BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 41 2942—2948 (1968)

3,4-Benzotropolone and Related Compounds. V.[1] Bromo- and Hydroxy-2,3-benzotropones

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(Received February 8, 1968)

Isomeric 5,7- and 4,7-dibromo-2,3-benzotropones were prepared, not *via* 2,3-benzotropone, but by the bromination and subsequent dehydrobromination of 2,3-benzocycloheptenone. The tropone structure of these compounds was based on spectral data and hydrogenation to 2,3-benzocycloheptenone. The dibromo-2,3-benzotropones, when treated with hydroxylamine, underwent cine-reaction to 5- and 4-bromo-6-hydroxylamino-2,3-benzotropone oximes, which were then hydrolyzed and debrominated to the same 6-hydroxy-2,3-benzotropone. 5,7,5′-Tribromo-2,3-benzotropone was obtained by the drastic bromination, followed by the dehydrobromination, of 2,3-benzocycloheptenone. The position of a hydroxyl group in 6-hydroxy-2,3-benzotropone was confirmed by oxidation to *o*-carboxycinnamic acid, while that of the 5′-bromo substituent in 5,7,5′-tribromo-2,3-benzotropone was confirmed by hydrogenation to 5′-bromo-2,3-benzocycloheptenone.

It has previously been found that the treatment of 2-cycloheptenone[2] or cycloheptanone[3] with bromine brings about bromination, followed by spontaneous dehydrobromination, to afford 2,4,7-tribromotropone. According to this reaction, an attempt was made to prepare a bromo-substituted benzotropone by treating 2,3-benzocycloheptenone (I) with bromine. The reaction of I with excess bromine, however, did not give a brominated benzotropone, but instead produced two isomeric tetrabromo-2,3-benzocycloheptenones (IIa, mp 142°C and IIb, mp 146.5°C). The application of less bromine to I gave tribromo-2,3-benzocycloheptenone, and the reaction of I with bromine in the presence of sodium acetate produced dibromo-acetoxy-2,3-benzocycloheptenone.*2

The dehydrobromination of IIa was then attempted. IIa remained unchanged when heated with sodium acetate in an ethanolic or acetic acid solution, and resinified when treated with diethylamine or potassium hydroxide in an ethanolic solution at room temperature. IIa was effectively dehydrobrominated when its pyridine solution was allowed to stand at room temperature for a week it yielded two isomeric dibromo-2,3-benzotropones (IIIa and IIIb), with a predominance of the former. Under the same conditions, IIb produced only IIIa. The tropone structure of IIIa and IIIb is assumed on the basis of the catalytic reduction to 2,3-benzotropone (in a low yield) and I (in a fair yield), the ultraviolet absorption spectra having peaks in the 220—270 and 300—350 mμ

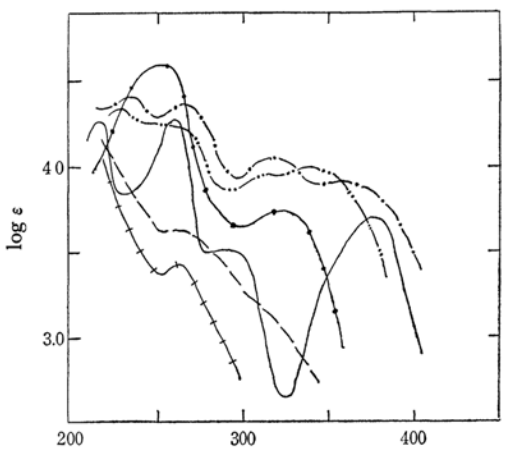

Fig. 1. Ultraviolet absorption spectra of isomeric tetrabromo-2,3-benzocycloheptenones (IIa, — — and IIb, +—+), isomeric dibromo-2,3-benzotropones (5,7-dibromo-, IIIa, —·— and 4,7-dibromo-, IIIb, —··—), uncharacterized compound (VII, ——) and 6-hydroxy-2,3-benzotropone (VIII, —•—•—) in methanol.

1) Part IV, This Bulletin, S. Ebine, **38**, 2029 (1965).

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2) H. J. Dauben and H. J. Ringold, *J. Am. Chem. Soc.*, **73**, 876 (1951).

3) T. Nozoe, Y. Kitahara, T. Ando and S. Masamune, *Proc. Japan Acad.*, **27**, 415 (1951); T. Nozoe, Y. Kitahara, T. Ando, S. Masamune and H. Abe, *Sci. Repts. Tohoku Univ., Ser. I*, **36**, 166 (1952).

*2 These brominated benzocycloheptenones, when oxidized with permanganate, gave phthalic acid, indicating that they possess all the bromo substituents in the cycloheptenone ring.

regions (Fig. 1), and the infrared absorption spectra having carbonyl bands at frequencies below 1650 cm^{-1} (Experimental), characteristics which are in accord with the spectral features of troponoid compounds.[4] IIIa and IIIb, like other troponoid compounds, dissolve in concentrated sulfuric acid and precipitate unchanged upon dilution with water. IIIa was not affected when heated with sodium acetate in a methanolic or an acetic acid solution at 120°C for 10 hr, with cupric acetate in a pyridine solution at 110°C for 12 hr, and with concentrated hydrochloric acid in an acetic acid solution at 150°C for 50 hr. It has been found that the out-of-plane deformation vibration of troponoid CH in halogenated benzotropolones is correlated with the position of the halogen substituents,[5] but the infrared absorption spectra of IIIa and IIIb made possible no definite conclusion regarding the position of substituents. IIIa showed an infrared absorption band at 898 cm^{-1}, hardly suggesting the presence of isolated hydrogen atoms.

