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The Electrophilic Substitution Reactions of 2-Aminotropone and Its *N*-Alkyl Derivatives[1]

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The electrophilic substitution reactions of 2-aminotropone (I), 2-methylaminotropone (II), and 2-dimethylaminotropone (III) were investigated. The structure of the products was proved by hydrolysis to lead to known tropolone derivatives. By the nitrosation of II, *N*-nitroso-2-methylaminotropone was obtained in a good yield; this compound is a new type of active troponoid compound. The substitution reactions of III gave tropolone derivatives, accompanied by the hydrolysis of the dimethylamino group. The mechanism of the hydrolysis is then discussed.

The relation of tropolone and 2-aminotropone (I) corresponds to the relation of phenol and aniline, and to investigate the chemical properties of I is both important and interesting. Althougth the reactivities of tropolones have been investigated in detail,[3] the chemical properties of I have been known for only a few examples of such cationoid substitution reactions as bromination and the azo-coupling reaction[4] and of reactions with active methylene compounds to synthesize 1-azaazulan-2-one and its derivatives.[5] No report has appeared about the chemical properties of 2-methylaminotropone (II)[4] and 2-dimethylaminotropone (III),[4] even though these compounds are an important family of I, corresponding to *N*-methylaniline and *N*-dimethylaniline. From this point of view, the electrophilic substitution reactions of 2-aminotropone and its *N*-alkyl derivatives, II and III, were undertaken. The authors wish to report here the results obtained.

Halogenations of 2-Aminotropone, 2-Methylaminotropone, 2-Dimethylaminotropone, and the Copper Complex of 2-Aminotropone. The bromination of I in acetic acid or chloroform was investigated in detail.[4] It was proved that substitution took place in the following order; at C-7 first, then at C-5, and finally at the C-3 position of I.[4] The halogenations of I, II, and III under a variety of conditions were then reinvestigated by comparison with the results previously obtained. The results of the reinvestigation

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3) a) P. L. Pauson, *Chem. Revs.*, **55**, 19 (1955). b) T. Nozoe, K. Takase and H. Matsumura, "Dai Yuki Kagaku" (Comprehensive Organic Chemistry), Vol. 13, ed. by M. Kotake, Asakura Shoten, Tokyo (1960).

4) T. Nozoe, S. Seto, M. Takeda, S. Morosawa and K. Matsumoto, *Sci. Repts. Tohoku Univ. Ser. I*, **36**, 126 (1952).

5) T. Nozoe, S. Seto, S. Matsumura and T. Terasawa, *Chem. & Ind.*, **1954**, 1356; T. Nozoe, S. Seto and S. Nozoe, *Proc. Japan Acad.*, **32**, 472 (1956); S. Seto and S. Nozoe, *ibid.*, **32**, 765 (1956); N. Soma and G. Sunagawa, *Yakugaku Zasshi*, **82**, 418 (1962); N. Soma, *ibid.*, **82**, 892, 898 (1962); H. Toda, *ibid.*, **87**, 1351 (1967); S. Matsumura, This Bulletin, **34**, 1362 (1961); K. Ogura, H. Sasaki and S. Seto, *ibid.*, **38**, 306 (1964); T. Toda, S. Seto and T. Nozoe, *ibid.*, **41**, 2102 (1968).

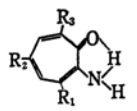
TABLE. 1. THE RESULTS OF HALOGENATION OF I, II AND III

Condition	Product % (recovery %) I	II	III
$Cl_2/CHCl_3$	V 31.5% (66.5%)		
$Br_2/AcOH$	VI 22%* (mixtures)**	VIII 28% (59%)	
$3Br_2/AcOH$	VI 83%*	VIII 80%	
$PPB/CHCl_3$***	VI 30% (55%)	VIII 27% (59%)	
$2PPB/CHCl_3$***	VI 55% (27%)	VIII 55% (mixtures)**	
$Br_2/MeOH$		IX 37% (44%)	XI 22%, XII 10% (67%)
$3Br_2/MeOH$		IX 85%	XII 92%
$I_2/MeOH \cdot H_2O$	VII 25% (66%)	X 94%	XIII 85%

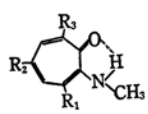
* The results of lit. 4.
** Mixtures of starting substance, mono- and di-bromo derivatives.
*** Pyridine perbromide.

are shown in Table 1, which shows that the halogenation of these compounds occurs at the C-7 position first, and then at the C-5 and C-3 positions. The reactivities of I and II are almost the same. On the other hand, III shows different properties and the hydrolysis of the dimethylamino group occurs during halogenation, giving tropolone derivatives.

