496. *Tropolones. Part III.* Halogenated Derivatives of Tropolone.*

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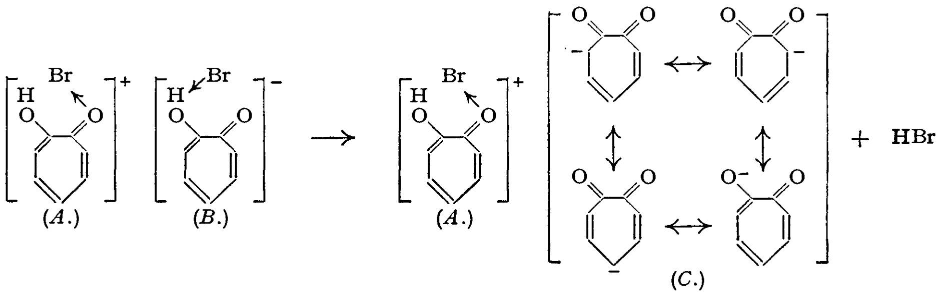
The courses of the bromination and iodination of tropolone are described and interpreted. The constitutions tentatively formulated in Part I (*J.*, 1951, 503) for the brominated tropolones have been confirmed by conversion of these derivatives into benzenoid compounds of known orientation.

As part of a detailed examination of the reactions of tropolone its bromination and iodination have been studied. Treatment of the compound in cold carbon tetrachloride or glacial acetic acid with a half-molecular proportion of bromine resulted in the immediate precipitation of a highly insoluble scarlet complex without the observable evolution of hydrogen bromide. The yield of this product was essentially the same when one and two molecular proportions of bromine were used, but was approximately halved when only a quarter-molecular proportion was employed. The complex was readily decomposed by water or methanol but could be crystallised unchanged from dry acetic acid; it remained unaltered for several months in a completely dry atmosphere. Analysis of the complex indicated that it contained one atom of bromine for each tropolone nucleus, a result confirming the stoicheiometry of the reaction. On being heated to 110° the complex decomposed to a colourless crystalline mass with concomitant evolution of hydrogen bromide; quantitative determination of the latter indicated that one molecule was formed from one molecule of the complex [on the assumption that this is $(C_7H_6O_2)_2,Br_2$]. Fractional sublimation of the colourless solid product gave tropolone, tropolone hydrobromide, and a mixture of brominated tropolones from which mono- and dibromotropolones could be isolated. Decomposition of the complex with water, sodium hydroxide solution, or methanol gave essentially similar products except that no tropolone hydrobromide was encountered.



To explain these phenomena the above ionic formulation (*A*–*B*) for the complex is proposed. The cation (*A*) is regarded as being formed by the donation of the carbonyl-oxygen lone pair to the unoccupied $4p$ orbital of the bromonium cation produced by heterolytic fission of the bromine molecule, thus yielding a structure analogous to the oxonium salts. The anion (*B*) is conceived to be the result of hydrogen bonding between the hydroxylic hydrogen atom of tropolone and the bromine anion, a construction closely resembling that of the well-established hydrofluoride ion $(F{-}H{\leftarrow}F^-)$. The formation of such a complex may thus be seen as a further manifestation of the amphoteric nature of the tropolone ring system.

It is reasonable to assume that thermal activation of the complex results in the ejection of one molecule of hydrogen bromide from the anion (*B*) to form the mesomeric anion (*C*). The cation (*A*) now functions as a source of the well-established brominating agent, bromonium cation, which interacts with the mesomeric anion (*C*) to produce brominated tropolones at the indicated points of electron access, tropolone itself being thereby regenerated from cation (*A*). Furthermore, the driving force of the reaction with hydroxylic solvents at room temperature may be taken to be the ease of formation of hydroxonium ion by interaction of anion (*B*) with a water molecule.

