52. Studies on Tropolone Derivatives¹⁾. VII. Halogen Derivatives of Tropolone (II).

By Tetsuo NOZOE, Shûichi SETO, Toshio MUKAI,
* Kameji YAMANE, and Akira MATSUKUMA.

Chemical Institute, Faculty of Science, Tôhoku University.

(Comm. by R. MAJIMA, M.J.A., May 16, 1951.)

The authors have obtained all the substitution products possible of formation by the bromination of tropolone^{2),3),5)}. Those include two kinds of monobromo compound (o-: m.p. 108°, p-: m.p. 191°), two kinds of dibromo compound (o, o-: m.p. 160°, o, p-: m.p. 153°) and one kind of tribromo compound (m.p. 124°). It had also been shown that during the bromination of tropolone or o-bromotropolone in carbon tetrachloride or chloroform, a red or a yellowish orange complex is obtained as an intermediate and that the decomposition of this complex with water yielded a mixture of variously substituted bromotropolones. A tentative formula of an unsaturated tropoquinonoid structure, as shown in (A), was given for this complex³⁾.

The present paper deals with the results of experiments recently conducted to obtain chloro- and chlorobromotropolones which had not been obtained previously, and a further consideration of the above-mentioned complex compounds.

(A)

Chlorination of Tropolone in Alcohol and Glacial Acetic Acid:

Previous experiments have shown^{2),3)} that the bromination of tropolone (I) in glacial acetic acid or ethanol results in the formation, not of monobromo compound, but of o, o-dibromotropolone (II) and tribromotropolone (III), and the same tendency was found in the chlorination.

Application of 2 moles of chlorine to (I) in glacial acetic acid at a room temperature, under the presence of sodium acetate, yields trichlorotropolone (IV), m.p. 125–125.5°, as pale yellow needles as crystallized from benzene and petroleum ether⁶⁾ (Anal. Calcd. for $C_7H_3O_2Cl_3$: C, 37.27; H, 1.34; M.W., 224. Found: C, 37.72; H, 1.72; M.W., 226.). p-Toluidine compd.: Yellow needles, m.p. 165° (Anal. Calcd. for $C_{14}H_{12}O_2NCl_3$: N, 4.21. Found: N, 4.09.).

Application of 2–2.5 moles chlorine in ethanolic solution of (I) yields besides (IV), dichlorotropolone (V), m.p. 171°, as colorless plates as crystallized from ethanol (Anal. Calcd. for $C_7H_3O_2Cl_2$: C,

44.01; H, 2.11; M.W. 191. Found: C, 44.68; H, 2.13; M.W., 190.). p-Toluidine compd.: Yellow needles, m.p. 136.5° (Anal. Calcd. for $C_{14}H_{13}O_2NCl_2$: N, 4.70. Found: N, 4.56).

From the manner of electrophilic substitution of the tropolone nucleus, it seems certain that the three chlorine atoms in (IV) are in o, o-, and p-positions³⁷).

The assumption of the substituted positions in (V) was drawn from following experiments. Bromination of (V) in acetic acid, under the presence of sodium acetate, yields a dichloro-bromotropolone (VI), m.p. 119–119.5°, as pale yellowish green plates as crystallized from a mixture of benzene and petroleum ether (Anal. Calcd. for $C_7H_5O_2BrCl_2$: C, 31.13; H, 1.13. Found: C, 31.20; H, 1.10.). p-Toluidine compd.: Yellow needles, m.p. 171–172° (Anal. Calcd. for $C_{14}H_{13}O_2NBrCl_2$: N, 3.72. Found: N, 3.41.).

On the other hand, chlorination of the structurally known p-bromotropolone (VII) by passing through over 2 moles of chlorine in its glacial acetic acid solution, under the presence of sodium acetate, results in the formation of colorless needles of m.p. 112–112.5° as crystallized from a mixture of benzene and petroleum ether, from the insoluble portion, and o, o-dichloro-p-bromotropolone (VIII), m.p. 116–118.5°, from the soluble portion, as pale yellowish green needles, as crystallized from a mixture of benzene and petroleum ether. p-Toluidine compd.: Yellow needles, m.p. 171–172°. Since the mixed fusion of (VIII) and its p-toluidine compd. with (VI) and its p-toluidine compd. failed to show any depression of the melting points, it can rightfully be assumed that (VI) is o, o-dichloro-p-bromotropolone, and (V), o, o-dichlorotropolone.