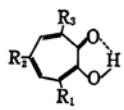
The bromination of the copper complex (IV)[4] of I was also investigated by comparison with the properties of the copper complex of tropolone.[6] In chloroform, IV with equimolar bromine gave



I: $R_1=R_2=R_3=H$
V: $R_1=R_2=R_3=Cl$
VI: $R_1=R_2=R_3=Br$
VII: $R_1=R_2=H$, $R_3=I$



II: $R_1=R_2=R_3=H$
VIII: $R_1=R_2=R_3=Br$
IX: $R_1=H$, $R_2=R_3=Br$
X: $R_1=R_2=H$, $R_3=I$



XI: $R_1=R_3=Br$, $R_2=H$
XII: $R_1=R_2=R_3=Br$
XIII: $R_1=I$, $R_2=R_3=H$

Fig. 1. The structures of the halogenation products of I, II and III.

6) T. Toda, H. Kubota and T. Nozoe, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **88**, 1234 (1967).

5,7-dibromo-2-aminotropone[4] in a 50% yield; the rest of the starting substance was recovered. This result is parallel with the properties[6] of the copper complex of tropolone.

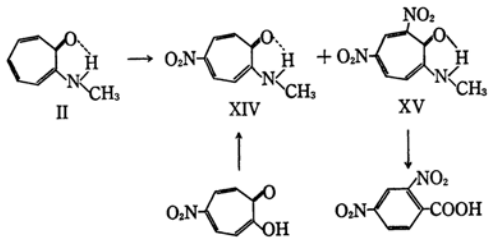
3,5,7-Trichloro-2-aminotropone (V), 7-iodo-2-aminotropone (VII), 3,5,7-tribromo-2-methylaminotropone (VIII), 5,7-dibromo-2-methylaminotropone (IX), and 7-iodo-2-methylaminotropone (X) are new compounds. The hydrolyses of these compounds gave known tropolone derivatives: 3,5,7-trichlorotropolone[7] from V, 3-iodotropolone (XIII)[8] from VII and X, 3,5,7-tribromotropolone (XII)[9] from VIII, and 3,5-dibromotropolone[9a] from IX. Thus, the structures of these compounds are proved. VII and X were also obtained from the methyl ether of XIII by treating it with ammonia and monomethylamine respectively.

Nitration, Azo-coupling Reaction and Sulfonation of 2-Methylaminotropone. As has been shown above, in properties I and II are very similar to each other. Because it is easy to handle, the nitration, azo-coupling reaction, and sulfonation of II were undertaken.

The nitration of II with an equimole of nitric acid in acetic acid afforded 5-nitro-2-methylaminotropone (XIV) in an 85% yield. Generally,

7) T. Nozoe, S. Seto, K. Yamane and A. Yoshikoshi, *Proc. Japan Acad.*, **27**, 224 (1951); W. von E. Doering and L. H. Knox, *J. Am. Chem. Soc.*, **74**, 5683 (1952).
8) Y. Kitahara and T. Arai, *Proc. Japan Acad.*, **27**, 423 (1951).
9) a) T. Nozoe, S. Seto, Y. Kitahara, M. Kunori and Y. Yamanaka, *ibid.*, **26**, (7) 38 (1950). b) J. W. Cook, A. R. Gibb, R. A. Raphael and A. R. Sommervill, *J. Chem. Soc.*, **1951**, 503.

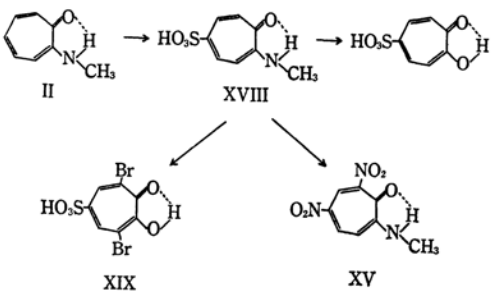
nitrotropolones give nitro-2-aminotropone derivatives when treated with amines.[3b,10] By the application of this method, the treatment of 5-nitrotropolone[10b,11] with methylamine afforded XIV. Thus, the structure of XIV is proved. In the same manner, the reaction of II with excess nitric acid gave a yellow, crystalline substance (XV) in a 60% yield besides 35% of XIV. XV was obtained when 3,5-dinitrotropolone[10b] was treated with methylamine; hence, XV is 5,7-dinitro-2-methylaminotropone. The treatment of XV with alcoholic alkali gave 2,4-dinitrobenzoic acid in a good yield, just as with nitrotropolones.[3b,10]



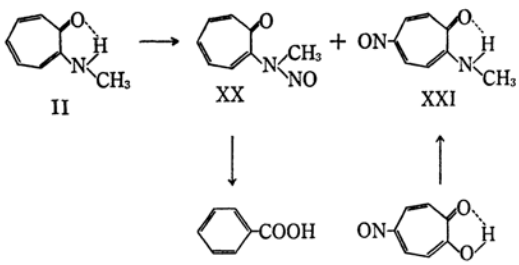
On the other hand, the treatment of I and III with excess nitric acid under the same reaction conditions as above resulted in the recovery of the starting substances.

