*Some Electrophilic Substitution Reactions of 4-Aminotropolone**

By Kozo Doi

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In the course of investigations of 4-aminotropolone (I) and its derivatives, the author has established general methods of their syntheses, which include amination of 3-iodotropolones with potassium amide in liquid ammonia⁽¹⁾, applications of the Schmidt reaction to acetyl-, formyl- and isopropenyltropolones⁽²⁾ and of the Curtius reaction to 4-carboxytropolones⁽¹⁾, and amination of 4-bromotropolone with aqueous ammonia⁽³⁾.

On the other hand, there have been little informations on reactivities of 4-aminotropolones except on a diazotization of 4-amino-6-methyltropolone (II)⁽⁴⁾, whereas the reactions of the isomeric 3- and 5-amino derivatives have been much investigated⁽⁵⁾. Recently the author has reported in brief the synthetic applications of I, involving preparations of some pyridotropolones⁽⁶⁾ and of 4-aminotropone⁽⁷⁾. In this communication the author wishes to take up some electrophilic substitution reactions of the aminotropolone (I).

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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) K. Doi, ibid., **34**, 501 (1961).

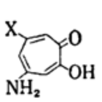
3) K. Doi, ibid., **34**, 504 (1961).

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

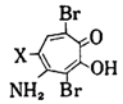
5) Cf. P. L. Pauson, *Chem. Revs.*, **55**, 9 (1955).

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

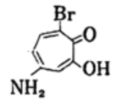
7) K. Doi, This Bulletin, **33**, 887 (1960).



I: X=H
II: X=Me



III: X=Br
V: X=H



IV

On bromination the aminotropolone (I) has been found to give nuclear substitution products in the same manner as many other tropolones. For example, in the presence of sodium acetate as a hydrogen bromide acceptor, I consumes three molar equivalents of bromine to afford in a good yield the tribromotropolone (III). On the other hand, in the absence of any hydrogen bromide acceptor, I reacts with one molar equivalent of bromine to give not only a monobromo derivative, IV, which was identified with that obtained from an application of the Schmidt reaction to the known 6-acetyl-3-bromotropolone[2], but also a dibromo compound, V, whose respective yield is better in the latter than the former. Such a preferential formation of dibromo compound by one molar equivalent of bromine has also been observed in the case of tropolone itself[5].

In Fig. 1 are indicated the ultraviolet absorption spectra of the above two substitution products, III and V, comparing with that of the monobromo compound IV. Tsuboi[8] observed that an introduction of one bromine atom into the 3 (or 7)- and 5-position of tropolone caused a red shift of the maximum in the longest wavelength by 10 and 15 mμ, respectively. Now, the above three bromotropolones (III, IV and V) have the maximum in the longest wavelength at 410, 380 and 390 mμ, respectively. The difference of the maxima of V and IV is 10 mμ, and that of III and V is 20 mμ, the fact of which suggests that the dibromotropolone (V) may be a 3, 7-dibromo derivative rather than a 3, 5-dibromo one.

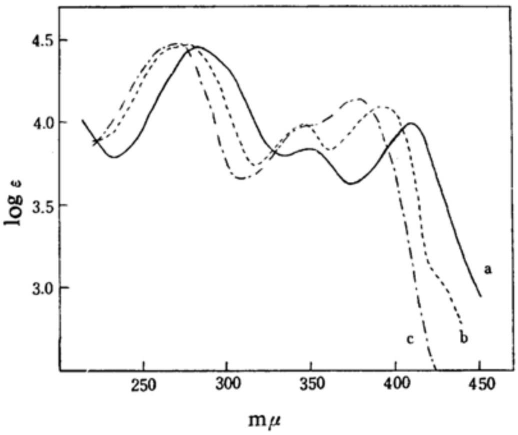


Fig. 1. The ultraviolet absorption spectra.
(a): 4-Amino-3, 5, 7-tribromotropolone (III)
(b): 4-Amino-3, 7-dibromotropolone (V)
(c): 6-Amino-3-bromotropolone (IV)

The position of the two bromine atoms of the dibromo compound V is also understood from a comparison of the characteristic bands due to the CH out-of-plane vibration (864 cm^{-1}) with those of some other 3, 4, 7-trisubstituted tropolones, which possess bands in the 820~875 cm^{-1} region[9], in the infrared absorption spectra. Table I indicates frequencies of the CH out-of-plane vibration of V, comparing with those of some other 3, 4, 7-trisubstituted tropolones.