It is seen that this structural concept accommodates both qualitatively and quantitatively the above-mentioned experimental results concerning the formation, properties, and dis-

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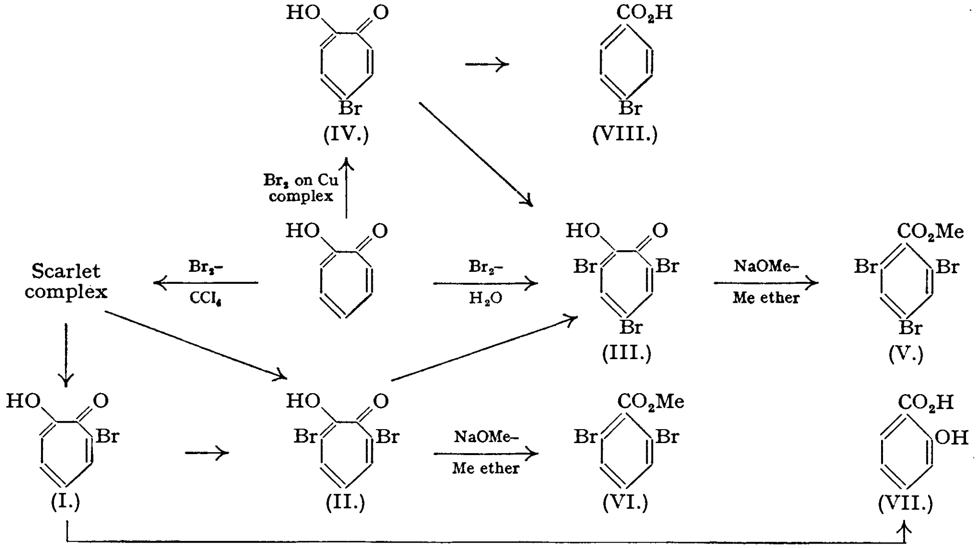
* Part II, *J.*, 1951, 695.

proportionation of the complex. The striking scarlet colour of the bromine complex is also in harmony with this formulation, being almost certainly due to that " type of absorption characterised by very great intensity, shown by certain crystals containing adjacent ions in different valency states " (Bowen, " Chemical Aspects of Light," Oxford Univ. Press, 1946, p. 144). Prussian-blue is the best-known example of this phenomenon. On this view, the intense long-wave absorption of the tropolone–bromine complex may be attributed to a ready anion–cation electron interchange resulting in an interconversion of their functions. That the colour is a crystal-structure effect is borne out by the fact that the acetic acid solution of the complex is pale yellow; this phenomenon is exactly paralleled in the case of $K_4Mn(CN)_6$, the dark blue crystals of which give a pale yellow solution (Bowen, *loc. cit.*). It is interesting that similar formation of highly coloured complexes with halogens has been observed in the case of a number of polycyclic aromatic compounds (for review see Cook, *Ann. Reports*, 1942, **39**, 167), and the recorded analyses of some of the compounds indicate a structure comparable with that of the above tropolone complex. Recently, evidence has accumulated that benzene itself forms complexes with halogens in solution, the aromatic nucleus functioning as an electron donor (for review and references see Keefer and Andrews, *J. Amer. Chem. Soc.*, 1950, **72**, 5170).

The mono- and di-bromotropolones obtained from the decomposition of the complex were found to be identical with the corresponding derivatives obtained by bromination of *cyclo*heptane-1 : 2-dione. Bromination of the monobromotropolone in acetic acid with one mole of bromine gave the same dibromotropolone. Further bromination of the dibromotropolone in acetic acid needed the application of heat and a tribromotropolone was obtained identical with that prepared by the exhaustive bromination of *cyclo*heptane-1 : 2-dione (Part I). The same tribromotropolone was also produced directly from tropolone by bromination in aqueous solution. In an attempt to avoid the aforementioned complications arising from the presence of the hydroxy-carbonyl system of tropolone, copper tropolone was brominated, as the formation of a chelate salt would be expected to annul the amphoteric nature of the parent compound. From the mixture of brominated tropolones thus obtained there was readily isolated in fair yield a new, higher-melting monobromotropolone (m. p. 188°). A small amount of this substance has also been isolated from the mother-liquors of the bromination of *cyclo*heptane-1 : 2-dione. Further bromination of this new product gave the same tribromotropolone encountered above. The formation and interrelationship of these bromo-derivatives may be formulated as in the annexed scheme.