The azo-coupling reaction of 2-aminotropones has been known to give 5-arylazo derivatives.[4,12] The treatment of II with phenyldiazonium salt and *p*-nitrophenyldiazonium salt gave the corresponding 5-phenylazo-2-methylaminotropone (XVI) and 5-(*p*-nitrophenyl)azo-2-methylaminotropone (XVII) in 45% and 95% yields respectively. XVI and XVII were also obtained from the corresponding methyl ethers[13] of 5-arylazotropolones by treatment with methylamine.

The reaction of 1.5 mol of sulfamic acid at 150—160°C gave a high-melting-point substance (XVIII) in a 50% yield, while II was also recovered (40%). The elemental analysis of XVIII is agreeable with the sulfonic acid derivative of II, and the hydrolysis of XVIII formed tropolone-5-sulfonic acid.[14] Hence, XVIII is 2-methylaminotropone-5-sulfonic acid. The nitration of XVIII with excess nitric acid resulted in XV in a 70% yield; there was also an exchange of the sulfonic acid group with the nitro group. The same type of exchange reaction was observed when tropolone-5-sulfonic acid was treated with nitric acid.[10b] On the other hand, the bromination of XVIII in an aqueous solution gave 3,7-dibromotropolone-5-sulfonic acid (XIX) in a 65% yield, while the 2-methylamino group was hydrolyzed.



Nitrosation of 2-Methylaminotropone. Although 2-aminotropone gave an unidentified powder when treated with nitrous acid,[4] it is expected that 2-methyaminotropone, as a secondary amine, would form an *N*-nitroso derivative. When II was treated with nitrous acid, white needles (XX) and yellow scales (XXI) were obtained in 80% and 10% yields respectively. The elemental analyses of them agree with those of the nitroso derivatives of II. The IR spectrum of XX does not show any NH stretching vibrations, while that of XXI possesses a broad NH stretching band at 3250 cm^{-1} (KBr pellet). Therefore, XX is assumed to be the *N*-nitroso derivative of II, and XXI, the 5-nitroso compound of II. It is known that 5-nitrosotropolones[11a,15] give 5-nitroso-2-aminotropones when treated with ammonia.[16] Since the treatment of 5-nitrosotropolone with methylamine afforded XXI, the structure of XXI is established to be 5-nitroso-2-methylaminotropone. On the other hand, the reaction of XX with alcoholic potassium hydroxide gave benzoic acid; hence, the structure of XX is 2-*N*-nitroso-2-methylaminotropone, as has been predicted. This is the first *N*-nitroso-2-methylaminotropone derivative obtained. XX is a new type



10) a) T. Nozoe, *Sci. Repts. Tohoku Univ., Ser. I*, **34**, 199 (1950). b) T. Nozoe, Y, Kitahara, K. Doi and T. Arai, *Bull. Chem. Res. Inst. Non-Aqueous Soln., Tohoku Univ.*, **7**, 13 (1957).

11) a) W. von E. Doering and L. H. Knox, *J. Am. Chem. Seoc.*, **73**, 828 (1951). b) T. Nozoe, Y. Kitahara, E. Kunioka and T. Ando, *Proc. Japan Acad.*, **27**, 190, 231 (1951). c) J. W. Cook, J. D. London and D. K. V. Steel, *J. Chem. Soc.*, **1954**, 530.

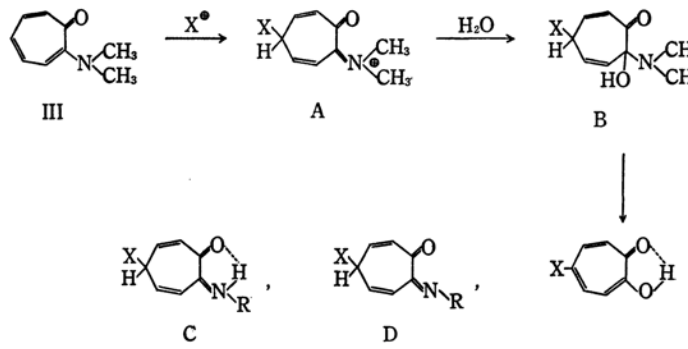
12) P. Akroyd, R. D. Howorth and J. D. Hobson, *ibid.*, **1951**, 3427.

13) Unpublished result of experiments made in the authors' laboratory.

14) T. Nozoe, S. Seto, T. Ikemi and T. Arai, *Proc. Japan Acad.*, **27**, 24 (1951).