TABLE I. FREQUENCIES OF THE CH OUT-OF-PLANE VIBRATION OF SOME 3, 4, 7-TRISUBSTITUTED TROPOLONES

Compound	ν_{CH} cm^{-1}	Ref.
4-Amino-3, 7-dibromotropolone (V)	864	
4-Isopropyl-3, 7-dibromotropolone	835	10
7-Bromo-3-iodo-4-methyltropolone	847	11
7-Bromotropolone-3, 4-dicarboxylic anhydride	872	12
7-Hydroxytropolone-3, 4-dicarboxylic anhydride	882	12

4-Aminotropolone (I), differing from its isomeric 3- and 5-amino derivatives, has been found to be fairly stable in pace of the action of nitric acid. Thus an attempt to obtain a nitro compound from I in an usual reaction condition for nitration of tropolones causes to yield not any substitution product but merely a nitrate, possessing a composition of $C_7H_7O_2N \cdot HNO_3 \cdot H_2O$. With fuming nitric acid, however, I reacts vigorously to form in a poor yield 4-amino-5-nitrotropolone (VI), whose structure was confirmed by the fact that the ultraviolet absorption is practically identical with that of the product obtained by an application of the Schmidt reaction to 4-acetyl-5-nitrotropolone[2].

In order to obtain further informations with respect to orientation of electrophilic substitution, nitration has also been carried out on 4-acetylaminotropolone (VII), which is readily prepared from the reaction of I and acetyl chloride in pyridine. Nitration of VII with fuming nitric acid in an acetic acid solution gives also a 5-nitro derivative, VIII, whose structure is confirmed by the formation of VI on its alkaline hydrolysis.

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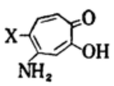
[8] M. Tsuboi, This Bulletin, 25, 369 (1952).

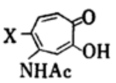
[9] Y. Ikegami, *J. Japanese Chem.* (*Kagaku-no-Ryoiki*), Extra No. 38, 33 (1959).

[10] T. Nozoe, E. Sebe, S. Mayama and S. Iwamoto, *Sci. Repts. Tohoku Univ. Ser. I*, 36, 184 (1952).

[11] T. Nozoe, K. Doi, K. Kitahara and K. Omura, to be published.

[12] T. Nozoe, K. Doi and T. Hashimoto, This Bulletin, 33, 1071 (1960).





VI : $X=NO_2$
IX : $X=NH_2$
X : $X=p$-Tolylazo

VII : $X=H$
VIII : $X=NO_2$

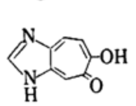
The absorption maximum at 400 mμ (log ε 3.90) of VIII indicates more decreased values both in wavelength and absorption intensity than that at 435 mμ (log ε 4.41) of 5-nitrotropolone itself[13]. This is not consistent with the bathochromic effect of the acetylamino group, having been attributed recently to the steric inhibition of resonance between the nitro group and the tropolone nucleus by the adjacent acetylamino group[14].

From a catalytic hydrogenation of the 5-nitro derivative VIII over palladized charcoal, 4, 5-diaminotropolone (IX) is readily obtained. In the previous paper[2], the author found that an application of the Schmidt reaction to 4-acetyltropolone resulted in the formation of 4-aminotropolone sulfate instead of the expected acetylamino derivative VII, attributing this mechanism to the hydrolyzable nature of VII in the condition employed. Actually it has now been found that the acetylamino compound VII affords easily 4-aminotropolone sulfate on being merely dissolved in concentrated sulfuric acid even at room temperature. This fact justifies the previous mechanism in the Schmidt reaction of the acetyltropolones.