Chlorination of the structurally known o-bromotropolone (IX) in acetic acid at room temperature yields, according to the reacting conditions, o, p-dichloro-o-bromotropolone (X), m.p. 116–117.5°, or monochloro-o-bromotropolone (XI), m.p. 163.5°. (X) is obtained as pale yellow needles or prisms from a mixture of benzene and petroleum ether (Anal. Calcd. for $C_7H_5O_2BrCl_2$: C, 31.13; H, 1.13. Found: C, 30.14; H, 1.05.). p-Toluidine compd.: Yellow needles, m.p. 165–165.5°. (Anal. Calcd. for $C_{14}H_{13}O_2NBrCl_2$: N, 3.72. Found: N, 3.68.). (XI) is obtained as pale yellow needles from ethanol (Anal. Calcd. for $C_7H_5O_2BrCl$: C, 35.70; H, 1.71. Found: C, 35.96; H, 1.78.). p-Toluidine compd.: Yellow needles, m.p. 128–129° (Anal. Calcd. for $C_{14}H_{13}O_2NBrCl$: N, 4.69. Found: N, 4.56.). The mixed fusion of (X) with (VI) showed a slight depression of m.p. and that of their p-toluidine compounds gave an intermediate value. Since (XI) differs from the previously reported o-bromo-p-chlorotropolone³, m.p. 128°, it must be o-chloro-o-bromotropolone. (V) submits to coupling with p-tolyldiazonium chloride to give an azo compound

of red scaly crystals, m.p. 187–188°. (Anal. Calcd. for $C_{14}H_{10}O_2N_2Cl_2$: N, 9.07. Found: N, 9.19.). Detailed studies on these are still being carried out.

Chlorination of Tropolone in CCl_4 :

Passage of 1 mole chlorine in a CCl_4 solution of tropolone (I) instantly yields colorless crystals (XII), m.p. 117–123° (sometimes a few degrees higher), which are insoluble in petroleum ether and benzene, but becomes slightly soluble when heated, by which it evolves HCl and returns to (I). (XII) is very easily soluble in water from which (I) and HCl are recovered, and gives strong coloration by $FeCl_3$. The CCl_4 mother liquor used in the chlorination yields an o, o-dichlorotropolone (V), m.p. 171°. It is certain, from these results, that the chlorination of (I) occurred first, and HCl generated in this instance, had instantly reacted with (I) to yield a salt of a conjugate acid (B) practically insoluble in CCl_4 . The results of titration gave the neutralization equivalent of 1.88, a value close to 2. In order to confirm this point, (I) was dissolved in CCl_4 and dry HCl passed through the solution by which the same colorless crystals, m.p. 120–130°, were obtained. No depression of m.p. was shown by their mixed fusion. Recently, Doering and Knox⁽⁷⁾ also recognized the fact that tropolone gives a hydrochloride in ether.

Bromination of Tropolone in CCl_4 and in $CHCl_3$:

(1) Addition of Br_2 to a CCl_4 or $CHCl_3$ solution of (I) at a room temperature results in the separation of reddish orange crystals (XIII), which sinter and turn white at 110° by liberating HBr, and melt at 155–158° (sometimes several degrees different). (XIII) is insoluble in benzene and petroleum ether and is difficultly soluble in $CHCl_3$, but can be recrystallized, by a cautious handling, to dark red needles, which change to pale yellow crystals by moisture in the air and sunlight. The crystals become colorless when they come in contact with water or ethanol. (XIII) colors the potassium iodide-starch paper blue. The analytical values approximately corresponded to formula $C_{14}H_{13}O_4Br_3$ which corresponds to tropolone and Br in 2:3 ratio, rather than the expected (A) formula. (Anal. Calcd. for $C_{14}H_{13}O_4Br_3$: C, 34.74; H, 2.96; Br, 49.48. Found: C, 34.84; 36.13; H, 2.45; 2.59; Br, 51.03; 45.25).

Titration of (XIII) gave neutralization equivalent of 4.03 and 4.01, if calculated as $C_{14}H_{13}O_4Br_3$ in the aqueous solution. The de-

composition products, in this case, are composed of (I), (II) and (IX), and possibly (III) as well. The neutralization equivalent of 3.13 and 3.09 are obtained when (XIII) is decomposed reductively in a conc. potassium iodide solution, and the liberated iodine removed by $\text{Na}_2\text{S}_2\text{O}_3$. The titration of iodine liberated by the decomposition of (XIII) in HCl solution of conc. potassium iodide gave an oxidation equivalent of 1.66 when calculated as $\text{C}_{14}\text{H}_{11}\text{O}_4\text{Br}_3$. In the reductive decomposition, (I), m.p. 47–50°, alone was obtained with none of its bromo compounds.

