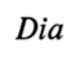
*Diazo Reactions of 4-Aminotropolones**

By Kozo Doi

(Received May 9, 1961)

Recently the author¹⁾ has synthesized 4-aminotropolone (I), 4-amino-6-methyltropolone (II) and 4-amino-6-isopropyltropolone (III) by an application of the elimination-addition mechanism²⁾ involving benzyne-type intermediate to the corresponding 3-iodotropolone. The author has also reported further synthetic methods of the aminotropolones, which include applications of the Curtius reaction to 4-carboxytropolones¹⁾ and of the Schmidt reaction to acetyl, formyl and isopropenyl derivatives of tropolones³⁾, and the reaction of 4-bromotropolone and ammonia⁴⁾.



I: X=H II: X=Me
III: X=*iso*-Pr

On the other hand, there have been rare observations of the reactivities of 4-aminotropolones, except in the case of the diazotization of a methyl analogue II, in which instance the corresponding hydroxytropolone (V) was obtained without detecting the intermediate diazonium salt⁵⁾. In the previous papers the author stated in brief some synthetic applications of the aminotropolone (I), involving preparations of some pyridotropolones⁶⁾ and of 4-aminotropone⁷⁾. Furthermore, the author has very recently reported that the aminotropolone (I), differing from the isomeric 3- and 5-aminotropolones, undergoes some electrophilic substitutions to give normal nuclear substitution products⁸⁾.

It is well-known that diazotization of 5-aminotropolones results in formation of diazonium salts, which undergo the Sandmeyer reaction in the presence of cuprous salt to replace the amino group by halogen, nitrile and alkoxyl groups⁹⁾. On the other hand, the diazotization of 3-aminotropolones is also known to undergo the Sandmeyer reaction¹⁰⁾, although accompanied by aromatization into the corresponding salicylic acid¹¹⁾, forming 3-halogenotropolones and 3-hydroxytropolones under a certain reaction condition¹²⁾.

In this communication the author wishes to describe the diazotizations of the above three 4-aminotropolones in comparison with those of the 3- and 5-isomers.

On diazotization in a sulfuric acid solution the aminotropolones afford the corresponding hydroxytropolones, in neither case of which the addition of alkaline β-naphthol to the diazotized solution causes red coloration, as observed by Haworth and his co-workers⁵⁾. The melting points and ultraviolet absorptions

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* This work was presented at the 12th Annual Meeting of the Chemical Society of Japan, Kyoto, April, 1959.

1) K. Doi, This Bulletin, **34**, 497 (1961).

2) J. D. Roberts et al., *J. Am. Chem. Soc.*, **75**, 3290 (1953); ibid., **78**, 601 (1956).

3) K. Doi, This Bulletin, **34**, 501 (1961).

4) K. Doi, ibid., **34**, 504 (1961).

5) W. D. Crow, R. D. Haworth and P. R. Jefferies, *J. Chem. Soc.*, **1952**, 3705.

6) K. Doi, *Bull. Chem. Res. Inst. Non-Aqueous Solutions, Tohoku Univ.*, **9**, 19 (1959).

7) K. Doi, This Bulletin, **33**, 887 (1960).

8) K. Doi, ibid., **34**, 1410 (1961).

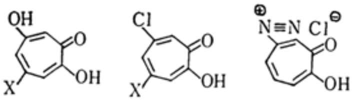
9) P. L. Pauson, *Chem. Revs.*, **55**, 9 (1955); T. Nozoe, S. Seto, S. Ebine and S. Ito, *J. Am. Chem. Soc.*, **73**, 1895 (1951).

10) T. Nozoe, Y. Kitahara and K. Doi, *Proc. Japan Acad.*, **27**, 282 (1951).

11) R. D. Haworth and P. R. Jefferies, *J. Chem. Soc.*, **1951**, 2067; T. Nozoe, Y. Kitahara and K. Doi, *J. Am. Chem. Soc.*, **73**, 1895 (1951).