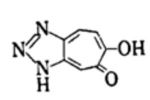
Bromination and nitration of 5-aminotropolones have already been reported, but in no cases has isolation of the substitution products been described[15]. With 3-aminotropolone, some electrophilic substitutions involving bromination, nitration, and azo coupling have been attempted with no isolation of any reaction products[16]. On the contrary, 4-aminotropolone (I) gives easily nuclear substitution products in some electrophilic reactions. This fact is probably considered to be connected with that the amino and hydroxyl groups in the aminotropolone (I) are situated at the positions where they cooperate with each other to increase the reactivity of the tropolone ring, whereas the two groups in the 3- and 5-isomers are not in such positions.

The aminotropolone (I), similarly to the other tropolones, undergoes azo coupling to give a nuclear substitution product of red dyestuff, not a diazoamino derivative. Thus on being treated with diazotized p-toluidine in an alkaline solution, I affords in a good yield 4-amino-5-p-tolylazotropolone (X), whose hydrogenolysis leads to the diaminotropolone (IX).

In a similar manner to o-phenylenediamine, the diamino compound IX gives an imidazole, XI, on being heated with formic acid, and a triazole, XII, on being diazotized. Informations on tautomerism between these reaction products and their possible isomers of the aza-azulene type have not been obtained in detail, but it is probably concluded that they may not be their possible dihydroxy-azaazulene derivatives, since their respective ultraviolet absorption is resembling that of imidazolo[d]tropone[17] and of triazolo[d]tropone[18] (Fig. 2).



XI



XII

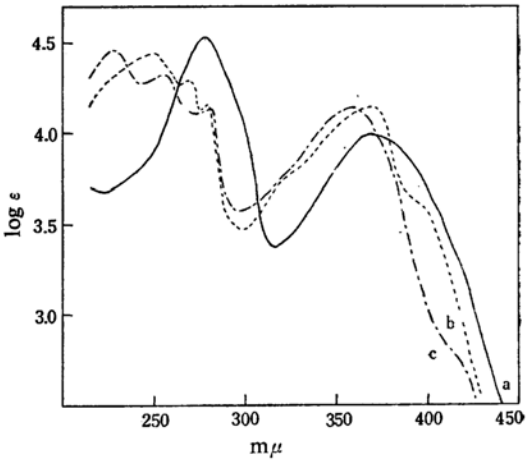


Fig. 2. The ultraviolet absorption spectra.
(a): 4, 5-Diaminotropolone (IX)
(b): Imidazolo[d]tropolone (XI)
(c): Triazolo[d]tropolone (XII)

Experimental

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

Tribromination of 4-Aminotropolone (I).—To a stirred mixture of I (70 mg.), sodium acetate trihydrate (200 mg.) and methanol (2 ml.) was added dropwise a cold solution of bromine (240 mg.) in methanol (2 ml.). The reaction mixture was

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

[14] Y. Kitahara, K. Doi and T. Hashimoto, ibid., **9**, 91 (1960).

[15] T. Nozoe, S. Ebine, S. Ito and A. Konishi, *Proc. Japan Acad.*, **27**, 10 (1951); T. Nozoe, S. Seto, S. Ito and M. Sato, ibid., **27**, 426 (1951).

[16] K. Doi, unpublished work.

[17] T. Nozoe, M. Sato, S. Ito, K. Matsui and T. Matsuda, *Proc. Japan Acad.*, **29**, 565 (1953).

[18] T. Nozoe, S. Ito and K. Matsui, ibid., **30**, 313 (1954).

diluted with water, and the precipitated solid, after collection by filtration, sublimation in vacuo, and subsequent recrystallization from acetic acid, gave 4-amino-3, 5, 7-tribromotropolone (III, 160 mg.) as yellow needles, m. p. 203°C.