The orientation of the derivatives was carried out in the following manner. The methyl ether of tribromotropolone on being heated for 30 minutes with methanolic sodium methoxide underwent smooth conversion into methyl 2 : 4 : 6-tribromobenzoate (V) identified by comparison with an authentic sample; this confirms the αα′γ-structure (III) for the parent compound. On similar treatment the methyl ether of dibromotropolone rearranged to methyl 2 : 6-dibromobenzoate (VI); this not only establishes the correctness of the αα′-structure (II) but also indicates that the lower-melting monobromotropolone from which (II) may be derived must be the α-compound (I). An attempt to confirm the latter assignment by rearrangement of α-monobromotropolone methyl ether was abortive; much ionic bromine was produced and a minute yield of an impure bromine-free tropolone-like material was obtained. Potassium hydroxide fusion of (I), however, gave a small yield of salicylic acid (B. J. Abadir, personal communication). These assignments indicated that the higher-melting monobromotropolone should be the γ-isomer (IV); this structure was confirmed by the sodium methoxide rearrangement of its methyl ether to methyl *p*-bromobenzoate, characterised by hydrolysis to the free acid (VIII). It is seen that these results confirm Dewar's predictions (*Nature*, 1950, **166**, 790) that the 3 (α), 5 (γ) and 7 (α′) positions of tropolone would be those most liable to electrophilic attack. They do not, with regard to bromination at least, support the author's contention that the γ-position should be more prone to such substitution than the α- and the α′-position.

Theoretically an alternative disruption of the tropolone–bromine complex (*A–B*) may be visualised, namely, direct recombination to regenerate tropolone and bromine. This does not appear to occur to any appreciable extent in the case of the bromine complex, but seems to be the major reaction in the case of the tropolone–iodine complex which was prepared by the action of aqueous iodine–potassium iodide on tropolone. This black, crystalline complex was unaffected by water but was intrinsically much less stable than the corresponding bromine complex, iodine being slowly evolved at room temperature. This process was hastened by sublimation whereupon the complex broke up into iodine and tropolone.

The action of iodine in alkaline solution (*i.e.*, hypoiodite) on tropolone was found to follow an entirely different course. On the reactants being mixed in the cold a yellow crystalline precipitate was immediately formed. This, after purification, was identified as iodoform. The crude material obtained in an earlier experiment gave tropolone colour reactions, and this was responsible for the mistaken suggestion (Part I; *loc. cit.*) that it was an iodotropolone. Acidification of the alkaline filtrate gave a product from which 2 : 4 : 6-tri-iodophenol could be readily isolated, in conformity with the recently reported finding by Doering and Knox (*J. Amer. Chem. Soc.*, 1951, **73**, 828), who do not seem to have observed the formation of iodoform. The yield of iodoform varied with the reaction conditions, and it is probably a secondary product rather than a product inherent in the rearrangement which leads to the iodinated phenol. It may be noted that stipitatic acid, a natural tropolone, has been found to give an iodoform reaction (Birkinshaw, Chambers, and Raistrick, *Biochem. J.*, 1942, **36**, 250). Many similar "exceptions" to the validity of the iodoform test have been noted by Booth and Saunders (*Chem. and Ind.*, 1950, 824).

Doering and Knox (*loc. cit.*) also reported the conversion of tropolone into benzoic acid by fusion with potash, and of its methyl ether into methyl benzoate by means of boiling sodium methoxide solution. These results, which we have confirmed, are at variance with those which we reported earlier (Part I, *loc. cit.*). In the case of the potash fusion the discrepancy is difficult to explain as the conditions were very similar, except that we used a hard-glass tube for the reaction whereas Doering and Knox used a nickel crucible. With the sodium methoxide reaction, however, our earlier failure is clearly due to the short reaction time (30 minutes) which we employed, in contrast to the longer time (12 hours) used by the American workers. These conversions into benzenoid compounds by alkaline hypoiodite and sodium methoxide have already been realised with colchiceine and colchicine, respectively, and the evidence that tropolone and its methyl ether undergo similar transformations provides valuable corroboration of the tropolone methyl ether structure of one of the rings of colchicine.