12) T. Nozoe, Y. Kitahara and K. Doi, *Science Repts. Tohoku Univ., Ser. I*, **40**, 121 (1957).

of 4-hydroxytropolone[13] (IV) and 4-hydroxy-6-methyltropolone[5] (V) respectively are in essentially good agreement with those reported. 4-Hydroxy-6-isopropyltropolone (VI) was also ascertained to agree with reaction product[14], obtained by high temperature alkaline hydrolysis of 3-bromo-6-isopropyltropolone.

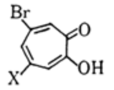


IV : X=H VII : X=H
V : X=Me VIII : X=Me X
VI : X=*iso*-Pr IX : X=*iso*-Pr

On diazotization in a dilute hydrochloric acid solution in place of sulfuric acid, the aminotropolones form corresponding 4-chlorotropolones in a good yield, even without any catalyst such as cuprous chloride or copper. 4-Chlorotropolone (VII) is in good agreement with an authentic sample[15] in both its melting point and ultraviolet absorption spectrum. The structures of 4-chloro-6-methyl-VIII and 4-chloro-6-isopropyltropolones (IX) are reasonably understood from the comparison of their ultraviolet absorptions with that of VII.

An isolation of a stable diazonium salt was possible in some cases. For instance, in a concentrated hydrochloric acid solution, 4-aminotropolone (I) results in facile diazotization, even in a state of suspension, and converts into yellow tropolone-4-diazonium chloride (X), which undergoes red coloration with alkaline β-naphthol. This diazonium salt gives the chloro derivative VII on being heated with copper powder under the vigorous evolution of nitrogen, 4-methoxytropolone on being heated with methanol, and 4-cyanotropolone on reaction with cuprous cyanide. From alkyl derivatives II and III, the corresponding diazonium salt has not been isolated in a solid state, but it seems to be formed as an intermediate in the above reactions.

In a similar manner, the use of hydrobromic acid in place of hydrochloric acid in the diazotization results also in the formation of corresponding bromotropolones without any catalyst. 4-Bromotropolone (XI) was identified with an authentic specimen[4] by the determination of the mixed melting point and by a comparison of the ultraviolet absorption. The structures of the other reaction products XII and XIII are assumed from the similarity of their ultraviolet absorptions to that of XI.



XI : X=H XII : X=Me
XIII : X=*iso*-Pr

Fig. 1 indicates the ultraviolet absorption spectra of hydroxyl (IV), chloro (VII), and bromo (XI) derivatives obtained from 4-aminotropolone (I). The ultraviolet spectra of the alkyl derivatives of the above three products resemble essentially that of the respective product from I.

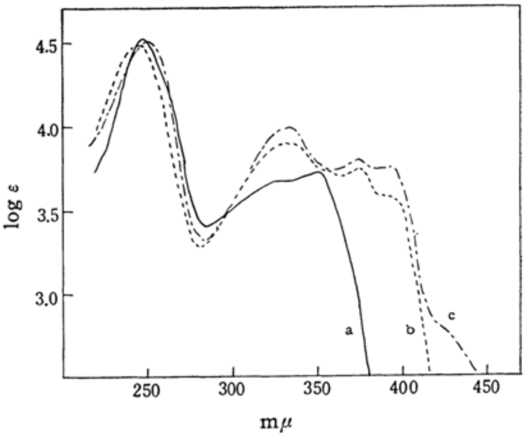
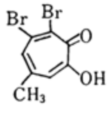
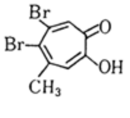


Fig. 1. The ultraviolet absorption spectra.
a : 4-Hydroxytropolone (IV)
b : 4-Chlorotropolone (VII)
c : 4-Bromotropolone (XI)

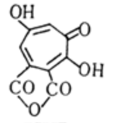
When diazotized in an concentrated hydrobromic acid solution, 4-amino-6-methyltropolone (II) has been found to yield not only 4-bromo-6-methyltropolone (XI) but also an unexpected



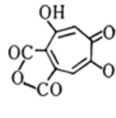
XIV



XV



XVI



XVII

product, dibromo-methyltropolone. The ultraviolet absorption spectrum of this anomalously produced dibromotropolone resembles not so much that of 3, 6-dibromotropolone as that of the 4-bromo derivative XI, although indicating a bathochromic shift by the introduction of one bromine atom (Fig. 2). For the above reason, the dibromo-methyltropolone is probably a nuclear substitution product, namely XIV or XV.