In order to elucidate the position of the bromo substituents, IIIa and IIIb were subjected to Diels-Alder reaction with maleic anhydride, and the NMR spectra of the adducts were examined. The spectrum of the IIIb - maleic anhydride adduct contained AB-type absorption bands at 7.05 and 6.30 ppm (J=9.5 cps) ascribable to adjacent two ethylenic hydrogens, indicating that the adduct carries the bromo substituents at the positions given in Formula XVIIIb. It follows, therefore, that IIIb is the 4,7-dibromo compound. The spectrum of the IIIa - maleic anhydride adduct contained a doublet at 6.61 ppm with a long-range coupling constant (J=1.8 cps) ascribable to an ethylenic hydrogen which couples with a distant hydrogen, suggesting that the adduct carries the bromo substituents as given in formula XVIIIa or XVIIIa'. Accordingly, IIIa is either the 5,7- or 4,6-dibromo compound. As will be described below, IIIa and IIIb gave isomeric bromo-hydroxy-benzotropones (VIa and VIb, respectively) when treated with hydroxylamine and then with sulfuric acid, and these two isomers gave the same hydroxy-benzotropone (VIII) upon debromination. This fact leads to the conclusion that IIIa is the 5,7-dibromo compound. The position of bromo substituents was further proved to be 5,7- in IIIa and 4,7- in IIIb from an NMR spectral study of IIIa, IIIb, and related compounds, the details of which will be published elsewhere.[6] IIIa is presumably identical with Buchanan's dibromo-2,3-benzotropone obtained by the bromination of 2,3-benzotropone or 2,3-benzo-2,4-cycloheptadienone.[7]

IIIa was allowed to react with methanolic potassium hydroxide at room temperature to yield 5-bromo-6-methoxy-2,3-benzotropone (V), 5-bromo-6-hydroxy-2,3-benzotropone (VIa), and an uncharacterized compound (VII),*3 along with a considerable amount of tar. The ultraviolet absorption spectrum of V (Fig. 1) is essentially superimposable upon that of isomeric 7-bromo-3,4-benzotropolone methyl ether.[8]

IIIa and IIIb were treated with hydroxylamine in a pyridine solution to give 5-bromo-6-hydroxylamino-2,3-benzotropone oxime (Xa) and the corresponding 4-bromo isomer (Xb), which were then hydrolyzed with sulfuric acid to 5-bromo-6-hydroxy-2,3-benzotropone (VIa) and the corresponding 4-bromo isomer (VIb) respectively. These, in turn, were debrominated with hydrogen over a palladium-charcoal catalyst to the same 5-hydroxy-2,3-benzotropone (VIII). VIII was also produced from Xa or Xb *via* 6-hydroxylamino-2,3-benzotropone oxime (XI). VIII is soluble in dilute alkali or in concentrated sulfuric acid, and can be precipitated unchanged upon the neutralization of its alkaline solution or on the dilution of its concentrated sulfuric acid solution with water. VIII gives no ferric chloride coloration. The tropone structure of VIII is based on its ultraviolet absorption spectrum, which shows two peaks at 255 and 335 mμ (Fig. 1), and its infrared absorption spectrum, which shows a carbonyl band below 1650 cm^{-1}.[4] The position of a hydroxyl group of VIII was confirmed by oxidation with alkaline hydrogen peroxide to *o*-carboxycinnamic acid (XII), and by hydrogenation with excess hydrogen over a platinum oxide catalyst to 4,5-benzocycloheptene-1,3-diol (IX), followed by oxidation with potassium permanganate to *o*-carboxyhydrocinnamic acid (XIII).

4) For a reference on the ultraviolet spectra of troponoid compounds, see M. Tsuboi, This Bulletin, **25**, 369 (1952). For references on the infrared spectra of troponoid compounds, see S. Kinumaki, K. Aida and Y. Ikegami, *Sci. Repts. Res. Inst. Tohoku Univ.*, **A-8**, 263 (1956), and E. Kloster-Jensen, N. Tarkoy, A. Eschenmoser and E. Heilbronner, *Helv. Chim. Acta*, **39**, 780 (1956).

