107. *Tropolones. Part I. The Preparation and General Characteristics of Tropolone.*

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Bromination of *cyclo*heptane-1 : 2-dione in glacial acetic acid with varying proportions of bromine gave a series of bromo-compounds. The inter-relationship of these products is interpreted by a self-consistent reaction scheme. One of them was a bromotropolone; its sparingly soluble sodium salt underwent smooth hydrogenolysis to tropolone which thus becomes readily available for detailed study. Some phases of this are recorded.

The inspired suggestion of Dewar (*Nature*, 1945, **155**, 50) that the properties of the mould metabolite, stipitatic acid, could be interpreted by assigning to it the structure of a derivative of 2-hydroxy*cyclo*hepta-2 : 4 : 6-trienone (tropolone; III) has attracted widespread interest and has been very fruitful in elucidating the structures of a variety of natural products (cf. Loudon, *Ann. Reports*, 1948, **45**, 187). Tropolone structures have been established for stipitatic acid (Corbett, Johnson, and Todd, *J.*, 1950, 147), puberulic acid (*idem, ibid.*, p. 6), α-, β-, and γ-thujaplicin (Erdtman, Gripenberg, and Anderson, *Acta Chem. Scand.*, 1948, **2**, 625, 639, 644), and purpurogallin (Haworth, Moore, and Pauson, *J.*, 1948, 1045). There is also strong, though less conclusive, evidence that colchicine is a tropolone derivative (Loudon,

loc. cit. ; Scott and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 240), as suggested by Dewar (*Nature*, 1945, **155**, 142).

By extrapolation of the known properties of these natural products a fairly complete picture may be constructed of the probable chemical attributes of the parent compound of the series, namely, tropolone itself. It was clearly desirable to devise methods of synthesis of tropolone for the dual purpose of providing material for a study of its chemistry and to extend these methods to the synthesis of natural tropolones. The present communication is concerned with the synthesis of tropolone and a general survey of its properties. A preliminary summary of some of this work has already been published (*Chem. and Ind.*, 1950, 427). The results fully confirm Dewar's prediction that the tropolone ring would have aromatic stability.
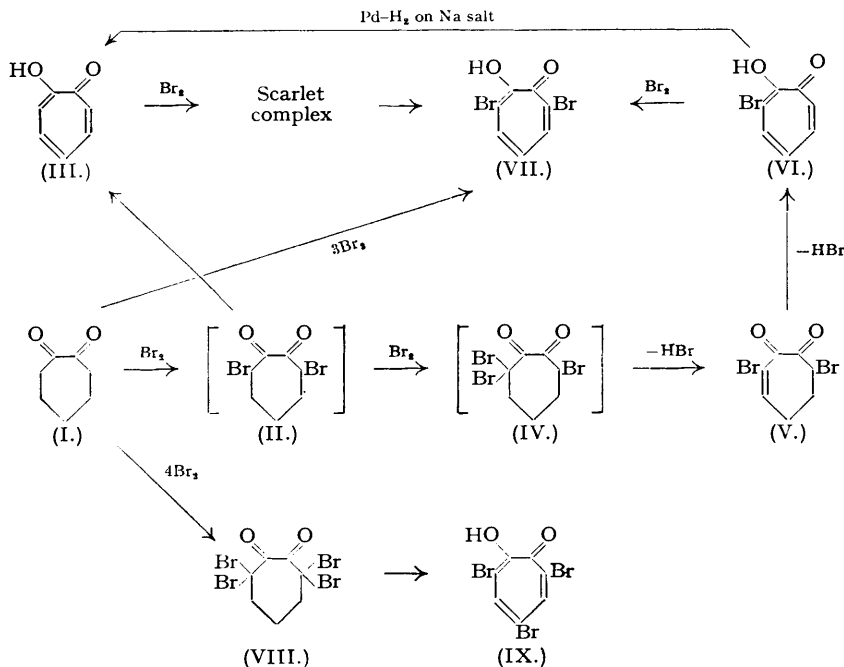
It was found that the most obvious and direct route to tropolone, *i.e.*, the dehydrogenation of *cyclo*heptane-1 : 2-dione (I) with reagents such as selenium, palladium, or chloranil, could not be used, as the dione resinified under such treatment. Failure of this approach led to the investigation of the natural alternative, the bromination–dehydrobromination of the dione. This reaction proved to be unexpectedly complex, the nature of the products being highly dependent on the proportion of bromine used. The action of one mole of bromine in glacial acetic acid on *cyclo*heptane-1 : 2-dione gave a small yield of a dense oil [presumably 3 : 7-di-bromo*cyclo*heptane-1 : 2-dione (II)] which, on dehydrobromination with sodium hydroxide solution, furnished tropolone (III) by way of its sodium salt. This procedure was attended by the formation of much tar, and the method cannot be regarded as preparative. When the dione was treated in glacial acetic acid with two moles of bromine and then heated for a short period, hydrogen bromide was profusely evolved and a sparingly soluble, crystalline compound separated. This did not possess tropolone-like properties, and analysis indicated its formula to be compatible with the structure (V) formed by the elimination of one mole of hydrogen bromide from the intermediate 3 : 3 : 7-tribromo*cyclo*heptane-1 : 2-dione (IV). Compound (V) was unstable and slowly evolved hydrogen bromide when kept. This elimination was rapid and quantitative when (V) was warmed with sodium hydroxide solution : dissolution rapidly occurred and the resulting deep yellow solution, on being cooled, deposited the sparingly soluble, highly crystalline sodium salt of bromotropolone (VI) ; the overall yield of the pure sodium salt based on the starting dione was 26%. If the intermediate compound (V) was not isolated, but heated further in the acetic acid reaction medium, it slowly dissolved with evolution of hydrogen bromide ; cooling resulted in the crystallisation of bromotropolone