Whether the dibromotropolone is XIV or XV is reasonably suggested by its infrared absorption spectra. Table I indicates the absorption bands in the CH out-of-plane vibration regions

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[13] Y. Kitahara, ibid., **39**, 258 (1956).
[14] T. Toda, private communication.
[15] T. Sato, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **80**, 1171 (1959).

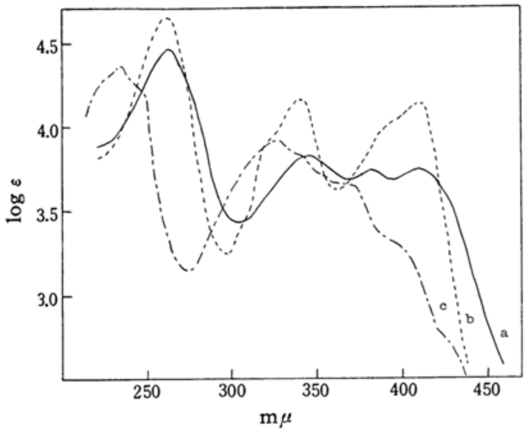


Fig. 2. The ultraviolet absorption spectra.
a : 3, 4-Dibromo-6-methyltropolone (XIV)
b : 3, 6-Dibromotropolone
c : 5-(β-Chloro-β-cyanoethyl)tropolone (XVIII)

Table I. Frequencies in the CH out-of-plane vibration region of the infrared spectra of some trisubstituted tropolones (cm^{-1})

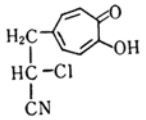
XIV	896	867	823	795	735
XVI	896	865	806	774	730
XVII	—	—	814	763 782	740

of the infrared spectra of the dibromotropolone, 6-hydroxytropolone-3, 4-dicarboxylic anhydride[16] (XVI) (3, 4, 6-trisubstituted tropolone), and stipitatonic acid[16] (XVII) (4, 5, 6-trisubstituted tropolone). Undoubtedly these absorptions of the dibromo-methyltropolone resemble not so much those of XVII as of XVI, and therefore, the dibromotropolone seems to be 3, 4-dibromo-6-methyltropolone (XIV) rather than 4, 5-dibromo-6-methyltropolone (XV).

The formation of this dibromotropolone (XIV) is probably interpreted to be due to further bromination of XI, which has been produced normally in the diazotization, with free bromine formed by an oxidation of hydrobromic acid with nitrous acid. A similar example was reported in the formation of 3, 5-dibromotropolone from 3- and 5-nitrotropolone when heated with hydrobromic acid[17].

The above description has demonstrated that the diazotizations of 4-aminotropolones result in the formation of diazonium salt, which reacts immediately with anions of the acid used to give the halogeno- or hydroxytropolones without any catalyst such as cuprous salt or copper. Such a fact has not been found in the other isomeric aminotropolones. This is probably to be understood as a competitive action of an electron-withdrawing effect of the diazonium group and a conjugate acid-forming effect of the tropolone ring with the acid used, resulting in promotion of the formation of a carbonium ion, which combines immediately with anions from the acid used to form substitution product.

In relation to the diazotization of the 4-aminotropolones, the author has investigated the reaction of 5-diazotized aminotropolone and acrylonitrile under the Meerwein condition to obtain 5-(β-chloro-β-cyanoethyl)tropolone (XVIII), although in a poor yield. The structure of this product XVIII is probably supported by the resemblance of the ultraviolet absorption (Fig. 2) to those of 5-alkyltropolones and by the result obtained in the reaction of diazotized aniline and acrylonitrile[18].