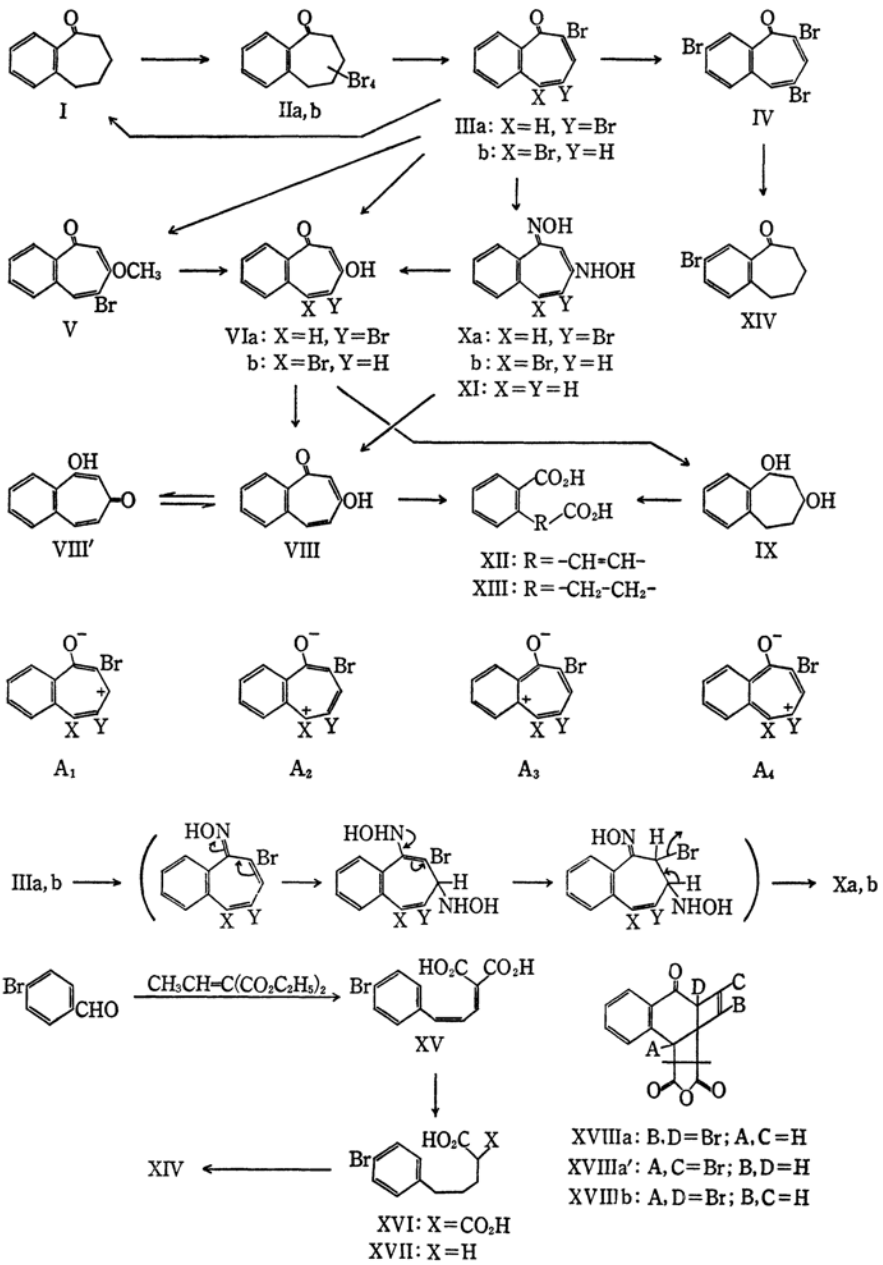
5) S. Ebine, This Bulletin, **35**, 119 (1962).

6) S. Ebine and M. Hoshino, This Bulletin, to be published.

7) G. L. Buchanan and D. R. Lockhart, *J. Chem. Soc.*, **1959**, 3586.

*3 The uncharacterized compound (VII) dissolves in alkali, shows a weak silver-mirror reaction, and produces a monoacetate. Its ultraviolet absorption spectrum (Fig. 1) deviates from those of general troponoid compounds and rather resembles those of hydroxynaphthaldehydes (N. C. Melchior, *J. Am. Chem. Soc.*, **71**, 3647 (1949).). The infrared absorption band at 1670 cm^{-1} (KBr) corresponds to carbonyl bands of hydroxynaphthaldehydes (I. M. Hunsberger, *ibid.*, **72**, 5626 (1950).). From these facts and by analogy with the transformation of 2-bromo-7-chlorotropone with alkali to 3-chlorosalicylaldehyde (T. Nozoe, S. Seto and S. Matsumura, *Proc. Japan Acad.*, **28**, 483 (1952); S. Seto, *Sci. Repts. Tohoku Univ., Ser. I*, **37**, 377 (1953).), VII is assumed to be hydroxy-methoxy-naphthaldehyde; however, it was not further investigated because we lacked a sample.

8) S. Ebine, This Bulletin, **35**, 115 (1962).



VIII is a novel isomer of previously-reported 4-hydroxy-2,3-benzotropone,[9] 3,4-benzotropolone,[10] and 4,5-benzotropolone.[11] VIII is capable of existing as a tautomeric mixture with 3-hydroxy-4,5-benzotropone (VIII'), but this compound gives a single methyl ether, acetate, and 2,4-dinitrophenylhydrazone. Although it is not clear which form predominates in the tautomeric mixture, the VIII formula is tentatively employed in this paper. VI and X would also hold under the same circumstances as VIII.

The halogenated troponoids tend to undergo abnormal "cine-reaction" on being treated with basic reagents.[12] The formation of V, VI and

9) G. L. Buchanan, *J. Chem. Soc.*, **1954**, 1060. G. L. Buchanan and J. K. Sutherland, *ibid.*, **1956**, 2620.

10) J. W. Cook and A. R. Somerville, *Nature*, **163**, 410 (1949). J. W. Cook, A. R. M. Gibb, A. R. Raphael and A. R. Somerville, *J. Chem. Soc.*, **1952**, 603.