EXPERIMENTAL.

Bromination of Tropolone.—(*a*) To a cold solution of tropolone (56·1 mg.) in dry carbon tetrachloride (3 c.c.) contained in a weighed filter beaker was added a solution of bromine in carbon tetrachloride (0·34 c.c. of a solution containing 110 mg. of bromine per c.c.; 0·5 mol.). The orange-red precipitate immediately formed was filtered off, washed with a little carbon tetrachloride, dried *in vacuo*, and weighed (68·4 mg., 74%). The yields obtained with 1 mol. (85%) and 2 mols. (81%) of bromine were similar, but that produced by 0·25 mol. was 31%. The complex dissolved in hot glacial acetic acid to give a yellow solution from which it crystallised on cooling as a mass of scarlet needles; accurate analysis was difficult owing to its ready reaction with atmospheric moisture [Found : C, 39·9; H, 3·5; Br, 40·3. $(C_7H_6O_2)_2,Br_2$ requires C, 41·6; H, 3·0; Br, 39·6%]. On being heated to 110° the substance sintered and rapidly decolorised to form a white, crystalline mass which melted unsharply to a clear liquid at 152—163°. On careful heating at 70° (bath-temp.)/10^{-5} mm. the complex slowly sublimed with only slight decomposition. A sample of the complex (84·2 mg.) was heated at 140° for 45 minutes in a slow stream of nitrogen, the issuing gases being bubbled through sodium hydroxide solution (5 c.c. of N.). The latter was treated with excess of nitric acid and silver nitrate, and the precipitated silver bromide was coagulated by boiling, filtered off, washed, dried, and weighed [Found: AgBr, 32·3 mg. Calc. for the production of one mol. of HBr from $(C_7H_6O_2)_2,Br_2$: AgBr, 39·2 mg.].

The complex (127 mg.) was heated in an oil-bath at 110° at atmospheric pressure in a sublimation apparatus until decolourisation was complete. The bath was then cooled to 60° and the apparatus evacuated to 20 mm.; the crystalline sublimate thus obtained (6 mg.) had m. p. 48—50° undepressed on admixture with tropolone. The bath-temperature was then raised to 120° and the pale yellow sublimate formed (42 mg.), m. p. 83—94°, was purified by repeated crystallisation from *cyclo*hexane to yield pure α-monobromotropolone (17 mg.), m. p. 105—107°, undepressed on admixture with an authentic specimen; from the number of crystallisations required to attain purity it is probable that the product contained a little of the higher-melting γ-monobromotropolone (see below). The residue remaining in the sublimation apparatus was dissolved in a small quantity of warm glacial acetic acid; on being cooled the solution deposited small rosettes of needles (11 mg.), m. p. 154—157° undepressed on admixture with dibromotropolone (m. p. 157—158°). Evaporation of the acetic acid mother-liquors to dryness under reduced pressure left a white crystalline mass (38 mg.), insoluble in hydrocarbon solvents but crystallising from a small volume of methanol or ethyl methyl ketone in long needles, m. p. 130—132° (Kofler block), resolidifying slowly on further heating to a mass of needles which did not melt below 250°. This compound was found to be *tropolone hydrobromide* identical with an authentic sample prepared by passing hydrogen bromide into a benzene solution of tropolone (Found: Br, 38·6. $C_7H_7O_2Br$ requires Br, 39·35%). On being heated under reflux with a small volume of ethyl acetate the hydrobromide slowly dissolved; evaporation to dryness gave tropolone (18 mg.), crystallising from light petroleum (b. p. 40—60°) in needles, m. p. 49—50° undepressed on admixture with an authentic specimen.