(VI) itself. This procedure, however, gave an inferior yield. On being shaken with hydrogen in the presence of a palladium–charcoal catalyst, the sodium salt of bromotropolone (VI) underwent smooth hydrogenolysis to give tropolone in 78% yield, the reaction ceasing after the absorption of one mole of hydrogen. The convenience and ease of this series of reactions render attainable relatively large amounts of tropolone for the detailed investigation of its physical and chemical properties. Recently, two further syntheses of tropolone have been described. The first consists of the permanganate oxidation of *cyclo*hepta-1 : 3 : 5-triene, itself prepared by photochemical diazomethane ring-expansion of benzene (Doering and Knox, *J. Amer. Chem. Soc.*, 1950, **72**, 2305), whereas the second involves the stepwise degradation of purpurogallin (Haworth and Hobson, *Chem. and Ind.*, 1950, 441). It seems unlikely that either of these procedures could be utilised on a preparative scale.

It might be supposed that the formation of bromotropolone (VI) could be more simply interpreted as the further bromination of initially formed tropolone. This explanation is untenable in view of the fact that bromination of tropolone under analogous conditions does not give bromotropolone (VI); as will be described more fully in a future communication, a scarlet complex is first formed which disproportionates into tropolone and dibromotropolone (VII).

The bromination of *cyclo*heptane-1 : 2-dione in glacial acetic acid with three moles of bromine led to the formation of a dibromotropolone (VII), m. p. 157—158°. The production of this compound may be satisfactorily explained as the further bromination of pre-formed bromo-tropolone (VI), a reaction which has been confirmed experimentally. Hydrogenolysis of the sodium salt of this dibromotropolone did not give the expected monobromotropolone, but a mixture of equal amounts of tropolone and dibromotropolone; addition of a further mole of sodium hydroxide and continuation of the hydrogenolysis led to complete debromination and conversion into tropolone. When the dione (I) was treated with four moles of bromine in the cold, no tropolone-like material was obtained, the only isolable product consisting of 3 : 3 : 7 : 7-tetrabromo*cyclo*heptane-1 : 2-dione (VIII), m. p. 84°. Attempts to dehydrobrominate this compound by means of sodium hydroxide solution or pyridine led only to tar formation. On being heated to 130°, the tetrabromo-compound evolved hydrogen bromide; the product, purified through its sodium salt, was found to be a tribromotropolone (IX), m. p. 123°. It is difficult to formulate a rational mechanism for the production of (IX) from (VIII) and the exact course of the reaction remains obscure.

The production and inter-relationship of these compounds may be satisfactorily interpreted by the above reaction scheme, but it should be emphasised that the structures assigned, although likely, are tentative and their confirmation, or otherwise, must await the results of orientation investigations which are now in progress. The above products are always more highly brominated than would seem to be compatible with the corresponding molar proportions of bromine employed in the reaction, *e.g.*, the dione (I) gives bromotropolone (VI) *via* (V) and (IV) by the use of only two instead of the expected three moles of bromine. This apparent anomaly is probably due to the fact that the dione (I) is an unstable compound which always undergoes some unproductive degradation during bromination. The true bromine : dione ratio of the reaction mixtures is therefore considerably higher than that indicated by the actual initial weights of the reactants.

The above procedure is obviously applicable to the preparation of substituted tropolones, and indeed application of the method to the relevant homologous diones has resulted in the synthesis of three naturally occurring tropolones, the α-, β- and γ-thujaplicins (forthcoming publication).

Tropolone crystallised from light petroleum in long, almost colourless needles, m. p. 49—50°, possessing a remarkably high vapour pressure, as volatilisation occurred readily at room temperature. If exposed at room temperature to the atmosphere, tropolone slowly coloured and became sticky, but it could be kept indefinitely without apparent change at temperatures below 0°. It was readily soluble in water and organic solvents. It dissolved rapidly in sodium hydrogen carbonate solution with effervescence and the production of the yellow sodium salt; electrometric titration with sodium hydroxide solution indicated a pK value of 7·00 $\pm$ 0·02 at 20° which is midway between the values obtained for a typical phenol (*e.g.*, pK 10·0 for phenol itself) and a simple carboxylic acid (pK 4·8 for acetic acid). With ferric chloride solution tropolone in aqueous solution gave an intense deep green colour. This colour reaction took place in two distinct stages : if a limited amount of ferric chloride was used a red precipitate was first formed; this redissolved on further addition of ferric chloride to form the deep green solution. The red solid was readily soluble in chloroform, from which it crystallised in reddish-black needles; analysis showed that these consisted of ferric tropolone. The ready formation

of this compound and the intense colour of its extremely dilute solutions in chloroform suggests its use for the colorimetric estimation of ferric ion. Similarly, treatment of tropolone with aqueous solutions of cupric and cuprammonium salts resulted in the formation of the chloroform-soluble cupric complex which readily crystallised from many organic solvents. In contra-distinction to sodium tropolone, which behaved as a true ionised salt, the ferric and cupric compounds showed the properties of typical co-ordination complexes. This reaction of tropolone with cupric and ferric ions recalls the analogous behaviour of the well-known analytical reagent cupferron (X) and some formal resemblance is indeed apparent between the structures of the two compounds.

No carbonyl reactions or ketonic derivatives could be obtained from any of the above tropolones; thus the action of semicarbazide acetate, hydroxylamine acetate, and 2 : 4-dinitro-phenylhydrazine sulphate left the compounds unchanged; moreover, treatment with *o*-phenylenediamine did not result in quinoxaline formation. The preparation, from the tropolones, of derivatives involving the hydroxyl group was unexpectedly troublesome; solid acetates could not be obtained and attempts to prepare, by standard procedures, the *p*-nitro-benzyl, 2 : 4-dinitrophenyl, and carboxymethyl ethers were fruitless. *S*-Benzylthiuronium and benzylamine salts were readily formed, but rapidly broke up into their constituents on attempted purification. 3 : 5-Dinitrobenzoates were obtainable, however, and treatment of the tropolones with diazomethane and diphenyldiazomethane gave respectively the crystalline methyl and diphenylmethyl ethers. As with the parent compounds these ethers did not exhibit carbonyl reactivity.