11) H. Fernholz, E. Hartwig and J. C. Salfeld, *Ann.*, **576**, 131 (1952).

12) T. Nozoe and Y. Kitahara, *Proc. Japan Acad.*, **30**, 204 (1954). T. Nozoe, S. Seto and T. Sato, *ibid.*, **32**, 473 (1956).

X from III falls in the same category. The reason why III brings about such a type of reaction is as follows: the resonance structure of III is much contributed to by the A_1 and A_2 formulas, but little by the A_3 and A_4 formulas, because the condensed benzene ring of the former is aromatic, while that of latter is quinonoid[5,8,13]; moreover, a substitution reaction at the 4-position encounters a slight steric hindrance caused by the *peri* position of the benzene ring.[5] The mechanism of the formation of X from III is illustrated in the chart.

5,7,5′-Tribromo-2,3-benzotropone (IV) was prepared by the further bromination of IIIa, or by the bromination of I under drastic conditions and by subsequent treatment with pyridine. The position of the 5′-bromo substituent was determined by its oxidation to 4-bromophthalic acid and by its hydrogenation to 5′-bromo-2,3-benzocycloheptenone (XIV), which was identified by a synthesis consisting of the successive reactions shown in the chart: the condensation of *p*-bromobenzaldehyde with diethyl ethylidenemalonate to *p*-bromocinnamylidenemalonic acid, hydrogenation, followed by decarboxylation to δ-(*p*-bromophenyl-)valeric acid, and ring-closure with polyphosphoric acid to XIV.

It is noteworthy that, upon being treated with anionoid reagents, a 7-bromo substituent of 2,3-benzotropone derivatives undergoes an abnormal "cine substitution" exclusively.

Experimental*4

Bromination of 2,3-Benzocycloheptenone (I). *Dibromo-acetoxy-2,3-benzocycloheptenone.* A solution of 4 g of bromine in an equal amount of acetic acid was added to a solution of 1 g of 2,3-benzocycloheptenone (I) in 20 m*l* of acetic acid containing 6.6 g of sodium acetate, and the mixture was heated on a water bath for 5 hr. The evaporation of the acetic acid, and the crystallization of the residue from petroleum ether gave 470 mg (20%) of colorless needles; mp 104—105°C, infrared spectrum (Nujol): 1748 cm^{-1} for an acetyl carbonyl and 1720 cm^{-1} for a cycloheptenone carbonyl.

Found: C, 41.63; H, 3.42%. Calcd for $C_{13}H_{12}O_3Br_2$: C, 41.51; H, 3.22%.

Tribromo-2,3-benzocycloheptenone. A solution of 1 g of I and 4.0 g of bromine in 6 m*l* of acetic acid was heated on a water bath for 15 hr. The subsequent recrystallization of the product from dilute ethanol afforded 0.57 g (23%) of a colorless crystalline powder; mp 133—134°C.

Found: C, 33.45; H, 2.30%. Calcd for $C_{11}H_9OBr_3$: C, 33.28; H, 2.29%.

Isomeric Tetrabromo-2,3-benzocycloheptenones (IIa and IIb). A solution of 10 g of I and 40 g of bromine in 50 m*l* of acetic acid was heated on a water bath for 7 hr. To this there was again added 40 g of bromine, and heating was continued for a further 7 hr. The fractional recrystallization of the product from ethanol gave 12.6 g (43%) of IIa and 0.8 g (2.8%) of IIb.

IIa, colorless granular crystals, mp 141.5—142°C, infrared spectrum (Nujol): 1712 cm^{-1} for carbonyl, ultraviolet spectrum (MeOH): 265 mμ (log ε 3.65).

Found: C, 27.82; H, 2.03%. Calcd for $C_{11}H_8OBr_4$: C, 27.76; H, 1.70%.

IIb, colorless plates, mp 145.5—146.5°C, infrared spectrum ($CHCl_3$): 1717 cm^{-1} for carbonyl, ultraviolet spectrum (MeOH): 263 mμ (log ε 3.47).

Found: C, 27.79; H, 1.75%. Calcd for $C_{11}H_8OBr_4$: C, 27.76; H, 1.70%.

The admixture of IIa and IIb showed a depression in the melting point to *ca.* 112°C. Crude IIa and IIb produce severe vesication on the skin, but purified samples are harmless and can be handled safely.

Oxidation of IIa and IIb. IIa or IIb (0.5 g) dissolved in 180 m*l* of acetone was oxidized with 5 g of potassium permanganate by heating it under reflux for 2 hr; this afforded phthalic acid in 60—65% yields; mp and mixed mp 192—194°C. (It was further identified by conversion to phthalanil; mp and mixed mp 201—202°C.)

Isomeric 5,7-Dibromo-2,3-benzotropone (IIIa) and 4,7-Dibromo-2,3-benzotropone (IIIb). A solution of 8 g of IIa in 24 m*l* of pyridine was set aside at room temperature for a week. The crystalline product which thus separated was filtered and recrystallized from ethanol (100 m*l*) to yield 3.30 g (63%) of IIa as pale yellow fibrous needles; mp 165°C, infrared spectrum, (KBr) in carbonyl region: 1620, 1595, 1535 cm^{-1}, ultraviolet spectrum (MeOH): mμ (log ε), 242 (4.37), 277 (4.33), 325 (4.03), 370 (3.87).