15) T. Nozoe, S. Seto, S. Ebine and S. Ito, *J. Am. Chem. Soc.*, **73**, 1875 (1951).

16) T. Nozoe, M. Sato and T. Matsuda, *Sci. Repts Tohoku Univ., Ser. I*, **37**, 407 (1953).



of active troponoid compound[17] and has interesting properties.

Azo-coupling Reaction, Nitrosation and Sulfonation of 2-Dimethylaminotropone. Substitution reactions do not occur when tropolone methyl ethers are treated with cationoid reagents, but addition reactions do take place.[18] However, the halogenation of III shows that the substitution reactions occur with the hydrolysis of the dimethylamino group, as has been mentioned before. Therefore, the reactions of III with cationoid reagents other than halogens were undertaken.

Although the nitration of III resulted in the recovery of the starting substance, as has been mentioned before, the nitrosation of III in ordinary ways gave 5-nitrosotropolone[11a,15] in a 95% yield. Also, 5-(*p*-nitrophenyl)azotropolone[19] was obtained quantitatively when III was treated with *p*-nitrophenyl diazonium salt. The reaction of III with 1.5 mol of sulfamic acid afforded tropolone-5-sulfonic acid[14] in a 35% yield; there was also a 50% recovery of III.

The electrophilic substitution reactions of III always resulted in the hydrolysis of the 2-dimethylamino group, thus forming tropolone derivatives as in the case of halogenations. It is possible that III is hydrolized to form tropolone first, and that then the attack of a cationoid reagent takes place. However, the treatment of III under the same conditions as in the substitution reactions, but without reagents, resulted in the recovery of III unchanged. Moreover, in the case of nitration, III was recovered quantitatively even if reagents were present. It is also known that if a reaction is carried out under anhydrous conditions, III and its derivatives give substituted derivatives of III without any hydrolysis of the 2-dimethylamino group.[20] Therefore, the mechanism of the reactions can be explained as follows: the nucleophilic attack of water on the C-2 position of the intermediate A to give tropolone derivatives *via* a B-type intermediate, because the steric interference of the dimethylamino group of A makes it difficult for A to keep the dimethylamino group in the same plane of the seven-membered ring.

On the other hand, II can form a C-type intermediate which possesses a hydrogen bond that contributes to the stability of C; the hydrogen is even able to leave to form D and other types of intermediates under some conditions. These entities do not have serious steric interference like that of A. This is the reason why only III gives hydrolized products during the electrophilic substitution reactions.

It is very interesting that, unlike tropolone methyl ethers,[18] not addition reactions but substitution reactions take place in the case of electrophilic reactions of III.

By cationoid substitution reactions under acidic conditions as in nitration, I and III were recovered unchanged, but only II afforded substitution products. This relation is parallel with the order of basicity of primary-, secondary-, and tertiary-amines.

Experimental[21]

3,5,7-Trichloro-2-aminotropone (V). To a solution of 0.60 g of I in 5 m*l* of chloroform cooled in an ice bath, 0.35 g of chlorine in 5 m*l* of chloroform was added drop by drop, and then the mixture was allowed to stand overnight at room temperature. The precipitate formed was separated by filtration; then the chloroform layer was washed with aqueous sodium bicarbonate and water and dried over sodium sulfate, and the chloroform was removed. The residue was recrystallized from benzene-methanol to give 0.35 g of V; yellow needles, mp 183—185°C.

Found: C, 37.85; H, 2.00; N, 6.62%. Calcd for $C_7H_5ONCl_3$: C, 37.45; H, 1.79; N, 6.24%.

The former precipitate was treated with aqueous sodium bicarbonate and extracted with chloroform. The chloroform layer was washed with water and dried

17) Recording the definition of active troponoid compounds, see Ref. 3b, p. 179.
18) M. Yasunami, D. Sc. thesis of Tohoku University, Feb., 1966.
19) T. Nozoe, S. Ito, S. Suzuki and K. Hiraga, *Proc. Japan Acad.*, **32**, 344 (1956).
20) T. Toda, Y. Miura and T. Mukai, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **89**, 804 (1968).
21) All melting points are uncorrected.

over sodium sulfate; the chloroform was then removed under reduced pressure to give 0.40 g of I.