XVIII

Experimental

All of the ultraviolet absorption spectra were measured in methanol solution with a Beckman model DU quartz spectrophotometer. The infrared spectra were measured on potassium bromide disks with a Perkin-Elmer model 21 infrared spectrometer, using a rock salt prism.

4-Hydroxytropolone (IV).—A solution of sodium nitrite (70 mg.) and water (1 ml.) was added, drop by drop, for 5 min. into a cold suspension of 4-aminotropolone (I, 140 mg.), concentrated sulfuric acid (0.5 ml.) and water (5 ml.). After 30 min., the reaction mixture was gradually warmed up to 50°C, by which means a complete solution was effected. Then the mixture was diluted with water (20 ml.) and extracted continuously with ether for 8 hr. The residue obtained by the evaporation of the ether extract, after sublimation in vacuo and subsequent crystallization from acetic acid, afforded IV (60 mg.) as colorless needles, m. p. 230∼231°C, undepressed on admixture with an authentic sample[13].

4-Hydroxy-6-methyltropolone (V).—A solution of sodium nitrite (70 mg.) and water (1 ml.) was added dropwise into a cold, stirred solution of 4-amino-6-methyltropolone (II, 150 mg.), concentrated sulfuric acid (0.5 ml.) and water (10 ml.). The reaction mixture was then treated as in the above case, and V (60 mg.) was obtained as colorless prisms, m. p. 241∼242°C, undepressed on admixture with an authentic specimen[5].

4-Hydroxy-6-isopropyltropolone (VI).—A solution of sodium nitrite (70 mg.) and water (1 ml.) was added dropwise into a cold, stirred solution of 4-amino-6-isopropyltropolone (III, 180 mg.), concentrated sulfuric acid (0.5 ml.), and water (10 ml.) for 5 min. After 30 min., the reaction mixture was

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[16] K. Doi and Y. Kitahara, This Bulletin, **31**, 788 (1958).

[17] T. Nozoe, Y. Kitahara, K. Doi and T. Arai, *Bull. Chem. Res. Inst. Non-Aqueous Solutions, Tohoku Univ.*, **7**, 13 (1957).

[18] C. F. Koelsch, *J. Am. Chem. Soc.*, **65**, 57 (1943).

extracted with three 20-ml. portions of chloroform, and the residue obtained by evaporation of the chloroform extract was sublimed in vacuo. Recrystallization of the sublimate from dilute methanol gave VI (100 mg.) as colorless prisms, m.p. 178~179°C, undepressed on admixture with an authentic sample[14].

4-Chlorotropolone (VIII).—To a cold, stirred mixture of 4-aminotropolone (I, 70 mg.), concentrated hydrochloric acid (1 ml.) and water (2 ml.) was added dropwise for 5 min. a solution of sodium nitrite (40 mg.) and water (0.5 ml). Then the mixture was warmed gradually to 40°C, by which the suspended solid dissolved with evolution of gas to form a clear solution. This solution was extracted with three 3-ml. portions of chloroform, and the residue therefrom was recrystallized from cyclohexane. VII (50 mg.) was obtained as pale yellow needles, m. p. 78~79°C, undepressed on admixture with an authentic sample[15].

4-Chloro-6-methyltropolone (VIII).—A solution of sodium nitrite (70 mg.) and water (1 ml.) was added dropwise into a cold, stirred solution of 4-amino-6-methyltropolone (II, 150 mg.), concentrated hydrochloric acid (5 ml.), and water (2 ml.). With the progress of the diazotization, the colorless solid separated out from the reaction mixture. After stirring for 2 hr., the reaction mixture was diluted with water (10 ml.) and extracted with three 20-ml. portions of chloroform. The residue obtained by evaporation of the extract, after sublimation in vacuo and subsequent crystallization from cyclohexane, yielded VIII (120 mg.) as colorless needles, m. p. 117°C.

Found: C, 56.19; H, 4.62. Calcd. for $C_8H_7O_2Cl$: C, 56.30; H, 4.16%. $\lambda_{\max}$ mμ (log ε): 246 (4.49), 334 (3.90), 373 (3.78).