No reaction took place on attempted catalytic hydrogenation of tropolone when palladium was employed as catalyst, thus providing some indication that the double bonds in the compound are not of the ordinary ethylenic type. The action of tetranitromethane in petroleum gave only a light yellow colour. When platinum was employed as catalyst in the hydrogenation a ready uptake of three moles of hydrogen occurred, followed by a much slower absorption of a further one mole. It is logical to suppose that the first stage leads to the formation of 2-hydroxy-*cyclo*heptanone which is then slowly reduced to a mixture of *cis*- and *trans*-*cyclo*heptane-1 : 2-diol; this reluctance of cyclic α-ketols (acyloins) to undergo hydrogenation has been noted before (Stoll *et al.*, *Helv. Chim. Acta*, 1947, **30**, 1820, 1828). Oxidative fission of the hydrogenation product with potassium permanganate gave pimelic acid; thus the presence of a seven-membered carbocyclic ring in tropolone was confirmed. Lithium aluminium hydride reduction of tropolone has as yet given no pure chemical entity as product.

It was obviously of interest to subject tropolone and its methyl ether to those reactions which involve the tropolone ring of colchiceine and its methyl ether, colchicine, in order to examine the degree of correspondence of properties. There is a marked superficial resemblance between the two systems; thus colchiceine gives a green ferric chloride colour, exhibits acidic properties, forms a chloroform-soluble copper salt, and shows no carbonyl reactivity. Further, tropolone methyl ether was far more soluble in water than tropolone, a surprising property exactly paralleled by colchicine and colchiceine. In contrast, however, there seems to be far less tendency for tropolone and its methyl ether to rearrange into benzenoid derivatives than is exhibited by colchiceine and colchicine. Thus colchicine on treatment with methanolic sodium methoxide is smoothly converted into *allo*colchicine, the tropolone-like ring undergoing contraction to form the methyl ester of a substituted benzoic acid (Fernholz, *Annalen*, 1950, **568**, 66; cf. Šantavý, *Helv. Chim. Acta*, 1948, **31**, 821); tropolone methyl ether was unaffected by sodium methoxide under the same conditions. Other naturally occurring tropolones (*e.g.*, γ-thujaplicin, stipitatic acid, purpurogallin) undergo a similar transformation into substituted benzoic acids on being heated to high temperatures with potassium hydroxide. Heating tropolone with potassium hydroxide at temperatures ranging from 180° to 250° left it to some degree unaltered and no benzoic acid could be isolated. Oxidation of colchiceine with alkaline hydrogen peroxide converts the tropolone ring into a phenolic ring with formation of *N*-acetyl-colchinol (Čech and Šantavý, *Coll. Czech. Chem. Comm.*, 1949, **14**, 532); tropolone was practically unaffected by this reagent although a small quantity of *cis* : *cis*-muconic acid could be isolated. The latter product was presumably formed by further oxidation of the primary fission product,

cis : *cis*-penta-1 : 3-diene-1 : 5-dicarboxylic acid; a similar oxidation of the *trans* : *trans*-isomer of the diene-acid to *trans* : *trans*-muconic acid has been recorded (Grundmann, *Ber.*, 1937, **70**, 1150). Another means of aromatisation of colchiceine was described by Windaus (*Sitzungsber. Heidelberg. Akad. Wiss., Math.-Nat. Kl., A.*, 1914, 18 Abh.; 1919, 16 Abh.) who found that it underwent conversion into the iodophenol, *N*-acetyliodocolchinol, when treated with cold sodium hypoiodite. Similar treatment of tropolone produced a compound which differed from all of the known iodinated derivatives of phenol; as will be described in a later communication, it exhibited typical tropolone properties and was presumably an iodotropolone. Tropolone coupled readily with *p*-toluenediazonium chloride, giving a red-brown dye; this reaction takes place with many of the naturally-occurring tropolones, but not with colchiceine, which gives only a faint brownish colour.

Heating of tropolone with maleic anhydride or *cyclo*pentadiene furnished no adduct.

