-Isopropenyl-5-(4-methylphenylazo)tropolone (**6b**).

This compound was obtained as orange needles, yield 950 mg (68%); mp 152-153°; ir (potassium bromide): ν max 3195 (OH), 1614 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.20 [3H, s, 3-C(CH₃)], 2.40 (3H, s, 4'-CH₃), 5.13 (1H, m, =CH_E), 5.30 (1H, m, =CH_Z), 7.2-8.5 (7H, m).

Anal. Calcd. for C₁₇H₁₆N₂O₂: C, 72.83; H, 5.75; N, 10.00. Found: C, 72.71; H, 5.93; N, 9.96.

3-Isopropenyl-5-(4-methoxyphenylazo)tropolone (**6c**).

This compound was obtained as orange needles, yield 830 mg (56%), mp 126-127°; ir (potassium bromide): ν max 3195 (OH), 1603 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.25 (3H, s, CH₃), 3.90 (3H, s, OCH₃), 5.12 (1H, m, =CH_E), 5.29 (1H, m,

=CH_Z), 6.9-8.3 (7H, m).

Anal. Calcd. for C₁₇H₁₆N₂O₃: C, 68.90; H, 5.44; N, 9.46. Found: C, 68.90; H, 5.31; N, 9.39.

5-(4-Chlorophenylazo)-3-isopropenyltropolone (**6d**).

This compound was obtained as reddish orange needles, yield 920 mg (61%), mp 140-141°; ir (potassium bromide): ν max 3201 (OH), 1628 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.21 (3H, s, CH₃), 5.12 (1H, m, =CH_E), 5.28 (1H, m, =CH_Z), 7.31 (1H, d, $J = 10.0$ Hz, H-7), 7.41 (2H, dm, $J = 8.0$ Hz, H-3',4'), 7.75 (2H, dm, $J = 8.0$ Hz, H-2',6'), 8.00 (1H, dd, $J = 10.0, 2.0$ Hz, H-4), 8.20 (1H, d, $J = 2.0$ Hz, H-6).

Anal. Calcd. for C₁₆H₁₃N₂O₂Cl: C, 63.90; H, 4.36; N, 9.32. Found: C, 63.90; H, 4.38; N, 9.39.

5-(4-Bromophenylazo)-3-isopropenyltropolone (**6e**).

This compound was obtained as reddish orange needles, yield 1.38 g (80%), mp 151-152°; ir (potassium bromide): ν max 3199 (OH), 1608 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.15 (3H, s, CH₃), 5.12 (1H, m, =CH_E), 5.29 (1H, m, =CH_Z), 7.2-8.3 (7H, m).

Anal. Calcd. for C₁₅H₁₃O₂Br₂: C, 55.67; H, 3.80; N, 8.12. Found: C, 55.76; H, 3.89; N, 8.13.

3-Isopropenyl-5-(4-nitrophenylazo)tropolone (**6f**).

This compound was obtained as orange red needles, yield 780 mg (50%), mp 170-171°; ir (potassium bromide): ν max 3107 (OH), 1609 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.15 (3H, s, CH₃), 5.15 (1H, m, =CH_E), 5.30 (1H, m, =CH_Z), 7.2-8.4 (7H, m).

Anal. Calcd. for C₁₆H₁₃N₃O₄: C, 61.73; H, 4.21; N, 13.50. Found: C, 61.44; H, 4.38; N, 13.56.

Reaction of 3-Isopropenyl-5-(4-methylphenylazo)tropolone (**6b**) with Bromine.

To an ice-cooled stirred solution of **5b** (280 mg, 1 mmole) in pyridine (6 ml) was added dropwise bromine (320 mg, 2 mmoles). After stirring for 2 hours, the reaction mixture was poured into water (10 ml). A yellow precipitate was collected and recrystallized from benzene to give 7-bromo-3-methyl-5-(4-methylphenylazo)-8*H*-cyclohepta[*b*]furan-8-one (**7**) as yellowish orange crystals, yield 170 mg (49%); mp 232-233°; ir (potassium bromide): ν max 1658 cm^{-1} (C=O); ^1H nmr (deuteriochloroform): δ 2.50 (3H, s, CH₃), 2.61 (3H, s, CH₃), 7.42 (2H, dm, $J = 8.0$ Hz, H-3',5'), 7.81 (1H, s, H-2), 8.01 (2H, dm, $J = 8.0$ Hz, H-2',6'), 8.32 (1H, d, $J = 1.8$ Hz, H-6), 9.21 (1H, d, $J = 1.8$ Hz, H-4).

Anal. Calcd. for C₁₇H₁₃N₂O₂Br: C, 57.16; H, 3.67; N, 7.84. Found: C, 56.91; H, 3.73; N, 7.56.

REFERENCES AND NOTES

- [1] T. Nozoe, K. Takase, and H. Matsumura, "Dai Yuki Kagaku", M. Kotake, ed, Asakura Shoten, Tokyo, 1960, Vol **13**, pp 1-437.
- [2] F. Pietra, *Chem. Rev.*, **73**, 293 (1973).
- [3] D. Lloyd, "Non-benzenoid Conjugated Carbocyclic Compounds", Elsevier, Amsterdam, 1984, pp 107-125.
- [4] K. Takase, T. Kusunose, and T. Meguro, 12th National Meeting of the Chemical Society of Japan, 1959, (Ref [1], p 173).
- [5] K. Imafuku, K. Yamaguchi, and H. Matsumura, *Bull. Chem. Soc. Japan.*, **53**, 745 (1980).
- [6] K. Imafuku and K. Arai, *Synthesis*, 501 (1989).
- [7] G. Komppa, *Ber.*, **28**, 2968 (1893).
- [8] R. Stromer and M. Simon, *Liebigs Ann. Chem.*, **342**, 1 (1905).