Hydrolysis of V; 3,5,7-Trichlorotropolone. A mixture of 0.10 g of V and 5 m*l* of 1.6 N potassium hydroxide was heated on a water bath for 4 hr. The V was then gradually dissolved, whereupon ammonia gas evolved. The solution was acidified with N hydrochloric acid and extracted with chloroform. The chloroform layer was washed with water and dried over sodium sulfate, and then the chloroform was removed under reduced pressure to give 70 mg of pale yellow needles, the melting point of which failed to show any depression on admixture with authentic 3,5,7-trichlorotropolone.[7]

Bromination of 2-Aminotropone Copper Complex (IV). To a solution of 1.21 g of IV in 100 m*l* of chloroform, 1.09 g of sodium acetate was added, and then 30 m*l* of chloroform containing 1.28 g of bromine was added, drop by drop. A dark green precipitate was formed immediately, and then the mixture was allowed to stand overnight. The precipitate formed was separated by filtration and recrystallized from chloroform to give greenish scales of the complex of VI, mp 253—255°C. The complex was dissolved in 100 m*l* of methanol containing a few drops of 1 N hydrochloric acid, and the mixture was treated with hydrogen sulfide. The solvent was removed, and the residue obtained was recrystallized from cyclohexane - acetone to give 1.00 g of yellow needles, mp 203—205°C, which was undepressed on admixture with an authentic sample of 5,7-dibromo-2-aminotropone.[4]

The chloroform layer was treated as above to give 0.38 g of recovered I.

Bromination of I with Pyridine Perbromide (PPB); 3,5,7-Tribromo-2-aminotropone (VI). *a) With 1 mol of PPB.* A solution of 0.37 g of I in 5 m*l* of chloroform cooled in an ice bath was treated with 0.72 g of PPB prepared by McElvain's method.[22] The precipitate thus formed was recrystallized from ethanol to give 0.32 g of yellow needles, mp 196—198°C, which were found to be identical with the 3,5,7-tribromo-2-aminotropolone[4] by a comparison of their mixed mp and IR spectra.

The chloroform layer was neutralized and concentrated to give 0.20 g of recovered I.

b) With 2 mol of PPB. From 0.37 g of I and 1.44 g of PPB, 0.60 g of VI and 0.10 g of recovered I were obtained.

Bromination of II by PPB; 3,5,7-Tribromo-2-*N*-methylaminotropone (VIII). *a) With 1 mol of PPB.* From 0.34 g of II and 0.60 g of PPB, 0.25 g of yellow needles of VIII was obtained; mp 197—199°C after recrystallization from cyclohexane - acetone.

Found: C, 26.26; H, 2.09; N, 4.03%. Calcd for $C_8H_6ONBr_3$: C, 25.84; H, 1.63; N, 3.78%.

From the chloroform layer, 0.20 g of II was recovered.

b) With 2 mol of PPB. From 0.34 g of II and 1.20 g of PPB, 0.51 g of VIII and 0.20 g of a mixture of mono- and dibromo-derivatives of II were obtained.

Bromination of II in Acid. *a) With 1 mol of Bromine.* Into a solution of 0.34 g of II in 5 m*l* of acetic acid cooled in an ice bath, 0.40 g of bromine in 2 m*l* of acetic acid was stirred, drop by drop: then the mixture was allowed to stand overnight at room temperature. The yellow precipitate thus formed was separated by filtration and washed with aqueous sodium bicarbonate and water. Recrystallization from cyclohexane - acetone gave 0.26 g of yellow needles of VIII. The acetic acid layer was diluted with water, and extracted with chloroform, and the chloroform layer was washed with water, and dried over sodium sulfate. After the chloroform had then been removed, the residue was recrystallized from cyclohexane to give 0.20 g of recovered II, mp 75—76°C.

b) With 3 mol of Bromine. From 0.34 g of II, 3 equivalent moles of sodium acetate, and 1.2 g of bromine, 0.82 g of VIII was obtained under the same reaction conditions.

Hydrolysis of VIII; 3,5,7-Tribromotropolone. A solution of 100 mg of VIII in 4 m*l* of 1.6 N methanolic potassium hydroxide was refluxed on a water bath for 4 hr. After cooling, the solution was acidified with 1 N hydrochloric acid and extracted with benzene. The benzene layer was washed with water, dried over sodium sulfate, and concentrated. The residue thus obtained was recrystallized from cyclohexane - benzene to give 60 mg of pale yellow needles, mp 125—127°C, which failed to show any depression upon admixture with 3,5,7-tribromotropolone.

Bromination of II in Methanol: 5,7-Dibromo-2-methylaminotropone (IX). *a) With 1 mol of Bromine.* Into a solution of 0.34 g of II in 5 m*l* of methanol cooled in an ice bath, 0.40 g of bromine in 10 m*l* of methanol was stirred drop by drop, and then the mixture was allowed to stand at room temperature overnight. The precipitate thus formed was separated by filtration, washed with aqueous sodium bicarbonate and water, and dried in a desiccator. Recrystallization from cyclohexane - acetone afforded 0.20 g of yellow needles of IX, mp 204—205°C.

Found: C, 32.77; H. 2.36; N, 4.73%. Calcd for $C_8H_7ONBr_2$: C, 32.80; H, 2.41; N, 4.75%.