(*b*) To a cold solution of tropolone (57 mg.) in water (5 c.c.) was rapidly added a solution of bromine (290 mg., 3·5 mols.) in potassium bromide solution. The yellow precipitate formed was filtered off, washed with water, and crystallised from methanol, from which solvent it formed yellow needles (116 mg.), m. p. 123° undepressed on admixture with the tribromotropolone obtained as described in Part I. The action of ethereal diazomethane gave *tribromotropolone methyl ether*, crystallising from a small volume of light petroleum (b. p. 40—60°) in yellow nodules, m. p. 123—124° (strongly depressed on admixture with starting material) (Found: C, 26·05; H, 1·5. $C_8H_5O_2Br_3$ requires C, 25·8; H, 1·35%).

Bromination of α-Monobromotropolone (I).—To a cold solution of α-monobromotropolone (200 mg.) in acetic acid (3 c.c.) was added an acetic acid solution of bromine (160 mg., 1 mol.). After a few minutes a yellow crystalline precipitate (210 mg.) separated. This was filtered off; evaporation of the filtrate to dryness gave dibromotropolone (60 mg.), m. p. 156—157° after one crystallisation from methanol.

The precipitate obtained melted at 80—85° with evolution of hydrogen bromide, rapidly resolidifying, and remelting at 145—153°. It rapidly dissolved in a small volume of warm methanol; on being cooled the solution deposited needles of pure dibromotropolone, m. p. 157—158° (118 mg.). The low-melting intermediate was found to be identical with dibromotropolone hydrobromide prepared by treating the parent compound with an acetic acid solution of hydrogen bromide.

Mixed-melting-point determination showed that the dibromotropolone prepared as above was identical with that obtained as described in Part I.

Bromination of Dibromotropolone (II).—A solution of dibromotropolone (47 mg.) in acetic acid (2 c.c.) was treated with an acetic acid solution of bromine (40 mg., 1·5 mols.). No action was apparent in the cold, but the bromine colour was slowly discharged when the reaction mixture was heated under gentle reflux for 30 minutes. Evaporation to dryness under reduced pressure and crystallisation from methanol gave tribromotropolone (42 mg.), m. p. 123° undepressed on admixture with an authentic specimen.

Bromination of Copper Tropolone.—To a cold solution of copper tropolone (176 mg.) in chloroform (20 c.c.) was rapidly added a solution of bromine in chloroform (1·51 c.c. of a solution containing 135 mg. of bromine per c.c.; 2 mols.); a black, powdery precipitate was formed. After 16 hours at room temperature an equal volume of water was added and the reaction mixture treated with hydrogen sulphide. Extraction with ether, followed by drying (Na_2SO_4) and evaporation, yielded a dark oil which rapidly solidified; sublimation of the product at 110—120°/0·5 mm. gave a pale yellow solid (196 mg.) melting over the range 85—110°. Fractional crystallisation from light petroleum (b. p. 60—80°) gave two main fractions, m. p. 96—103° (28 mg.) and m. p. 176—180° (46 mg.) respectively. Two crystallisations of the latter from a small quantity of ethanol gave pure *γ-monobromotropolone* (22 mg.) as needles, m. p. 188° with vigorous sublimation (Found: C, 41·9; H, 2·7. $C_7H_5O_2Br$ requires C, 41·8; H, 2·5%). The lower-melting fraction, whose melting range was not markedly improved by further crystallisation, consisted of slightly impure α-monobromotropolone. The action of ethereal diazomethane on γ-monobromotropolone gave the *methyl ether* crystallising from light petroleum (b. p. 60—80°) in needles, m. p. 135—137° (Found: C, 44·9; H, 3·3. $C_8H_7O_2Br$ requires C, 44·7; H, 3·3%); a marked change in crystal form occurred before melting.

γ-Monobromotropolone (160 mg.) was also obtained by subjecting the crude fractions (2 g.; m. p. 68—80°) obtained from the bromination of *cyclo*heptane-1 : 2-dione to fractional crystallisation from ethanol.

Heating γ-monobromotropolone in acetic acid with excess of bromine (2·5 mols.) gave an almost quantitative yield of tribromotropolone, m. p. and mixed m. p. 123°.