4-Chloro-6-isopropyltropolone (IX).—To a cold, stirred solution of 4-amino-6-isopropyltropolone (III, 180 mg.), concentrated hydrochloric acid (2 ml.) and water (2 ml.), was added dropwise a solution of sodium nitrite (70 mg.) and water (1 ml.). With the progress of the diazotization, the colorless solid precipitated out. The reaction mixture was treated as above and recrystallization of the final sublimate from petroleum ether (b. p. 40~60°C) afforded IX (110 mg.) as pale yellow needles, m. p. 42~43°C.

Found: C, 60.23; H, 5.86. Calcd. for $C_{10}H_{11}O_2Cl$: C, 60.46; H, 5.59%. $\lambda_{\max}$ mμ (log ε): 248 (4.51), 334 (3.94), 373 (3.78).

Tropolone-4-diazonium Chloride (X).—A solution of sodium nitrite (280 mg.) and water (1 ml.) was added dropwise into a cold, stirred mixture of 4-aminotropolone (I, 550 mg.), concentrated hydrochloric acid (20 ml.) and water (6 ml.), and then the reaction mixture was stirred for an hour at 0°C. The colorless solid turned gradually into a yellow solid with the progress of the diazotization. The residual yellow solid was collected by filtration to give X (0.31 g.), m. p. 100~103°C (decomp.). From the filtrate 4-chlorotropolone (120 mg.) was obtained.

The diazonium salt X showed red coloration on being added into an alkaline solution of β-naphthol, and yielded 4-chlorotropolone on being heated with copper bronze in benzene.

4-Methoxytropolone from X.—To a cold, stirred mixture of the diazonium salt (X, 100 mg.) and methanol (5 ml.) was added copper bronze (10 mg.). The reaction mixture turned into a deep red solution with the evolution of nitrogen, and then it was stirred for an hour at room temperature. The filtrate, after removal of copper, evaporation of the solvent, sublimation in vacuo and subsequent crystallization from methamol, gave 4-methoxytropolone (20 mg.) as colorless leaflets, m. p. 95°C, undepressed on admixture with an authentic sample[13].

4-Cyanotropolone from X.—To a stirred mixture of potassium cyanide (700 mg.), cuprous cyanide (450 mg.) and water (2 ml.), was added the diazonium salt (X, 400 mg.) at room temperature. The mixture was stirred for another hour and then warmed gradually to 50°C. Hydrogen sulfide was passed through the mixture, chloroform (10 ml.) was added, and some insoluble matter was removed by filtration. The chlorform solution, after evaporation of the solvent in vacuo, gave 4-cyanotropolone (40 mg.) as yellow needles, m. p. 194°C, undepressed on admixture with an authentic sample[4].

4-Bromotropolone (XI).—A solution of sodium nitrite (70 mg.) and water (1 ml.) was added dropwise under cooling into a stirred mixture of the aminotropolone (I, 140 mg.), concentrated hydrobromic acid (4 ml.) and water (2 ml.). With the progress of the diazotization, the reaction mixture became a clear solution under evolution of nitrogen. After 2 hr., the reaction mixture was diluted with water (40 ml.) and extracted with three 30-ml. portions of chloroform. The residue obtained by evaporation of the solvent of the extract, after sublimation in vacuo and subsquent crystallization from cyclohexane, afforded XI (100 mg.) as pale yellow needles, m. p. 85~86°C, undepressed on admixture with an authentic specimen[4].

4-Bromo-6-methyltropolone (XII).—A mixture of the aminotropolone (II, 150 mg.), concentrated hydrobromic acid (2 ml.) and water (4 ml.) was diazotized with a solution of sodium nitrite (70 mg.) and water (1 ml.). As treated similarly to the above case, the reaction mixture afforded XII (120 mg.) as pale yellow needles (cyclohexane), m. p. 116~117°C.

Found: C, 44.50; H, 3.34. Calcd. for $C_8H_7O_2Br$: C, 44.68; H, 3.28%. $\lambda_{\max}$ mμ (log ε): 253 (4.50), 336 (3.87), 370 (3.76), 395 (3.49).