Found: C, 41.97; H, 1.78%. Calcd for $C_{11}H_6OBr_2$: C, 42.07; H, 1.93%.

After the IIIa had been removed, the pyridine filtrate was diluted with water (50 m*l*) to give a precipitate of a second product. Recrystallization from petroleum ether gave 1.00 g (19%) of IIIb as pale yellow fibrous needles melting at 65.5°C; infrared spectrum (KBr) in carbonyl region: 1627, 1607, 1592, 1561, 1532 cm^{-1}, ultraviolet spectrum (MeOH): mμ (log ε), 235 (4.33), 270 (4.22), 320 (3.97), 340 (3.95).

Found: C, 42.29; H, 2.17%. Calcd for $C_{11}H_6OBr_2$: C, 42.07; H, 1.93%.

Hydrogenation of IIIa. a) A solution of 500 mg of IIIa in 250 m*l* of acetic acid was hydrogenated in the presence of 250 mg of 5% palladium-on-charcoal and 500 mg of anhydrous sodium acetate at an ordinary temperature and pressure. The uptake of hydrogen amounted to 4 mol equiv. After a usual work-up, crude I was obtained in good yield and identified by conversion to its 2,4-dinitrophenylhydrazone; red crystals, mp 204—205°C, undepressed on admixture with an authentic specimen of 2,3-benzocycloheptenone 2,4-dinitrophenylhydrazone. (Found: C, 59.74; H, 4.48; N, 16.53%. Calcd for $C_{17}H_{16}O_4N_4$: C, 59.99; H, 4.74; N, 16.46%).

b) A solution of 500 mg of IIIa in 100 m*l* of ethanol was hydrogenated as above until 2 mol equivalent of hydrogen had been taken up. The oily product was treated with 2,4-dinitrophenylhydrazine, giving 75 mg of 2,3-benzotropone 2,4-dinitrophenylhydrazone, mp 227—228°C. (Found: C, 61.07; H, 3.51; N, 16.06%. Calcd for $C_{17}H_{12}O_4N_4$: C, 60.71; H, 3.61; N, 16.66%).

13) S. Ebine, This Bulletin, **34**, 887 (1961).

*4 Thanks are due to the Department of Chemistry, Faculty of Science, Tohoku University, for the microanalyses.

Reaction of IIIa with Methanolic Potassium Hydroxide. A solution of 3.2 g of IIIa and 8 g of potassium hydroxide in 800 m*l* of methanol was allowed to stand at room temperature for 24 hr. The solution was acidified with 2 N hydrochloric acid and then concentrated to a semi-solid mass. The fractional recrystallization of the product from ethanol afforded 205 mg (6.4% recovery) of an unchanged material (IIIa), 360 mg (13%) of 5-bromo-6-methoxy-2,3-benzotropone (V), 50 mg (2.0%) of 5-bromo-6-hydroxy-2,3-benzotropone (VIa), and 50 mg of an uncharacterized product (VII).

5-Bromo-6-methoxy-2,3-benzotropone (V), colorless prisms, mp 140.5°C, infrared spectrum (KBr) in carbonyl region: 1617, 1578, 1565 cm^{-1}, ultraviolet spectrum (MeOH): mμ (log ε), 260 (4.58), 337 (3.76). V was also obtained in an excellent yield by the methylation of VIa with diazomethane.

Found: C, 54.43; H, 3.55%. Calcd for $C_{12}H_9O_2Br$: C, 54.36; H, 3.42%.

5-Bromo-6-hydroxy-2,3-benzotropone (VIa), described below.

An Uncharacterized Compound (VII), assumed to be hydroxy-methoxy-naphthaldehyde, pale yellow needles, mp 186°C, infrared spectrum (KBr) above 1500 cm^{-1}: 3447, 1670, 1621, 1601 cm^{-1}, ultraviolet spectrum (MeOH): mμ (log ε), 220 (4.32), 265 (4.26), 290 (3.52), 380 (3.64).

Found: C, 70.70; H, 4.74%. Calcd for $C_{12}H_{10}O_3$: C, 71.28; H, 4.99%.

Acetate of VII, colorless needles, mp 60—61°C.

Found: C, 68.78; H, 4.98%. Calcd for $C_{14}H_{12}O_4$: C, 68.84; H, 4.95%.

Isomeric 5-Bromo-6-hydroxylamino-2,3-benzotropone Oxime (Xa) and 4-Bromo-6-hydroxylamino-2,3-benzotropone Oxime (Xb). A solution of 5 g of IIIa (or IIIb) and 3.5 g of hydroxylamine hydrochloride in 160 m*l* of pyridine was allowed to stand at room temperature for 24 hr. The pyridine was then distilled below 30°C under reduced pressure, and the residue was recrystallized from ethanol; this yielded 2.40 g (71%) of Xa (or 2.47 g, 73%, of Xb).

Xa, colorless needles, mp 228°C (dec.).

Found: C, 46.92; H, 3.30; N, 9.66%. Calcd for $C_{11}H_9O_2N_2Br$: C, 47.00; H, 3.23; N, 9.97%.

Diacetate, colorless needles, mp 148—149°C.