(2) Application of one molecular equivalent of Br_2 to o-bromotropolone (IX) in CCl_4 or CHCl_3 solution at a room temperature or under ice-cooling, yields orange yellow needle microcrystals (XIV), which turns colorless at 141°, and melts at 164–168°. Its qualitative properties, such as the solubility, its action against water, and its oxidizability, are all identical with those of (XIII). (XIV) is barely recrystallized from CHCl_3 and seems to be the most stable of these complexes. The mother liquor of CCl_4 , from which (XIV) has been removed, yields crystals of m.p. 113–133° which contains (II) and (IX). The analytical values of the complex in this case approximates those of $\text{C}_{14}\text{H}_{11}\text{O}_4\text{Br}_5$ which corresponds to a compound of (IX) and Br in 2:3 ratio, and do not support the tropoquinonoid structure. (Anal. Calcd. for $\text{C}_{14}\text{H}_{11}\text{O}_4\text{Br}_5$ which corresponds to a compound of (IX) and Br_2 in 2:3 ratio, and do not support the tropoquinonoid structure. Anal. Calcd. for $\text{C}_{14}\text{H}_{11}\text{O}_4\text{Br}_5$: C, 26.15; H, 1.72; Br, 62.16, Found: C, 26.80, 25.99; H, 2.24, 1.00; Br, 63.50). Neutralization equivalent obtained by titration were 3.65, 4.13 and 3.96, when calculated as $\text{C}_{14}\text{H}_{11}\text{O}_4\text{Br}_5$, and the decomposition product is a mixture of (IX), (II) and (III). Titration of iodine liberated by decomposition with HCl solution of conc. potassium iodide showed the oxidation equivalent to be 1.64 and 1.57 when calculated as $\text{C}_{14}\text{H}_{11}\text{O}_4\text{Br}_5$ for (XIV). Reductive decomposition of (XIV) yields (IX), m.p. 105–107°, alone.

(3) Application of Br_2 to CCl_4 solution of p-bromotropolone (VII) gives reddish orange crystals (XV), precipitation of which sometimes takes a long time, and the product seems to be very easily decomposed, as they generally contain some colorless crystals. (XV) turns white at 110°, sinters at 180°, and melts at 197–203° (sometimes several degrees lower). Decomposition of (XV) with water yields crystals of m.p. 165–180°, from which p-bromotropolone (VII) was identified. (VII) and a bromo compound of m.p. 120–140° were obtained from the CCl_4 mother liquor. The decomposition of (XV) by KI-HCl, similar to the cases of (1) and (2), gave the oxidation equivalent of 1.30 when

calculated as $C_{14}H_{11}O_4Br_5$, and the large difference in this value from those of (1) and (2) must be due to the unstability of (XV).

(4) The dropwise addition of Br_2 to CCl_4 solution of tropolone methyl ether (XVI) results in an instant separation of an orange-colored oil which crystallized all at once during the reaction. The reddish orange crystals (XVII) thus obtained melts, as is, at $75-80^\circ$ with effervescence. The aqueous solution of (XVII) gives a very faint coloration with ferric chloride but the color deepens by heating. This shows that the hydrolysis of the methyl ether occurred after being dissolved in water. The decomposition product contains tribromo-tropolone (III). The CCl_4 mother liquor yielded crystals of m.p. $97-108^\circ$ and some oil. (Anal. Calcd. for $C_{16}H_{17}O_4Br_3$: C, 37.45; H, 3.34. Found: C, 37.82; H, 3.62.) The oxidation equivalent of 1.47 when calculated as $C_{16}H_{17}O_4Br_3$, was obtained by the titration of the liberated iodine by KI-HCl decomposition, and the decomposition product was an oil.

Consideration of the Results obtained:

(1) Bromination of (I), (VII), (IX) and (XVI) in non-ionic solvents such as CCl_4 results in the formation of orange yellow to red complex practically insoluble in these solvents, prior to direct substitution. These complexes, when heated or thrown into water, lose the characteristic color and yields a mixture of variously substituted bromotropolones and the original material.

(2) These colored complexes are very susceptible to sunlight and moisture, and have a tendency to liberate a part of bromine when left standing. The analytical values, therefore, would not necessarily be correct but generally they correspond to those of a compound in which 3 atoms of bromine have been combined with 2 moles of tropolone or its derivatives. It has, therefore, excluded the previous assumption of a tropoquinonoid structure (A) possessing 2 bromine atoms in 1 mole of tropolone.

(3) Reductive decomposition of these complexes results in a sole recovery of the original material so that the 3 bromine atoms in these complexes must not be in a state of complete covalent bonding to the tropolone molecule. The results of quantitative determinations approximately corresponds to the assumption that only 2 out of the three bromine atoms exist as free bromines (or as a bromine cation).