From the methanol layer, 0.15 g of II was recovered.

b) With 3 mol of Bromine. From 0.34 g of II and 1.2 g of bromine, 0.62 g of IX was obtained.

Bromination of III in Methanol. *a) With 1 mol of Bromine.* A methanol solution (5 m*l*) of 0.15 g of III was cooled in an ice bath, and then into this solution 0.16 g of bromine in 1 m*l* of methanol was stirred, drop by drop. The color of the bromine disappeared gradually. The solution was allowed to stand at room temperature for 1 hr and then the methanol was removed under reduced pressure. The addition of water caused the precipitation of a crystalline substance, 62 mg, the melting point of which was 156—158°C after recrystallization from methanol. This substance was found to be identical with 3,5-dibromotropolone by a comparison of their IR spectra and by a mixed-melting-point determination.

To the filtrated mother layer, 5 m*l* of 1 N sodium hydroxide was added, and then the mixture was extracted with chloroform. From the water layer, 37 mg of pale yellow crystals were obtained, mp 126—127°C, which were found to be identical with 3,5,7-tribromotropolone by comparison of thir IR spectra and by a mixed-melting-point determination.

From the chloroform layer 0.10 g of a yellow oil was obtained; this oil was found to be identical with be original substance by a comparison of their IR spectra

22) S. M. McElvain and L. R. Morris, *J. Am. Chem. Soc.*, **73**, 206 (1951).

and the mixed mp of the picrate, mp 155°C.

b) With 3 mol of Bromine. From 0.15 g of III and 3 equivalent moles of bromine, 0.38 g of 3,5,7-tribromotropolone was obtained by the treatment described above.

7-Iodo-2-aminotropone (VII). I (0.60 g) and potassium carbonate (1.5 g) were dissolved in 6 m*l* of water and methanol (1 : 1) cooled in an ice bath, and into this, a solution of 1.4 g of iodine and 1.0 g of potassium iodide in 10 m*l* of cold water was stirred, drop by drop. The mixture was then allowed to stand at room temperature overnight. The mixture was slightly acidified by the addition of 1 N hydrochloric acid; the precipitate thus formed was then recrystallized from cyclohexane to give 0.28 g of pale green needles of VII, mp 202—203°C.

Found: C, 35.72; H, 2.50; N, 5.76%. Calcd for C_7H_6ONI: C, 35.45; H, 2.55; N, 5.92%.

The mother layer was extracted with chloroform, after which the chloroform layer was treated as before to give 0.35 g of recovered I.

7-Iodo-2-methylaminotropone (X). From 0.67 g of II, 1.5 g of potassium carbonate, and a solution of 1.4 g of iodine and 1.0 g of potassium iodide, 1.22 g of X, mp 179—180°C, was obtained by the treatment described above.

Found: C, 36.35; H, 3.46; N, 5.03%. Calcd for C_8H_8ONI: C, 36.81; H, 3.09; N, 5.37%.

Hydrolysis of VII and X; 3-Iodo-tropolone (XIII). A solution of 0.10 g of VII in 5 m*l* of 1.6 N methanolic potassium hydroxide was heated under reflux for 4 hr; then it was concentrated, and water was added. The water layer was neutralized with 1 N hydrochloric acid and extracted with benzene. After the benzene had been removed, the residue was sublimated under reduced pressure. The recrystallization of the sublimated from cyclohexane - benzene afforded 60 mg of a pale yellow, crystalline substance, mp 101—102°C, which was identical with authentic 3-iodotropolone. By the same procedure, 0.10 g of X gave 70 mg of XIII.

Iodination of III. A solution of 0.75 g of III and 1.5 g of potassium carbonate in 4 m*l* of methanol and water (1 : 4), and a solution of 1.4 g of iodine and 1.0 g of potassium iodide in 10 m*l* of water were treated in the same way as I and II. After recrystallization from cyclohexane, 1.02 g of XIII were obtained.

Nitration of II. *a) With 1 mol of Nitric Acid, 5-Nitro-2-methylaminotropone (XIV).* A solution of 0.40 g of II in 3 m*l* of acetic acid was cooled in an ice bath, and into this, 0.33 g of 60% nitric acid in 2 m*l* of acetic acid was added stirred, drop by drop. The reaction mixture was then poured into crushed ice, and the prepipitate thus formed was separated by filtration and dried in a desiccator overnight. Recrystallization from cyclohexane - benzene afforded 0.45 g of green-yellow, micro needles of XIV, mp 214—216°C.