Found: C, 49.61; H, 3.33; N, 7.49%. Calcd for $C_{15}H_{13}O_4N_2Br$: C, 49.82; H, 3.59; N, 7.67%.

Xb, colorless needles, mp 185—186°C (dec.).

Found: C, 47.16; H, 3.18; N, 9.59%. Calcd for $C_{11}H_9O_2N_2Br$: C, 47.00; H, 3.23; N, 9.97%.

Isomeric 5-Bromo-6-hydroxy-2,3-benzotropone (VIa) and 4-Bromo-6-hydroxy-2,3-benzotropone (VIb). a) Xa or Xb (2 g) dissolved in 75 m*l* of 80% sulfuric acid was heated at 160—165°C for 2.5 hr. After dilution with 1 *l* of water, the solution was extracted with ethyl acetate and the extract was shaken with 1 N sodium hydroxide. The acidification of the alkaline layer gave a crude product, which was then recrystallized from dilute ethanol or acetic acid to yield 1.52 g (85%) of VIa or 1.61 g (90%) of VIb.

VIa, pale yellow needles, mp 234°C (dec.).

Found: C, 52.67; H, 2.97%. Calcd for $C_{11}H_7O_2Br$: C, 52.61; H, 2.81%.

Acetate of VIa, colorless scales, mp 164.5°C.

Found: C, 53.00; H, 3.06%. Calcd for $C_{13}H_9O_3Br$: C, 53.27; H, 3.10%.

Methyl ether of VIa, described above as V.

VIb, pale yellow needles, mp 201—202°C (dec.).

Found: C, 52.59; H, 3.04%. Calcd for $C_{11}H_7O_2Br$: C, 52.61; H, 2.81%.

b) V (500 mg) was heated with 100 m*l* of concentrated hydrochloric acid on a water bath for 3.5 hr, this afforded VIa in a quantitative yield. The action of methanolic potassium hydroxide on IIIa also gave VIa, as has been described above.

Oxidation of VIa and VIb. VIa or VIb (350 mg) dissolved in 50 m*l* of 0.5 N sodium hydroxide was oxidized with 4 m*l* of 35% hydrogen peroxide in the same way as will be described below for the oxidation of VIII; this afforded phthalic acid in 40—45% yields.

6-Hydroxylamino-2,3-benzotropone Oxime (XI). a) The catalytic debromination of Xa or Xb (1 g) in ethanolic solution, using 5% palladium-on-charcoal (400 mg) and anhydrous sodium acetate (400 mg), was allowed to proceed until the hydrogen uptake amounted to 1 mol equivalent. The product was then recrystallized from ethanol, giving XI (590 mg, 82%), colorless needles, mp 205°C (dec.).

Found: C, 65.19; H, 4.72; N, 13.33%. Calcd for $C_{11}H_{10}O_2N_2$: C, 65.53; H, 4.98; N, 13.86%.

b) XI (130 mg, 74%) was also obtained by the reaction of VIII (150 mg) with hydroxylamine hydrochloride (150 mg) in a pyridine solution at 100°C for 2 hr in the same way as has been described for the formation of Xa and Xb.

6-Hydroxy-2,3-benzotropone (VIII). A solution of 1 g of VIa or VIb in 100 m*l* of ethanol, containing 200 mg of 5% palladium-on-charcoal and 660 mg of anhydrous sodium acetate, was shaken under a hydrogen atmosphere and at an ordinary temperature and pressure until 1 mol equivalent of hydrogen had been taken up. The product was recrystallized from ethanol to yield 540 mg (79%) of VIII, pale yellow needles, mp 208.5°C (dec.), infrared spectrum (KBr) above 1500 cm^{-1}: 3400, 3040, 2640, 2550, 1640, 1582, 1557, 1535 cm^{-1}, ultraviolet spectrum (MeOH): mμ (log ε), 255 (4.57), 335 (3.72).

VIII (70 mg, 21%) was also obtained by the hydrolysis of XI (400 mg) with 80% sulfuric acid (30 m*l*) at 160—165°C.

Found: C, 76.50; H, 4.46%. Calcd for $C_{11}H_8O_2$: C, 76.73; H, 4.68%.

Methyl Ether, colorless needles, mp 73—74°C.

Found: C, 77.71; H, 5.09%. Calcd for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41%.

Acetate, colorless needles, mp 97—98°C.

Found: C, 72.72; H, 4.78%. Calcd for $C_{13}H_{10}O_3$: C, 72.89; H, 4.71%.

VIII reacted with 2,4-dinitrophenylhydrazine to give 6-(2,4-dinitrophenylhydrazino-)2,3-benzotropone 2,4-dinitrophenylhydrazone, reddish-brown granular crystals, mp 273—275°C.

Found: C, 51.70; H, 2.81; N, 20.94%. Calcd for $C_{23}H_{16}O_8N_8$: C, 51.88; H, 3.03; N, 21.05%.

VIII reacted with hydroxylamine in pyridine at 100°C to give XI, mp and mixed mp 205°C.