(4) The results of neutralization titration gave values close to 4 equivalents when decomposed in water, while on reductive decomposition ca. 3 equivalent. This, and the fact that the decomposition product is a mixture of various substitution compounds show that the bromination of the tropolone nucleus by free bromine

occurred in the aqueous solution, and a further one molar equivalent of HBr had been liberated.

It has already been shown³⁾⁹⁾ that, in order to explain the various specificity of hinokitiol and tropolone, a resonance among a large number of structures divided into three types of ionic and non-ionic formulae had been taken into consideration. From the tendency of recent studies in this field, it seems more appropriate to assume highly mobile tautomers rather than a resonance hybrid due to hydrogen bonding. Details on this point will be given in a following report⁹⁾.

The first reaction to take place, by the application of Cl_2 or Br_2 to tropolones in such non-ionic solvents as CHCl_3 or CCl_4 , is the ordinary electrophilic substitution but the hydrogen halide that is here produced instantly reacts with the tropolones to produce a conjugate acid cation. In the chlorination, crystals of chloride ($\text{B:X} = \text{Cl}$) that are insoluble in these solvents precipitate out. In the presence of bromine, however, this conjugated acid salt ($\text{B:X} = \text{Br}$), seems to immediately combine with bromine to give colored complexes of some particular type.

In order to explain the experimental results as outlined above, the authors have assumed a structure as shown by (C) as a working hypothesis. The initially formed conjugate acid cation is a very strong acid and the ring-carbons are positively charged so that it

(C₁)

polarizes another mole of amphoteric tropolone molecule, and the acid cation pulls this polarized tropolone in a negatively charged form (Type-C)⁹⁾. Further absorption of one mole of bromine to this double-molecule pair, completes the formation of a special complex such as (C₁).

These colored complexes possess a fair amount of stability, and are very difficultly soluble in CHCl_3 but can be recrystallized from it that they may be assumed to be essentially an ionic bonding.

Thus, it seems more probable to assume a resonance of Br_2 or Br_3 , in any form, between these two tropolone molecules, rather than a pure ionic bonding such as in (C₁). In the case of chlorination, however, it produces no colored precipitate, only white one, and when the conjugate acid and tropolone is mixed, there is no

coloration. It is possible to suppose that not only the bromine atom but the proton in the conjugate acid contributes on resonance or oscillation between two molecules of tropolone, in red complex salt. In this sense, it seems more appropriate to show these complexes by the formula (C₂), rather than by (C₁). These complexes may be taken as the quinhydrone-like molecular compounds characteristic of tropolones. In short, the formation of such complexes is due to the coplaner structure of tropolone together with its possession of a π -electron system of large polarizability and amphoteric properties.

Recently, Cook¹⁰⁾ and Haworth¹¹⁾ have also recognized the similar formation of scarlet or red complexes by the bromination of tropolone and methyltropolone in CHCl₃, but none of them touched on their structures.

Further detailed studies are being carried out and the results will be published in the near future.

The authors take this opportunity to extend their sincere gratitude to the Ministry of Education for the donation of its Grant in Aid of Scientific Research and the Takasago Chemical Industrial Co., Ltd. for its financial help.

References.

- 1) Presented at the 4th Annual Meeting of the Chemical Society of Japan in Tokyo April 7, 1951.
- 2) T. Nozoe, S. Seto, Y. Kitahara, M. Kunori, and Y. Nakayama, *Proc. Japan Acad.*, **26**, (No. 7) 38 (1950).
- 3) T. Nozoe, Y. Kitahara, K. Yamane, and A. Yoshikoshi, *ibid.*, **27**, 18 (1951).
- 4) T. Nozoe, S. Seto, T. Ikemi, and T. Arai, *ibid.*, **27**, 24 (1951).
- 5) T. Nozoe, Y. Kitahara, T. Andô, and E. Kunioka, *ibid.*, **27**, 190 (1951); *ibid.*, **27**, 231 (1951).
- 6) Microanalyses were carried out by Messrs. Hirai, Hayatsu, and Kawamoto of Sankyô & Co., Ltd.
- 7) W. E. Doering and L. H. Knox, *J. Am. Chem. Soc.*, **73**, 828 (1951).
- 8) T. Nozoe, *Proc. Japan Acad.*, **26**, (No. 9), 30 (1950).
- 9) T. Nozoe, S. Seto, and Y. Kitahara, to be published soon.
- 10) T. W. Cook, A.R. Gibb, R.A. Raphael, and A.R. Somerville, *J. Chem. Soc.*, 1951, 503.
- 11) R. B. Haworth and J. B. Hobson, *ibid.*, 1951, 561.