4-Bromo-6-isopropyltropolone (XIII).—A solution of the aminotropolone (III, 90 mg.), concentrated hydrobromic acid (1 ml.) and water (2 ml.) was diazotized with a solution of sodium nitrite (40 mg.) and water (1 ml.). The procedure followed for isolating the product was essentially the same as above, and the reaction product XIII (20 mg.) was obtained. Analytical sample was crystallized from petroleum ether (b. p. 40~60°C) as pale yellow needles, m. p. 52~53°C.

Found: C, 49.19; H, 4.32. Calcd. for $C_{10}H_{11}O_2Br$: C, 49.38; H, 4.52%. $\lambda_{\max}$ mμ (log ε): 255 (4.49), 335 (3.38), 370 (3.74), 393 (3.48).

3, 4-Dibromo-6-methyltropolone (XIV).—A solution of sodium nitrite (70 mg.) and water (1 ml.) was added dropwise into a cold, stirred mixture of the aminotropolone (II, 150 mg.), concentrated hydrobromic acid (8 ml.) and water (2 ml.). After being stirred for 3 hr. further, the reaction mixture was diluted with water (20 ml.), extracted with three 20-ml. portions of chloroform, and the solvent of the extract was evaporated in vacuo. The residual solid, m. p. 104~110°C, was dissolved in cyclohexane (50 ml.) and chromatographed on a column of silica gel (1.5×20 cm.). From the more soluble eluate, the monobromotropolone (XII, 40 mg., m. p. and mixed m. p. 116~117°C), was obtained, and from the less soluble eluate the dibromotropolone (XIV, 60 mg.) was obtained as pale yellow prisms (from ligroin), m. p. 127°C.

Found: C, 32.41; H, 2.31. Calcd. for $C_8H_6O_2Br_2$: C, 32.69; H, 2.06%. λ_{max} mμ (log ε): 264 (4.47), 345 (3.83), 383 (3.74), 410 (3.74).

5-(β-Chloro-β-cyanoethyl)tropolone (XVIII).—A cold solution of 5-aminotropolone (4.1 g.), concentrated hydrochloric acid (6 ml.), water (12 ml.), and dioxane (10 ml.) was diazotized with a solution of sodium nitrite (2.2 g.) and water (4 ml.). This diazonium salt solution was added dropwise under cooling to a stirred mixture of acrylonitrile (1.6 g.), sodium acetate trihydrate (4.1 g), cupric chloride (4 g.), water (6 ml.), and acetone (50 ml.), and the reaction mixture was stirred overnight at room temperature. Then the mixture was separated by filtration into the solid and the filtrate. The former afforded, after treatment with hydrogen sulfide, 5-chlorotropolone, m. p. and mixed⁹⁾ m. p. 180~181°C.

The filtrate was diluted with water (50 ml.), extracted with three 50-ml. portions of chloroform, and hydrogen sulfide was introduced into this extract. The chloroform solution, from which copper sulfide was removed, was evaporated in vacuo and the residual resinous matter was re-extracted with hot cyclohexane (100 ml.). The residue obtained on evaporation of the cyclohexane extract was separated by fractional sublimation into the two parts, A, which sublimed up to 120°C/2 mmHg (bath temp.), and B, which sublimed up to 170°C. The fraction. A was crystallized from cyclohexane to afford XVIII (20 mg.) as colorless leaflets, m. p. 119~120°C.

Found: C, 57.40; H, 3.72; N, 6.73. Calcd. for $C_{10}H_8O_2NCl$: C, 57.29; H, 3.80; N, 6.67%. λ_{max} mμ (log ε): 235 (4.36), 325 (2.92).

From the fraction B, 5-chlorotropolone (0.7 g.) was obtained.

The author wishes to express his deep gratitude to Professor Yoshio Kitahara for his kind guidance, to Professor Sekio Mitsui for supplying acrylonitrile, to Mr. Hideji Aono for infrared spectral measurements, and to Messrs. Shin-ichi Ohyama, Kuni Kato and Ayako Iwanaga for microanalyses.

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