Found: N, 3.80. Calcd. for $C_7H_4O_2NBr_3$: N, 3.75%.

λ_{max} mμ (log ε): 282 (4.47), 350 (3.84), 410 (4.00).

Monobromination of I.—To a stirred cold solution of I (0.41 g.) in methanol (10 ml.) was added dropwise a solution of bromine (0.48 g.) in methanol (2 ml.). After 30 min., the solution was evaporated in vacuo, the residue was diluted with water (5 ml.), and the deposited solid, after collection by filtration, was crystallized fractionally from methanol to give less soluble 4-amino-3,7-dibromotropolone (V, 016 g.) as yellow prisms, m. p. 224~225°C.

Found: N, 5.01. Calcd. for $C_7H_5O_2NBr_2$: N, 4.75%.

λ_{max} mμ (log ε): 276 (4.46), 345 (3.99), 390 (4.10). From the more soluble portion, 6-amino-3-bromotropolone (IV) as yellow needles, m. p. and mixed2) m. p. 214°C, was obtained. Further bromination of the preceding products, IV and V, afforded respectively the tribromotropolone (III).

Nitration of 4-Aminotropolone (I).—a) To a stirred solution of I (0.41 g.) and acetic acid (3 ml.) was added dropwise at room temperature a solution of fuming nitric acid (0.2 g., *d* 1.84) and acetic acid (1 ml.). After evaporation of the solvent, the residual solid was recrystallized from a mixed solvent of acetic acid and methanol to give 4-aminotropolone nitrate (0.26 g.) in the form of colorless needles, m. p. 163~164°C (decomp.).

Found: C, 41.96; H, 4.06; N, 13.80. Calcd. for $C_7H_7O_2N \cdot HNO_3 \cdot H_2O$: C, 42.00; H, 4.03; N, 14.00%. This substance is soluble in water and its aqueous solution decomposes sodium hydrogen carbonate.

b) Addition of fuming nitric acid (0.2 g.) to the aminotropolone (I, 0.41 g.) resulted in a vigorous reaction to form a deep red solution, which was immediately chilled in ice and allowed to stand for 30 min. Then this solution was diluted with water (2 ml.), the residual solid was collected by filtration, and crystallized from acetic acid to yield 4-amino-5-nitrotropolone (VI) as yellow needles, m. p. above 300°C, which was identified with an authentic specimen2) through ultraviolet absorption.

4-Acetylaminotropolone (VII).—After acetyl chloride (3.1 g.) was added dropwise during 10 min. to a stirred cold solution of I (2.8 g.) in pyridine (10 ml.), the reaction mixture was allowed to stand for 4 hr. The mixture was diluted with water, allowed to stand overnight, and then acidified to Congo red with dilute hydrochloric acid. The solid which separated on chilling this mixture was collected and recrystallized from methanol to afford 4-acetylaminotropolone (VII, 2.2 g.) as colorless needles, m. p. 166~167°C.

Found: C, 55.43; H, 5.33; N, 7.14. Calcd. for $C_9H_9O_3N \cdot H_2O$: C, 54.82; H, 5.62; N, 7.10%.

λ_{max} mμ (log ε): 267 (4.54), 365 (3.84).

4-Acetylamino-5-nitrotropolone (VIII). — To a stirred mixture of VII (1.3 g.) and acetic acid (4 ml.) was added dropwise at room temperature a solution of fuming nitric acid (0.5 g.) and acetic acid (1 ml.), the deep red solution so formed was allowed to be stirred for further 1 hr., diluted with water (40 ml.), and extracted with four 25-ml. portions of ether. The ether extract, after evaporation of the solvent followed by recrystallization from a mixed solvent of acetic acid and methanol, gave VIII (0.46 g.) as yellow needles, m. p. 230°C (decomp.).