Rearrangement of Brominated Tropolone Methyl Ethers.—(*a*) Tribromotropolone methyl ether (60 mg.) was added to a solution of sodium (50 mg.) in dry methanol (5 c.c.), and the reaction mixture heated under reflux for 30 minutes. The solvent was removed under reduced pressure, and water and ether were added to the residue. Evaporation of the dried (Na_2SO_4) ethereal layer furnished an oil which rapidly solidified; crystallisation of the product from aqueous ethanol gave methyl 2 : 4 : 6-tribromobenzoate (26 mg.) as plates, m. p. 69—70° undepressed on admixture with an authentic specimen (m. p. 69—70°).

(*b*) Dibromotropolone methyl ether (46 mg.) was treated in a manner exactly analogous to (*a*). The product (32 mg.) crystallised from aqueous ethanol in platelets, m. p. 61—62° undepressed on admixture with authentic methyl 2 : 6-dibromobenzoate (m. p. 61—62°) (Found : C, 32·6; H, 2·3. Calc. for $C_8H_6O_2Br_2$: C, 32·7; H, 2·05%). The ester was prepared by the action of ethereal diazomethane on 2 : 6-dibromobenzoic acid obtained by Olivier's method (*Rec. Trav. chim.*, 1924, **43**, 872). On the two previous occasions that this ester has been mentioned in the literature the m. p. has been recorded as 83° (Buning, *Rec. Trav. Chim.*, 1921, **40**, 350) and 78° (Sudborough, *J.*, 1895, **67**, 595); in these cases the compound was prepared by reaction of the acid chloride with methanol or sodium methoxide. Dimorphism seems to be the most likely explanation of this discrepancy; the m. p. of our ester was not changed by repeated crystallisation from various solvents or by melting and resolidification.

(*c*) γ-Monobromotropolone methyl ether (108 mg.) was treated as in (*a*) with a solution of sodium (100 mg.) in methanol (5 c.c.). The residue obtained after removal of the solvent was treated with sodium hydroxide solution (5 c.c. of 2N.), and the mixture heated under reflux for 1 hour. The cooled solution was extracted once with ether to remove neutral impurities, and the aqueous layer acidified with dilute sulphuric acid. Extraction with ether, drying (Na_2SO_4), and evaporation furnished a brown solid which was purified by sublimation (140°/0·5 mm.). Crystallisation of the sublimate from benzene gave *p*-bromobenzoic acid (33 mg.) as tiny needles, m. p. 245—247° with rapid sublimation, undepressed on admixture with an authentic sample (m. p. 248—250°).

Iodination of Tropolone.—(*a*) To a solution of tropolone (100 mg.) in water (15 c.c.) was added a solution of iodine (150 mg.) in potassium iodide solution (5 c.c. of 10%). The black precipitate immediately formed (160 mg.) was filtered off, dried on porous tile, and crystallised from chloroform from which solvent it formed black lustrous needles decomposing at *ca.* 140°. Accurate analysis was difficult as the *complex* slowly evolved iodine even at room temperature [Found : I, 49·5. $(C_7H_6O_2)_2,I_2$ requires I, 50·9%]. When a solution of the complex in chloroform was shaken with sodium thiosulphate solution the colour was immediately discharged and evaporation of the colourless chloroform layer furnished tropolone. Attempted sublimation of the complex in a high vacuum resulted in complete dissociation into iodine and tropolone.

(*b*) To a cold solution of tropolone (200 mg.) in N-sodium hydroxide (30 c.c.) was rapidly added a solution of iodine (3 g.) in potassium iodide solution. The yellow crystalline precipitate immediately formed (140 mg.) was filtered off and crystallised from ethanol to give yellow plates, m. p. 119—120° undepressed on admixture with iodoform (m. p. 119—120°). The alkaline filtrate was acidified with dilute sulphuric acid, the iodine colour discharged with a little sodium hydrogen sulphite solution, and the resulting solid filtered off. Crystallisation of this product from acetic acid gave needles (260 mg.), m. p. 153—155° undepressed on admixture with 2 : 4 : 6-tri-iodophenol (m. p. 155—156°).

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