The question of the fine structure of the tropolone ring system is obviously of fundamental interest from the theoretical standpoint, and purely chemical investigations can clearly contribute in only a limited degree to the solution of the problem. Chemical studies have therefore been supplemented by some of the modern physico-chemical techniques. As a first approximation the structure of tropolone may be written as
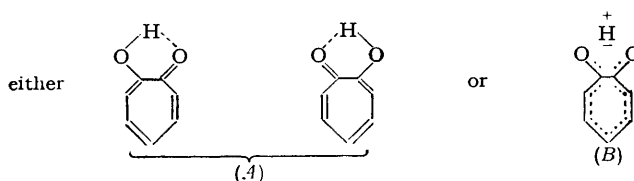
where the two equivalent forms of (A) are to be regarded as tautomers involving rapid inter-change rather than as extreme canonical forms of a true electronic resonance hybrid such as the alternative ionic " benzenoid " formulation (B). The infra-red absorption properties of tropolone and its derivatives would obviously provide crucial data for discrimination between the two concepts, and the required investigation has been carried out by Dr. Koch, whose results and the deductions therefrom are described fully in the following paper; it may be stated here that the spectroscopic evidence rules out the possibility of electronic resonance degeneracy involving two equivalent bonds between the proton and the two oxygen atoms, as in (B), and points with a strong degree of probability to a structure such as (A) for tropolone in which the hydroxylic hydrogen atom is regarded as being symmetrically located *on a time average basis* between the two oxygen atoms which will thus become chemically equivalent. It should be pointed out that the structure of salts of tropolone may well differ in their degree of attaining complete " benzenoid " resonance degeneracy.
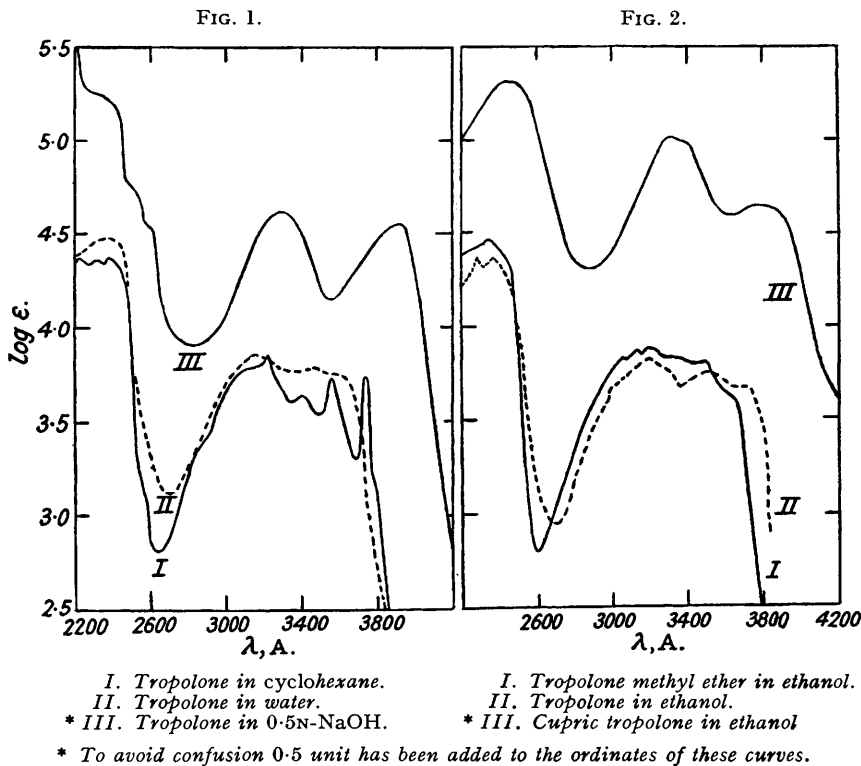
The calculated resonance energy of tropolone based on this model is seen from the following paper to be in excellent agreement with that found experimentally. The thermochemical data for the computation of the latter value were very kindly provided by Dr. G. R. Nicholson of the Dyestuffs Division of Imperial Chemical Industries Limited. He has determined the standard heat of combustion of tropolone (at 25° and 1 atmosphere pressure), ΔH_c, to be $-806\cdot2 \pm 0\cdot9$ kcals./mole and the heat of sublimation at 25°, ΔH_s, to be $+20\cdot0 \pm 0\cdot2$ kcals./mole. From the first of these results the heat of combustion of tropolone (solid) may be deduced as $-57\cdot1$ kcals./mole and thence, by use of the heat of sublimation, the heat of combustion of tropolone (gaseous) at 25° is found to be $-37\cdot1$ kcals./mole. Hence, by use of the heats of atomisation C $126\cdot3$, H $51\cdot71$, and O $58\cdot9$ kcals./g.-atom, the heat of formation of gaseous tropolone from its elements in their gaseous atomic states is found to be $-1349\cdot3$ kcals./mole. By means of the relevant bond energies (as given by Coates and Sutton, *J.*, 1948, 1187) the energy of the formal chemical bonds in tropolone may be calculated as $1320\cdot7$ kcals./mole. The difference between these experimental and theoretical values, *i.e.*, the resonance energy of tropolone, is thus seen to be $28\cdot6$ kcals./mole.

The ultra-violet absorption spectra of tropolone and its derivatives are consistent with the above concept of the fine structure. Thus the close similarity between the absorption curves of tropolone and its methyl ether (Fig. 2) would appear to tell against any formulation of tropolone as a true resonance hybrid of type (B). The absorption curve of tropolone in sodium hydroxide solution (Fig. 1), *i.e.*, that of the yellow tropolone anion, is seen, however, to be markedly different; this indicates a radical change of structure in the ion which may plausibly be attributed to its existence as a " benzenoid " resonance hybrid. Copper tropolone,

whose properties are those of a typical co-ordination complex in contrast to the undoubtedly strongly ionised sodium salt, exhibits an absorption (Fig. 2) different again from the above derivatives. The ultra-violet absorption curves of the brominated tropolones are similar in shape to that of tropolone itself, although the corresponding maxima occur at longer wavelengths.

Detailed *X*-ray crystallographic analysis of tropolone and its derivatives would obviously provide much vital information (*e.g.*, bond lengths) bearing on the fine structure of tropolone, and such investigations are now being carried out by Professor J. M. Robertson and his collaborators.

The tropolone structure may be regarded formally as a vinylogue of a carboxyl group and this concept would appear to be endowed with a modicum of reality if comparison be made between the resonance energy of simple carboxylic acids ($\sim$25 kcals., to which must be added

FIG. 1.   FIG. 2.