Found: C, 48.53; H, 3.88; N, 12.31. Calcd. for $C_9H_8O_5N_2$: C, 48.53; H, 3.60; N, 12.50%.

λ_{max} mμ (log ε): 274 (4.53), 400 (3.90).

Hydrolysis of VIII.—A mixture of VIII (0.2 g.), potassium hydroxide (0.2 g.), and water (8 ml.) was heated at 60°C on a water bath for 30 min., and then the resulting red solution was acidified with dilute hydrochloric acid to separate the aminotropolone (VI, 0.15 g.), whose structure was confirmed by the comparison of the ultraviolet absorption with that of an authentic sample2).

4, 5-Diaminotropolone (IX).—A mixture of the nitroamine (VI, 0.18 g.), 5% palladium-on-carbon (50 mg.) and methanol (100 ml.) was shaken in an hydrogen atmosphere until the uptake of hydrogen had ceased. Then the catalyst was removed by filtration, the filtrate evaporated in vacuo, and the residue crystallized twice from ethyl acetate to give 4,5-diaminotroplone (IX, 60 mg.) as yellow prisms, m. p. 215°C (decomp.).

Found: C, 54.98; H, 5.21; N, 18.57. Calcd. for $C_7H_8O_2N_2$: C, 55.25; H, 5.30; N, 18.41%.

λ_{max} mμ (log ε): 278 (4.54), 371 (3.99).

4-Amino-5-*p*-tolylazotropolone (X).—A diazonium chloride solution prepared from *p*-toluidine (2 g.) was added dropwise during 10 min. to a stirred cold solution of I (2.8 g.), potassium hydroxide (6 g.) and water (100 ml.). After 30 min., the reaction mixture was acidified with acetic acid, the solid which separated was collected, and recrystallized from ethyl acetate to afford X (4.5 g.) of red needles, m. p. 230°C (decomp.).

Found: N, 16.22. Calcd. for $C_{14}H_{13}O_2N_3$: N, 16.46%.

λ_{max} mμ (log ε): 260 (4.37), 300 (4.38), 375 (4.11), 470 (4.41).

Hydrogenation of X in methanol over 5% palladized carbon afforded easily a diamino derivative IX.

Imidazolo[d]tropolone (XI).—A mixture of IX (0.15 g.) and 80% formic acid (10 ml.) was heated under reflux for 2 hr., the solvent was evaporated to dryness, and the residue, after sublimation in vacuo, was recrystallized from acetic acid to give XI (60 mg.) of colorless prisms, m. p. above 275°C

Found: C, 59.08; H, 3.55; N, 17.60. Calcd. for $C_8H_6O_2N_2$: C, 59.26; H, 3.73; N, 17.28%.

λ_{max} mμ (log ε): 250 (4.44), 268 (4.28), 280 (4.14), 372 (4.14).

Triazolo[d]tropolone (XII).—A solution of sodium nitrite (60 mg.) in water (1 ml.) was added dropwise during 5 min. to a stirred cold solution of IX (0.15 g.), acetic acid (0.2 ml.), concentrated hydrochloric acid (0.4 ml.) and water (6 ml.). After 2 hr., the mixture was diluted with water (40 ml.), neutralized with sodium hydrogen carbonate, and extracted continuously with ether for 5 hr. The ether extract, after evaporation of the solvent, sublimation of the residue in vacuo followed by crystallization from acetic acid, gave XII (50 mg.) of colorless prisms, m. p. 265°C (decomp.).

Found: C, 51.20; H, 2.98; N, 25.78. Calcd. for $C_7H_5O_2N_3$: C, 51.54; H, 3.09; N, 25.76%.

λ_{max} mμ (log ε): 228 (4.48), 256 (4.34), 282 (4.14), 360 (4.17).

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The Chemical Research Institute
of Non-Aqueous Solutions
Tohoku University
Katahira-cho, Sendai