Found: C, 54.85; H, 4.32; N, 15.30%. Calcd for $C_8H_8O_3N_2$: C, 55.33; H, 4.48; N, 15.55%.

b) With Excess Nitric Acid. XIV and 5,7-Dinitro-2-methylaminotropone (XV). From 0.40 g of II and 1.0 m*l* of 60% nitric acid, 0.70 g of a crude substance was obtained by the same treatment as above. Recrystallization from ethanol gave 0.19 g of pale green needles, mp 214—216°C, which were identical with XIV. Ethanol-layer condensation afforded 0.41 g of a residue the recrystallization of which from cyclohexane-benzene gave orange-yellow needles of XV, mp 195—196°C.

Found: C, 43.04; H, 3.39; N, 18.26%. Calcd for $C_8H_7O_5N_3$: C, 42.70; H, 3.14; N, 18.64%.

Treatment of Nitrotropolones with Monomethylamine. *a) XIV.* A solution of 0.20 g of 5-nitrotropolone in 20 m*l* of benzene cooled in an ice bath, was saturated with dry monomethylamine, then the mixture was allowed to stand overnight. After the benzene and monomethylamine had been removed under reduced pressure, the residue was recrystallized from cyclohexane - benzene to give 0.16 g of yellow needles, mp 210—213°C, which did not show any depression on admixture with XIV.

b) XV. 3,5-Dinitrotropolone (0.20 g) was treated as above to give 0.14 g of XV.

Nitration of I. Nitric acid (60%, 1 m*l*) was stirred into a solution of 0.60 g of I in 2 m*l* of acetic acid cooled in an ice bath, and then the mixture was allowed to stand overnight. The reaction mixture was poured into crushed ice, the precipitate thus formed was separated by filtration, dried in a desiccator, and recrystallized from cyclohexane to give 0.55 g of the starting material.

Nitration of III. III (0.45 g) was treated with 1 m*l* of 60% nitric acid as above. An oily substance was obtained; this was found to be identical with III by a comparison of their IR spectra. This oil afforded 0.75 g of the picrate of III, mp 143—145°C.

5-Phenylazo-2-methylaminotropone (XVI). a) Into a solution of 0.135 g of II in 0.4 m*l* of 4 N of hydrochloric acid cooled in an ice bath, a phenyldiazonium chloride solution, prepared from 0.10 g of aniline in the ordinary way, was stirred. After 2 hr, the pH of the solution was adjusted to about 7.5 with aqueous sodium bicarbonate and extracted with benzene. The benzene layer was washed with water, dried over sodium salfate and chromatographed on alumina. From the cyclohexane-benzene elution part, 0.10 g of red needles of XVI was obtained; mp 145—146°C from the same mixed solvent.

Found: C, 70.65; H, 5.34; N, 17.26%. Calcd for $C_{14}H_{13}ON_3$: C, 70.27; H, 5.48; N, 17.56%.

From the benzene-acetone elution part, 40 mg of II were recovered.

b) 5-Phenylazotropolone methyl ether (0.20 g) was treated with excess methylamine in a sealed tube at room temperature for 4 days. After the methylamine had then been removed, the residue was recrystallized from cyclohexane-benzene to give 0.20 g of red needles of XVI, mp 140—141°C.

5-(*p*-Nitrophenylazo)-2-methylaminotropone (XVII). a) From 0.28 g of II and 1.5 equimoles of *p*-nitroaniline, 0.54 g of dark red scales of XVII, mp 254—256°C from cyclohexane - benzene was obtained by the same treatment as above.

Found: C, 59.87; H, 4.70; N, 20.52%. Calcd for $C_{14}H_{12}O_3N_4$: C, 59.15; H, 4.26; N, 19.71%.

b) 5-*p*-(Nitrophenylazo)tropolone methyl ether (50 mg) was treated with excess methylamine as above; 40 mg of XVII, mp 214—216°C from cyclohexane-benzene were thus obtained. The azo compounds obtained by the a and b method were found to be identical with each other by a comparison of their IR spectra and by a mixed-melting-point determination.

Azo-coupling Reaction of 2-Dimethylaminotropone (III); 5-(*p*-Nitrophenylazo)tropolone. *p*-Nitrophenyl diazonium chloride prepared from 0.60 g

of *p*-nitroaniline was added, drop by drop, to a solution of 0.45 g of III in 5 m*l* of dioxane, and then the mixture was allowed to stand for 2 hr while being stirred. The reaction mixture was neutralized with aqueous sodium bicarbonate.

The precipitate thus formed was separated by filtration, dried in a desiccator, and recrystallized from benzene to give 0.78 g of orange scales, mp 233—235°C, which were found to be identical with 5-(*p*-nitrophenylazo)tropolone by a comparison of their IR spectra and by a mixed-melting-point determination.