I. *Tropolone in* cyclo*hexane.*
II. *Tropolone in water.*
* III. *Tropolone in* 0·5N-NaOH.

I. *Tropolone methyl ether in ethanol.*
II. *Tropolone in ethanol.*
* III. *Cupric tropolone in ethanol*

* *To avoid confusion* 0·5 *unit has been added to the ordinates of these curves.*

an increment of $\sim$6 kcals. contributed by the presence of the conjugated *cyclo*heptatriene system; cf. Wheland, " The Theory of Resonance " pp. 56—58, 69) and tropolone (28·6 kcals.). Further, Dr. Nicholson has suggested that the rather high value for the latent heat of sublimation of tropolone may indicate that the hydrogen bonds are between groups in neighbouring molecules and not within the molecule, thus giving rise to a structure analogous to the well-established hydrogen bond dimers of carboxylic acids. However, the value for the molecular weight of tropolone as determined by ebullioscopic and cryoscopic methods is that expected for the monomer, thus providing evidence that the hydrogen bonding is intra- rather than inter-molecular. Again, neither the C=O nor the O–H characteristic frequencies displayed in the infra-red absorption of tropolone are close to those normally encountered in solid carboxylic acids. A further argument against this vinylogy postulate arises from the fact that compounds such as 3-methyl*cyclo*pent-3-ene-1 : 2-dione (Dane *et al.*, *Annalen*, 1937, **532**, 29; 1938, **536**, 196; 1938, **537**, 246; Stork and Singh, *Nature*, 1950, **165**, 816) and the many *cyclo*pentane-1 : 2 : 4-triones do not possess tropolone properties although they may be formally regarded as lower vinylogues of tropolone and hydroxytropolone respectively; these compounds behave as typical α-diketones, forming carbonyl derivatives and quinoxalines with great ease.

The marked antifungal properties exhibited by γ-thujaplicin and 3 : 4-benzotropolone (Baillie, Freeman, Cook, and Somerville, *Nature*, 1950, **166**, 65) suggested the examination in this respect of the tropolones obtained as above. Dr. G. G. Freeman and Mr. A. J. Baillie of the Nobel Division of Imperial Chemical Industries Limited have tested the fungistatic and bacteriostatic activity of the compounds against seven fungal species and four test bacteria at concentrations of 80—0·6 mg./l. The organisms were inoculated on to Petri dishes containing nutrient medium including the tested concentration of the compounds. Growth of the fungi was read after 5 days at 25° and growth of bacteria after 2 days at 35°. Tropolone, bromo-tropolone (VI), and dibromotropolone (VII) showed slight fungistatic and bacteriostatic activity at 80 mg./l., and no significant activity at 16 mg./l. In view of the low fungistatic activity no fungicidal tests were carried out.

EXPERIMENTAL.

*cyclo*Heptanone was prepared by the diazomethane ring expansion of *cyclo*hexanone (Kohler, Tishler, Potter, and Thomson, *J. Amer. Chem. Soc.*, 1939, **61**, 1057). From the former ketone *cyclo*-heptane-1 : 2-dione was obtained by selenium dioxide oxidation (Vanderhaar, Voter, and Banks, *J. Org. Chem.*, 1949, **14**, 836).

Bromination of cyclo*Heptane*-1 : 2-*dione.*—(a) *Reaction with one mole of bromine.* To a cooled (0°) and stirred solution of *cyclo*heptane-1 : 2-dione (10 g.) in glacial acetic acid (10 c.c.) was added dropwise, during 15 minutes, bromine (12·8 g.) in glacial acetic acid (10 c.c.). After 1 hour the reaction mixture was heated by steam until the evolution of hydrogen bromide ceased (*ca.* 1 hour). It was then distilled in steam, and the distillate (800 c.c.) made alkaline with solid sodium carbonate and extracted with ether. Drying and evaporation of this extract furnished a brown oil; this did not exhibit tropolone-like properties but, on being warmed with sodium hydroxide solution (5N.), it rapidly dissolved to give a yellow solution. Acidification (2N-sulphuric acid) and isolation by means of ether furnished impure tropolone as a gum from which pure tropolone sublimed on heating. Further small quantities could be obtained by acidification of the alkaline steam-distillation mother-liquor and by alkali treatment of the tarry non-volatile residue. The total yield of tropolone by this procedure was 1·4 g. (15%).

(b) *Reaction with two moles of bromine.* To a cooled (0°) and stirred solution of the dione (200 g.) in glacial acetic acid (200 c.c.) was added dropwise, during 4 hours, a solution of bromine (520 g.) in glacial acetic acid (200 c.c.), and the reaction mixture set aside at room temperature for 16 hours. The resulting dark orange solution was then heated by steam for 20 minutes; hydrogen bromide was profusely evolved and a dense, crystalline solid (130 g.) was precipitated, which, after being cooled, was filtered off, washed with a little cold acetic acid, and dried on porous tile. This compound could be crystallised rapidly from acetic acid but its instability precluded an accurate analysis; it slowly evolved hydrogen bromide even at room temperature. The bromine analysis, which indicated the presence of two atoms of bromine for each *cyclo*heptane nucleus, and its general properties, were in harmony with the structure (V) (Found : Br, 53·7. Calc. for $C_7H_6O_2Br_2$: Br, 56·7%). This product was then heated with excess of sodium hydroxide solution until completely dissolved (*ca.* 4 l. of 6N-sodium hydroxide are needed) and the resulting yellowish-brown solution cooled to 0°. The separated crystalline mass was filtered off and washed with a little cold brine. A further small quantity of product was obtained by steam-distillation of the acetic acid mother-liquor and extraction of the tarry residue with hot sodium hydroxide solution. The combined product was crystallised from aqueous alcohol (75%) from which the sodium salt of bromotropolone (107 g., 26%) crystallised as the *dihydrate* in lustrous, deep yellow plates, m. p. 308° (decomp.) (Found : C, 32·65; H, 2·9. $C_7H_4O_2BrNa,2H_2O$ requires C, 32·7; H, 3·1%). Dehydration of the *salt* was accomplished by heating it at 100° *in vacuo* for some time; analysis of the dried material indicated a tenacious retention of a small proportion of water (Found : C, 36·7; H, 1·6. $C_7H_4O_2BrNa$ requires C, 37·7; H, 1·8%).