Oxidation of VIII. To a solution of 200 mg of VIII in 20 m*l* of 0.5 N sodium hydroxide, 10 m*l* of 35% hydrogen peroxide were added; the resulting solution

14) F. Ramirez and A. F. Kirby, *J. Am. Chem. Soc.*, **75**, 6226 (1953).

was allowed to stand at room temperature (25°C) for 10 days. The product that separated on acidification was recrystallized from ethanol to give 130 mg (58%) of *o*-carboxycinnamic acid, mp 196—197°C (Found: C, 62.61; H, 4.19%. Calcd for $C_{10}H_8O_4$: C, 62.50; H, 4.20%). The mp was not depressed on admixture with an authentic sample,[15] and the infrared spectra of the two samples were superimposable in all respects.

4,5-Benzocycloheptene-1,3-diol] (IX). VIa (1 g), dissolved in 100 m*l* of ethanol, was hydrogenated over 200 mg of platinum oxide and 660 mg of anhydrous sodium acetate until the hydrogen uptake ceased. The semisolid product was then dissolved in benzene and chromatographed on silica gel, yielding 600 mg (85%) of colorless needles of IX, mp 98.5°C.

Found: C, 73.94; H, 7.73%. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92%.

Oxidation of IX. To a solution of 570 mg of IX in 50 m*l* of acetone, 990 mg of powdered potassium permanganate were added in small portions over a period of an hour, after which the reaction mixture was heated at 30°C for 5 hr. After the manganese dioxide had been removed by filtration, the filtrate was acidified, evaporated, and extracted with ether. The extract was evaporated to a syrup, which was then allowed to crystallize in an ice-chest. The recrystallization of the product from benzene gave 75 mg (12%) of *o*-carboxyhydrocinnamic acid, colorless needles, mp 165°C[16] (Found: C, 61.84; H, 4.98%. Calcd for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19%).

5,7,5′-Tribromo-2,3-benzotropone (IV). a) Bromine (25 g) was dropped into 5 g of 2,3-benzocycloheptenone (I) under ice-cooling; the resulting solution was allowed to stand at room temperature for 2 days and was then heated on a water bath for 15 hr. After the evaporation of the excess bromine, a dark brown, syrupy residue was dissolved in 10 m*l* of pyridine and set aside overnight to give a crystalline mass. The recrystallization of the product from acetic acid gave 2.7 g (24%) of IV, yellow needles, mp 205°C, and 1.0 g (11%) of IIIa.

Found: C, 33.89; H, 1.40%. Calcd for $C_{11}H_5OBr_3$: C, 33.62; H, 1.28%.

b) A solution of 300 mg of 5,7-dibromo-2,3-benzotropone (IIIa) in 1.5 g of bromine was refluxed for 3 hr. The excess bromine was evaporated, and the residual solid was crystallized from acetic acid to give 110 mg (29%) of IV, mp 205°C, (Found: C, 33.77; H, 1.38%).

Hydrogenation to 5′-Bromo-3,2-benzocycloheptenone (XIV). A solution of 400 mg of IV in 350 m*l* of acetic acid was shaken with hydrogen in the presence of 200 mg of 5% palladium-on-charcoal and 330 mg of fused sodium acetate at an ordinary temperature and pressure. After 4 mol equivalents (97 m*l*) of hydrogen had been taken up, the catalyst and the solvent were removed, the residue was extracted with ether, and the extract was evaporated. The crude XIV thus obtained was identified by converting it to its 2,4-dinitrophenylhydrazone, yellowish-orange needles, mp 243°C, (Found: C, 48.35; H, 3.45; N, 13.06%. Calcd for $C_{17}H_{15}N_4O_4Br$: C, 48.70; H, 3.61; N, 13.37%.), not depressed on admixture with a synthetic sample to be described below.

Oxidation to 4-Bromophthalic Acid. To a boiling solution of 500 mg of IV in 100 m*l* of acetone was added, portion by portion, 7.0 g of potassium permanganate; the solution was then refluxed for 3 hr. The excess potassium permanganate was decomposed by the addition of a little methanol, and the manganese dioxide that precipitated was collected and washed with 1 N potassium hydroxide. The acetone filtrate and alkaline washings were combined, acidified with hydrochloric acid, concentrated to a small volume, and extracted with ether. The ether extract was evaporated and the residual 4-bromophthalic acid was sublimed to give 245 mg (85%) of 4-bromophthalic anhydride, colorless granular crystals, mp and mixed mp 108—109.5°C.[17]

5,5′-Dibromo-6-hydroxylamino-2,3-benzotropone Oxime. A solution of 1 g of 5,7,5′-tribromo-2,3-benzotropone (IV) and 0.4 g of hydroxylamine hydrochloride in 80 m*l* of pyridine was treated in the same way as in the case of Xa. The product was recrystallized from ethanol to give 0.6 g (67%) of colorless crystals, mp 225°C.

Found: C, 37.01; H, 2.30; N, 7.39%. Calcd for $C_{11}H_8O_2N_2Br_2$: C, 36.69; H, 2.24; N, 7.68%.

5,5′-Dibromo-6-hydroxy-2,3-benzotropone. A solution of 500 mg of the above 5,5′-dibromo-6-hydroxylamino-2,3-benzotropone oxime in 22 m*l* of 66% sulfuric acid was heated at 160°C for 2 hr and then treated as has been described for VIa, b. The recrystallization of the product from ethanol gave 350 mg (76%) of pale yellow prisms melting at 243°C (dec.).