Sulfonation of II; 2-Methylaminotropone-5-sulfonic acid (XVIII). A well-ground mixture of 2.70 g of II and 2.90 g of sulfamic acid was heated in fusion at 160°C for 6 hr under a nitrogen atmosphere. After the reaction, the reaction mixture was extracted with chloroform and hot water. The concentration of the chloroform afforded 1.07 g of recovered II. The water layer was concentrated under reduced pressure to give pale yellow needles which, when recrystallized from methanol, afforded 2.01 g of pale yellow needles of XVIII, mp>350°C. This was treated with an equimole of benzylthiourea in diluted methanol; the recrystallization of the benzylthioronium salt thus obtained afforded pale yellow needles, mp 172—174°C.

Found: C, 50.37; H, 4.81; N, 10.77%. Calcd for $C_{16}H_{19}O_4N_3S_2$: C, 50.31; H, 5.02; N, 11.01%.

Sulfonation of III; Tropolone-5-sulfonic Acid. III (0.40 g) and sulfamic acid (0.39 g) were treated at 180°C for 10 hr in the way described above. From the chloroform extract, 0.51 g of III was recovered as its picrate, mp 145°C. The water layer showed a positive ferric chloride test and the addition of *p*-toluidine afforded colorless needles, mp 236—238°C. The melting point did not show any depression on admixture with *p*-toluidinium salt of tropolone-5-sulfonic acid, and their IR spectra were identical.

Hydrolysis of XVIII. On a water bath, 0.10 g of XVIII was heated for reflux in 2 m*l* of 1.6 N ethanolic potassium hydroxide for 4 hr. The pH of the solution was then adjusted about 3 with 1 N hydrochloric acid and 0.10 g of *p*-toluidine was added. The needles thus formed, mp 237—239°C, were identical with the *p*-toluidinium salt of tropolone-5-sulfonic acid.

Nitration of XVIII; 5,7-Dinitro-2-methylaminotropone (XV). Into a solution of 0.20 g of XVIII in 20 m*l* of acetic acid cooled in an ice bath, 1.0 m*l* of 60% nitric acid was stirred. After it had been allowed to stand for a couple of hours, the reaction mixmixture was poured onto ice; the precipitate thus formed was then separated by filtration and dried in a desiccator. Recrystallization from cyclohexane - benzene gave 0.15 g of orange yellow scales, mp 197—199°C, which were identical with 5,7-dinitro-2-methylaminotropone.

Bromination of XVII; 3,5-Dibromotropolone-5-sulfonic Acid (XIX). XVIII (0.20 g) was dissolved in 10 m of water and methanol (1 : 1), and then the mixture was cooled in an ice bath. Into this, 0.60 g of bromine was stirred, drop by drop, and then the reaction was continued for 30 min. The concentration of the solution caused the precipitation of a crystalline substance, the recrystallization of which from ethanol afforded 0.22 g of white rhombo prisms, mp 217—220°C.

Found: C, 23.50; H, 1.52%. Calcd for $C_7H_4O_5SBr_2$: C, 23.35; H, 1.12%.

Nitrosation of II; 2*N*-Nitrosomethylaminotropone (XX) and 5-Nitroso-2-methylaminotropone (XXI). Into a cold solution of 0.68 g of II in 5 m*l* of 10% hydrochloric acid, 0.43 g of sodium nitrite dissolved in 10 m*l* of water was stirred; the mixture was then allowed to stand for a couple of hours. The reaction mixture was then poured onto crushed ice, and the precipitate thus formed was separated by filtration and dried in a desiccator. Recrystallization form cyclohexane afforded 0.70 g of white needles of XX, mp 98—99°C.

Found: C, 58.74; H, 4.78; N, 16.78%. Calcd for $C_8H_8O_2N_2$: C, 58.53; H, 4.91; N, 17.07%.

The water layer was neutralized with aqueous sodium bicarbonate and extracted with benzene. The benzene layer was dried over sodium sulfate, and then filtered off, and the residue was recrystallized from cyclohexane - benzene to give 80 mg of brown-yellow scales of XXI, mp 128—130°C.

Found: C, 58.98; H, 5.18; N, 16.84%. Calcd for $C_8H_8O_2N_2$: C, 58.53; H, 4.91; N, 17.07%.

5-Nitrosotropolone (0.30 g) was dissolved in 20 m*l* of benzene, and the mixture was cooled in an ice bath. This was then saturated with dry methylamine. The precipitate thus formed was then separated by filtration and recrystallized from cyclohexane - benzene to give 0.15 g of brown-yellow scales, mp 123—125°C, which were identical with the XXI obtained above.

Rearrangement of XX. XX (0.16 g) was refluxed in 3 m*l* of 1.6 N ethanolic potassium hydroxide for 4 hr. After cooling, the solution was acidified with N hydrochloric acid and extracted with ether. The ether layer was washed with water and dried over sodium sulfate, and the ether was removed. White needles, mp 120—121°C, were obtained; the melting point did not show any depression on admixture with benzoic acid.