Acidification (2N-sulphuric acid) of an aqueous solution of this sodium salt caused the precipitation of *bromotropolone* (VI) itself, which could be obtained in polymorphic forms. Crystallisation from aqueous acetic acid gave pale green nacreous plates, whereas the compound separated from *cyclo*hexane in cream-coloured needles, which, when kept, changed to pale yellowish-green polyhedra; all these forms had m. p. 103—106° (Found : C, 41·75; H, 2·6; Br, 39·9. $C_7H_5O_2Br$ requires C, 41·8; H, 2·5; Br, 39·75%). Light absorption in ethanol : $\lambda_{max.}$, 2520, 2570, 3270, 3680, 3800 A.; log ε = 4·47, 4·48, 3·82, 3·76, 3·72. $\lambda_{infl.}$, 2330, 3180, 3860 A.; log ε = 4·14, 3·76, 3·60. Bromotropolone was also prepared by heating the originally obtained suspension of the intermediate compound (V) in acetic acid until no further evolution of hydrogen bromide was apparent and all the solid had dissolved; cooling to 0° caused the separation of bromotropolone. This procedure, however, favoured the formation of tarry by-products, and the yield was correspondingly reduced. Conversion of the intermediate (V) directly into bromotropolone was accomplished by warming it with aqueous methanol; dissolution rapidly occurred and the product separated on cooling.

Bromotropolone dissolved in sodium hydrogen carbonate solution with effervescence giving a yellow solution; with ferric chloride a deep green colour was immediately formed. The bromine atom in (VI) was very firmly bound; the compound was recovered unchanged after treatment with hot alcoholic potassium hydroxide, and alcoholic silver nitrate gave only the bright yellow, unstable silver salt decomposing vigorously at 178°. With cuprammonium sulphate solution an aqueous solution of sodium bromotropolone gave the corresponding *cupric* salt, which crystallised from tetrachloroethane as an infusible, light green powder (Found : C, 36·4; H, 1·75. $C_{14}H_8O_4Br_2Cu$ requires C, 36·4; H, 1·75%).

Bromotropolone reacted with ethereal diazomethane to give the *methyl ether*, which crystallised from light petroleum (b. p. 80—100°) in needles, m. p. 89—90° (Found : C, 44·7; H, 3·5; OMe, 14·0.

$C_8H_7O_2Br$ requires C, 44·7; H, 3·3; OMe, 14·4%). Light absorption in ethanol : $\lambda_{max.}$, 2540, 3270, 3610 A.; log ε = 4·63, 3·90, 3·87. $\lambda_{infl.}$, 3120, 3740 A.; log ε = 3·82, 3·77. The 3 : 5-*dinitrobenzoate*, obtained by the usual procedure, formed stout needles, m. p. 105—106°, from benzene–light petroleum (b. p. 60—80°) (Found : C, 42·8; H, 2·1. $C_{14}H_7O_7N_2Br$ requires C, 42·55; H, 1·8%). These homogeneous derivatives were unaccompanied by the position isomers which are theoretically possible.

(c) *Reaction with three moles of bromine* (by G. L. BUCHANAN). To a cooled (0°) and stirred solution of the dione (20 g.) in glacial acetic acid (20 c.c.) was added dropwise, during 20 minutes, a solution of bromine (78 g.) in glacial acetic acid (80 c.c.). After 2 hours at room temperature the dark solution was heated by steam until the evolution of hydrogen bromide ceased, and then evaporated under reduced pressure to half its bulk. On being cooled to 0°, the reaction mixture deposited a crystalline mass of *dibromotropolone* (VII) (13·5 g.), crystallising from alcohol or toluene in cream-coloured needles, m. p. 157—158° (Found : C, 30·2; H, 1·45; Br, 57·6. $C_7H_4O_2Br_2$ requires C, 30·0; H, 1·45; Br, 57·1%). Light absorption in ethanol : $\lambda_{max.}$, 2640, 3350, 3730, 3890 A.; log ε = 4·44, 3·77, 3·64, 3·71. $\lambda_{infl.}$, 3190, 4230 A.; log ε = 3·64, 2·66. The compound gave a deep green ferric chloride colour in alcohol. It dissolved with effervescence in warm aqueous sodium carbonate, to give a yellow solution of the sparingly soluble *sodium* salt, which crystallised from hot water in yellow needles, m. p. 296° (decomp.) (Found : C, 28·0; H, 1·1. $C_7H_3O_2Br_2Na$ requires C, 27·85; H, 1·0%). Action of ethereal diazomethane on dibromotropolone gave the *methyl ether*, crystallising from toluene–light petroleum (b. p. 100—120°) in colourless needles, m. p. 130—131° (Found : C, 33·0; H, 2·15; OMe, 10·85. $C_8H_6O_2Br_2$ requires C, 32·7; H, 2·05; OMe, 10·55%). Light absorption in ethanol : $\lambda_{max.}$, 2660, 3360 A.; log ε = 4·38, 3·77.

(d) *Reaction with four moles of bromine.* To a cooled (0°) stirred solution of the dione (5 g.) in glacial acetic acid (20 c.c.), bromine (25 g.) was rapidly added. After 1 hour at room temperature the solution was poured into water; the precipitated oil slowly solidified and crystallisation from aqueous acetic acid and then from benzene–light petroleum (b. p. 60—80°) gave 3 : 3 : 7 : 7-*tetrabromocycloheptane*-1 : 2-*dione* (VIII) (3·5 g.) as colourless plates, m. p. 82—84° (Found : C, 18·5; H, 1·75; Br, 72·2. $C_7H_6O_2Br_4$ requires C, 19·0; H, 1·35; Br, 72·4%). The product gave no colour with ferric chloride, and warming with sodium hydroxide solution and pyridine produced tars. On being heated to 130°, however, (VIII) rapidly evolved hydrogen bromide, to give a product which dissolved in hot sodium hydroxide solution to form a deep yellow solution. On cooling, this deposited a yellow sodium salt. Acidification of the salt, followed by crystallisation of the product from a small volume of alcohol, gave *tribromotropolone* (IX) as pale yellow needles, m. p. 122—123° (Found : C, 23·7; H, 1·1; Br, 66·5. $C_7H_3O_2Br_3$ requires C, 23·45; H, 0·85; Br, 66·8%). Light absorption in ethanol : $\lambda_{max.}$, 2580, 2710, 3500, 4400 A.; log ε = 4·85, 4·85, 4·38, 4·09. An alcoholic solution of the compound gave a deep green colour with ferric chloride.