Found: C, 40.10; H, 1.57%. Calcd for $C_{11}H_6O_2Br_2$: C, 40.03; H, 1.83%.

Acetate: colorless needles (recrystallized from ethanol), mp 193—193.5°C.

Found: C, 41.93; H, 1.87%. Calcd for $C_{13}H_8O_3Br_2$: C, 41.97; H, 2.17%.

Synthesis of 5′-Bromo-3,2-benzocycloheptenone (XIV). The synthesis was carried out according to the reported method for the preparation of 2,3-benzocycloheptenone derivatives.[18]

p-Bromocinnamylidenemalonic Acid (XV). To a solution of 34.6 g of diethyl ethylidenemalonate and 11.3 g of *p*-bromobenzaldehyde in 113 m*l* of absolute ethanol, there was added, in small portions, 24.5 g of powdered potassium hydroxide; the resulting solution was allowed to stand at room temperature (18°C) for 2 days. The solution was then acidified with dilute hydrochloric acid, and the precipitate that separated was recrystallized from dilute acetone to yield 11.73 g (65%) of XV, yellow prisms, mp 199°C.

Found: C, 48.31; H, 3.37%. Calcd for $C_{12}H_9O_4Br$: C, 48.51; H, 3.02%.

δ-(p-Bromophenyl-)valeric Acid (XVII). A solution of 12 g of XV in 1200 m*l* of methanol was hydrogenated in the presence of 400 mg of platinum oxide. The hydrogenation was stopped after the uptake of 2 mol equivalents of hydrogen, the catalyst and the solvent were removed, and the residual γ-(*p*-bromophenyl)-propylmalonic acid (XVI) was decarboxylated by

15) J. Boesekin, *Rec. Trav. Chim.*, **30**, 146 (1911).
16) F. Strauss and A. Rohrbadher, *Ber.*, **54**, 66 (1921).
17) F. F. Blicke and F. D. Smith, *J. Am. Chem. Soc.*, **51**, 1871 (1929).
18) P. D. Gardner, W. J. Horton, G. Thompson and R. R. Twelves, *ibid.*, **74**, 5527 (1952).

heating it at 145—150°C under 10 mmHg. The recrystallization of the product from benzene - petroleum ether (1 : 1) gave 3.5 g (34%, based on XV) of XVII, colorless granular crystals, mp 91—92°C, along with a considerable amount of δ-phenylvaleric acid.

Found: C, 51.47; H, 4.91%. Calcd for $C_{11}H_{13}O_2Br$: C, 51.38; H, 5.10%.

5'-Bromo-2,3-benzocycloheptenone (XIV). XVII (3 g) was added, portion by portion, to hot (90°C) and stirred polyphosphoric acid prepared from 107 g of phosphoric acid and 95 g of phosphorus pentoxide. After heating at 100°C for 5 hr, the solution was poured onto crushed ice and extracted with ether. The extract was washed with dilute alkali. The acidification of the alkaline washings gave 2.0 g (66.7% recovery) of unreacted XVII, and the evaporation of the ether extract gave 0.8 g (28.6%) of crude XIV. 2,4-Dinitrophenylhydrazone of XIV: yellowish orange needles (from acetic acid), mp 243°C.

Found: C, 48.40; H, 3.51; N, 13.11%. Calcd for $C_{17}H_{15}N_4O_4Br$: C, 48.70; H, 3.61; N, 13.37%.

Diels-Alder Reaction of IIIa and IIIb. *Adduct of IIIa with Maleic Anhydride.* A mixture of 500 mg of IIIa and 500 mg of maleic anhydride was heated at 165°C for 30 min. After cooling, ether was added to the reaction mixture and an insoluble product was collected by filtration. The product was recrystallized from ether to give 400 mg (68%) of XVIIIa, colorless granular crystals, mp 216—217°C. The NMR spectrum in deuteriochloroform: 8.33—7.37 ppm (4H, multiplet, aromatic hydrogens), 6.61 ppm (doublet, J=1.8 cps, an ethylenic hydrogen), 4.40 ppm (multiplet, a benzylic hydrogen), 3.97 ppm (1H, a doublet, J=9 cps, of doublets, J=2.5 cps) and 3.70 ppm (1H, doublet, J=9 cps) (the latter two bands are attributable to two α-hydrogens of maleic anhydride part).

Found: C, 43.78; H, 2.33%. Calcd for $C_{15}H_8O_4Br_2$: C, 43.72; H, 1.96%.

Adduct of IIIb with Maleic Anhydride (XVIIIb). This was obtained in a similar manner by heating a mixture of 500 mg of IIIb and 500 mg of maleic anhydride at 165°C for 5 hr. Colorless needles, mp 255—256°C (dec.). Yield, 320 mg (55%). The NMR spectrum in acetonitrile; 8.20—7.25 ppm (4H, multiplet, aromatic hydrogens), 7.05 and 6.30 ppm (2H, AB-type doublets, J=9.5 cps, adjacent two ethylenic hydrogens), 4.65 and 4.20 ppm (2H, AB-type doublets, J=10.8 cps, adjacent two α-hydrogens of the maleic anhydride part).

Found: C, 44.22; H, 2.27%. Calcd for $C_{15}H_8O_4Br_2$: C, 43.72; H, 1.96%.

The present work has been supported in part by a Grant for Scientific Research from the Ministry of Education.