In another experiment the dione (10 g.), glacial acetic acid (30 c.c.), and bromine (54 g.) were heated by steam until no further hydrogen bromide evolution occurred, and the reaction mixture was taken to dryness under reduced pressure. The dark red, viscous residue did not give a colour with ferric chloride and did not dissolve in warm alkali. On being heated to 130°, the material briskly evolved hydrogen bromide, and hot sodium hydroxide solution extracted from the product the sodium salt of tribromotropolone (1·7 g.) which was converted into the parent compound as described above.

Tropolone (III).—A suspension of finely-powdered sodium bromotropolone dihydrate (25 g.) in alcohol (200 c.c.) was stirred under hydrogen in the presence of palladium–charcoal (2·5 g.; 10%). The smooth absorption of hydrogen ceased after the uptake of 1 mole (3 hours). The cherry-red filtrate was evaporated under reduced pressure (temperature ≯40°) and the residue extracted with boiling light petroleum (b. p. 40—60°). On being cooled to —10° the extract deposited long, cream-coloured needles of tropolone (9·8 g., 78%) [Found : C, 68·75; H, 4·8; neutr. equiv., 126; *M* (ebullioscopic in acetone), 125, (cryoscopic in benzene), 126. $C_7H_6O_2$ requires C, 68·85; H, 4·95%; *M*, 122·1]. Light absorption : In *cyclo*hexane (Fig. 1) : $\lambda_{max.}$, 2220, 2320, 2380, 3220, 3400, 3560, 3740 A.; log ε = 4·37, 4·36, 4·37, 3·84, 3·64, 3·73, 3·74; $\lambda_{infl.}$, 2840, 3070 A.; log ε = 3·34, 3·77. In ethanol (Fig. 2) : $\lambda_{max.}$, 2280, 2370, 3200, 3510 A.; log ε = 4·36, 4·36, 3·83, 3·76; $\lambda_{infl.}$, 3030, 3710 A.; log ε = 3·70, 3·68. In water (Fig. 1) : $\lambda_{max.}$, 2380, 3160, 3470 A.; log ε = 4·48, 3·86, 3·79; $\lambda_{infl.}$, 3620 A.; log ε = 3·75. In 0·5N-sodium hydroxide (Fig. 1) : $\lambda_{max.}$, 3290, 3920 A.; log ε = 4·12, 4·05; $\lambda_{infl.}$, 2400, 2340, 2590 A.; log ε = 4·70, 4·21, 4·04. The compound was highly volatile and could be sublimed with great ease; it was readily soluble in all the common organic solvents and in water, and dissolved with effervescence in sodium hydrogen carbonate solution to give the very soluble yellow sodium salt. With excess of ferric chloride solution tropolone gave an intense deep green colour, but with a limited amount of the reagent the red, insoluble *ferric tropolone* was precipitated; this compound crystallised from chloroform–carbon tetrachloride in lustrous, intensely red needles which did not melt or decompose below 360°. Sparingly soluble in water and most organic solvents, it dissolved readily in chloroform (Found : C, 60·1; H, 3·7. $C_{21}H_{15}O_6Fe$ requires C, 60·15; H, 3·6%). It is the presence of a few mg. of this compound that imparts the red colour to the solution during the preparation of tropolone; it may be extracted from the residue of sodium bromide by chloroform. Its formation is probably due to a trace of iron in the charcoal. Treatment of tropolone with cupric or cuprammonium salt solutions gave an immediate green precipitate, sparingly soluble in most organic solvents, but very soluble in chloroform. This *copper* chelate compound crystallised well from benzene or alcohol in lustrous green needles, decomposing at 300° (Found : C, 55·5; H, 3·25. $C_{14}H_{10}O_4Cu$ requires C, 55·0; H, 3·30%). Light absorption in ethanol (Fig. 2) : $\lambda_{max.}$, 2470, 3310, 3800 A.; log ε = 4·82, 4·51, 4·14; $\lambda_{infl.}$, 3400 A.; log ε = 4·48.

Tropolone reacted briskly with ethereal diazomethane, to give a quantitative yield of the *methyl ether*, which crystallised from ether or carbon tetrachloride as its hemihydrate, prismatic needles, m. p. 37—38° (Found : C, 66·5; H, 6·1; OMe, 21·8. $C_8H_8O_2,0·5H_2O$ requires C, 66·2; H, 6·25; OMe, 21·4%). Light absorption in ethanol (Fig. 2) : $\lambda_{max.}$, 2350, 3140, 3190, 3500 A.; log ε = 4·46, 3·87, 3·88, 3·81; $\lambda_{infl.}$, 3060, 3360, 3630 A.; log ε = 3·83, 3·83, 3·64. The water of crystallisation was

removed under reduced pressure over silica gel, yielding the anhydrous ether as an oil; analysis of this oil was not possible owing to its extremely rapid reaction with atmospheric moisture to re-form the crystalline hemihydrate. The methyl ether was rapidly reconverted into tropolone on being warmed with 2N-sulphuric acid. The *picrate* of the methyl ether crystallised from methanol in yellow needles, m. p. 119—120° (Found : C, 45·8; H, 3·25. $C_8H_8O_2,C_6H_3O_7N_3$ requires C, 46·05; H, 3·05%). The *diphenylmethyl ether*, prepared by heating tropolone with a benzene solution of diphenyldiazomethane (Hardegger, El Heweihi, and Robinet, *Helv. Chim. Acta*, 1948, **31**, 439), crystallised from light petroleum (b. p. 100—120°) in rosettes, m. p. 142—143° (Found : C, 83·4; H, 5·6. $C_{20}H_{16}O_2$ requires C, 83·4; H, 5·6%). *Tropolone* 3 : 5-*dinitrobenzoate*, prepared by the standard method in poor yield, formed prismatic plates, m. p. 169—171°, from toluene–light petroleum (b. p. 100—120°) (Found : C, 53·6; H, 2·75. $C_{14}H_8O_7N_2$ requires C, 53·15; H, 2·55%). Treatment of an alkaline solution of tropolone with excess of *p*-toluenediazonium chloride solution resulted in the precipitation of p-*tolylazotropolone*, which crystallised from ethanol as a reddish-brown microcrystalline powder, sintering at 140° and finally melting at 190—193° (Found : N, 12·0. $C_{14}H_{12}O_2N_2$ requires N, 11·65%). An alcoholic solution of the azo-compound gave a green colour with ferric chloride and a deep green copper salt with copper sulphate solution.

Hydrogenation of Tropolone.—A solution of tropolone (160 mg.) in alcohol (25 c.c.) was stirred under hydrogen in the presence of pre-reduced platinum (from platinic oxide, 100 mg.). Three moles of hydrogen were absorbed rapidly (30 minutes); the rate of uptake then suddenly changed and absorption of the fourth mole of hydrogen was only complete after 3 hours. Removal of catalyst and solvent gave a thick oil which hardened to a waxy solid at −15°. To an emulsion of the oil in water (10 c.c.) and sodium carbonate solution (2 c.c.; 2N.) was slowly added powdered potassium permanganate (200 mg.). After 10 minutes the mixture was acidified to Congo-red with 2N-sulphuric acid, and sulphur dioxide was passed in until the solution was clear. The reaction mixture was shaken with ether, and the acidic product extracted into sodium carbonate solution and finally isolated by acidification and ether-extraction. Drying (MgSO₄) and evaporation gave a solid residue (125 mg.), crystallising from benzene in small needles, m. p. 99—101° undepressed on admixture with authentic pimelic acid.

Hydrogenolysis of Sodium Dibromotropolone.—A suspension of sodium dibromotropolone (1 g.) in alcohol (50 c.c.) was stirred under hydrogen in the presence of palladium–charcoal (200 mg.; 10%). Absorption of hydrogen was very slow and finally ceased after the uptake of 1 mole. It restarted when sodium hydroxide solution (1 mole of N.) was added to the reaction mixture and a further mole of hydrogen was absorbed. Removal of catalyst and solvent, and extraction of the residue with light petroleum (b. p. 40—60°), gave tropolone (360 mg.) identical with that prepared as above. When the reaction mixture was worked up after the absorption of 1 mole of hydrogen, the product consisted of a mixture of tropolone and unchanged dibromotropolone, separated by crystallisation from light petroleum; no monobromotropolone was encountered.

Attempted Conversion of Tropolone and its Methyl Ether into Benzenoid Compounds.—(a) To a solution of tropolone (50 mg.) in water (ca. 0·5 c.c.) was added solid potassium hydroxide (500 mg.), and the mixture heated to 180° in a metal-bath for 15 minutes. The light brown melt was dissolved in water, acidified, and cooled. As no solid was deposited, the solution was extracted with ether; drying followed by evaporation yielded a brown gum which gave a strong green colour with ferric chloride. Extraction with light petroleum (b. p. 40—60°) gave a small amount (ca. 10 mg.) of unchanged tropolone, leaving a small residue of brown resin. Similar results were obtained at temperatures ranging from 180° to 250°.

(b) A solution of tropolone (244 mg.) in sodium hydroxide solution (5 c.c. of N.) was treated with hydrogen peroxide (1 c.c.; 30%) and set aside in the dark for 48 hours. No colour change from the original yellow took place. The solution was acidified (2N-sulphuric acid) to Congo-red and extracted with ether. The oily residue obtained by drying and evaporation was extracted with *cyclo*hexane; the extract on cooling deposited needles of unchanged tropolone (180 mg.). The hydrocarbon-insoluble residue (ca. 10 mg.) consisted of an acidic solid which was purified by dissolution in sodium carbonate and precipitation by acid; it then melted at 182—184° undepressed on admixture with authentic *cis* : *cis*-muconic acid (cf. Elvidge, Linstead, Sims, and Orkin, *J.*, 1950, 2235).

When the oxidation was carried out in the presence of light the fission product had m. p. 154—162°. A similar m. p. range for *cis* : *cis*-muconic acid prepared in the light has been noted by Grundmann (*Ber.*, 1936, **69**, 1755).

(c) To a solution of sodium (100 mg.) in methanol (3 c.c.) was added tropolone methyl ether hemihydrate (50 mg.), and the mixture heated under reflux for 30 minutes. The solution was then evaporated to dryness under reduced pressure and extracted with ether. The residue was acidified, but no benzoic acid could be detected. The ethereal extract was evaporated to small bulk, seeded with tropolone methyl ether, and cooled; filtration gave unchanged tropolone methyl ether (35 mg.). The mother-liquors were evaporated to dryness and the residue heated with a few drops of alcoholic potassium hydroxide; evaporation and acidification again gave no trace of benzoic acid. The presence of methyl benzoate, even in traces, should have been readily detectable by smell.

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