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The Synthesis and Reactions of Benzo-1, 4-thiazinotropone Derivatives*[1]

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Three isomeric benzo-1, 4-thiazinotropones were obtained. Benzo-1, 4-thiazino[3, 2-b]tropones substituted with the chloro, the bromo, the nitro or the acetamido group at the seven-membered ring were synthesized by the reaction of di- or trihalotropolone, or 3-bromotropolones with the nitro or the acetamido group, with *o*-aminothiophenol. The bromination of benzo-1, 4-thiazino[3, 2-b]tropone (I) and its 8-isopropyl derivative (II) afforded 7- and/or 9-substituted compounds. In the case of nitration, 5-oxide and 5-oxide of 7-nitro derivative were obtained. The reaction of I or II with thionyl chloride unexpectedly gave the 7, 9-dichloro derivative of I, or four kinds of chloro derivatives of II.

The preparation of benzo[b]tropothiazine (cyclohepta[b]benzo[e]-1, 4-thiazine) (I), benzo-1, 4-thiazino[3, 2-b]tropone (cyclohepta[b]benzo-1, 4-thiazine-10(11*H*)-one) (II), and their alkyl and methoxyl derivatives by the reaction of 2-halotropones or 3-halotropolones with *o*-aminothiophenol has been reported.[1] The present paper will deal with the synthesis of the isomeric compounds and the various derivatives of II, and with some electrophilic substitution reactions of these compounds.

The condensation of 2-chloro-3-hydroxytropone[2]

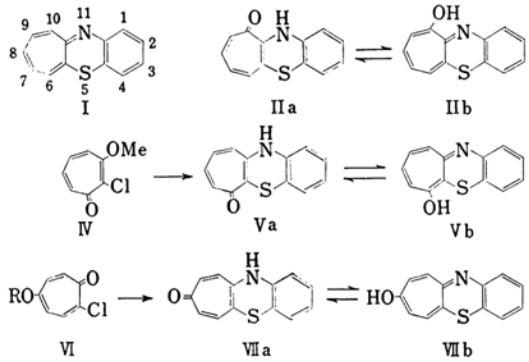
*1 Presented at the 13th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1960.

1) T. Nozoe, T. Asao and K. Takahashi, This Bulletin, **34**, 146 (1961).

2) S. Seto, *Sci. Repts. Tohoku Univ.*, **I, 73**, 275 (1953).

with *o*-aminothiophenol (III) in methanol gave a small amount of a compound which could not be purified. However, when a solution of 2-chloro-3-methoxytropone (IV)[2] and III in methanol was allowed to stand in an ice bath, benzo-1, 4-thiazino[2, 3-b]tropone (V) was obtained as violet needles in a 23% yield. The condensation of 2-chloro-5-methoxytropone (VI; R=Me)[3] with III at 0°C gave an oily substance (VII). The analytical values of VII satisfied the formula, $C_{13}H_9ONS$, and the infrared and ultraviolet spectra of VII were completely in agreement with those of the product obtained from the reaction of 2-chloro-5-hydroxytropone (VI; R=H)[3] and III. These facts indicate that the methoxy group of 2-chloro-5-methoxytropone was hydrolyzed during the reaction with III.

It is known[1] that II exists as the keto form (IIa) rather than the enol form (IIb). The structure of V and VII were also examined for the



presence of any keto-enol tautomerism. The compounds V and VII were slightly soluble in an acidic medium but not in an alkaline medium, and they did not form any molecular compound such as a picrate.

The ultraviolet spectra (Fig. 1) of V in methanol and in an acidic medium are essentially similar to those of II, and the infrared spectrum of V displays

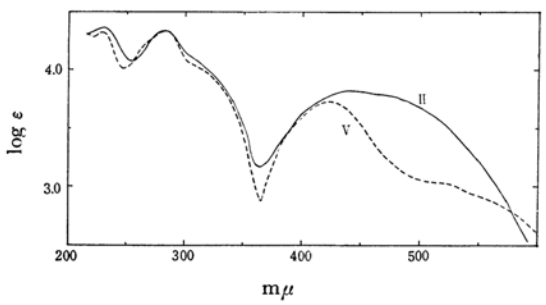


Fig. 1. Ultraviolet absortion spectra of II and V in MeOH.

3) T. Nozoe, T. Asao, E. Takahashi and K. Takahashi, This Bulletin, **39**, 1310 (1966).

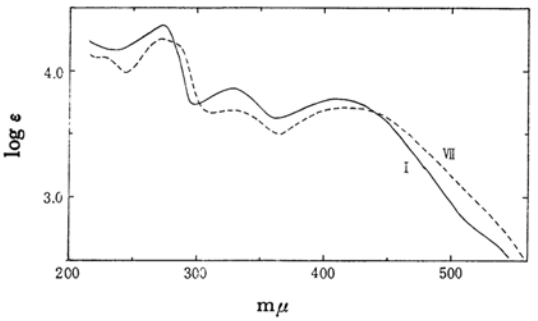


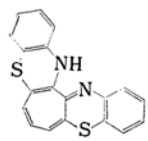
Fig. 2. Ultraviolet absorption spectra of I and VII in MeOH.

peaks at 3280, 3200, 1633 and 1615 cm^{-1} which are not observed in the spectrum of I. From these observations, it may be assumed that V exists as its keto form (Va) rather than as the enol form (Vb). The ultraviolet spectra (Fig. 2) of VII in methanol and in an acidic medium are similar to those of I rather than to those of II; however, the infrared spectrum of VII shows a peak at 1630 cm^{-1} (C=O). From these facts alone, it is difficult to draw any conclusions regarding the tautomerism of VII. A further, detalied investigation of the tautomerism of these isomeric thiazinotropones will, therefore, be carried out.

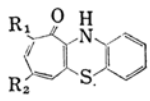
The reactions of *o*-aminothiophenol (III) with the following halotropolones have been studied. 3, 6-Dibromotropolone,[4] when treated with two molar equivalents of III in methanol, gave three compounds, as deep violet plates (VIII), red crystals (IX) and violet plates (X). From their analysis and absorption spectra, VIII was shown to be a pentacyclic compound formed by the condensation of two molecules of III with one molecule of 3, 7-dibromotropolone, as is shown in the scheme, while IX and X were shown to be the 9-*o*-aminophenylthio- and 9-bromo-derivatives of II respectively.

The application of one molar equivalent of III to 5, 7-dibromohinokitiol (3, 5 - dibromo - 6 -isopropyltropolone)[5] afforded the 7-*o*-aminophenylthio-8-isopropyl derivative of II (XI), plus a small amount of a compound which is assumed to be the 7-bromo-8-isopropyl derivative (XII). The 7-bromo-9-isopropyl derivative of II (XIII) was obtained by refluxing 5, 7-dibromo-α-thujaplicine (3, 5-dibromo-7-isopropyltropolone)[6] and III in methanol for 5 hr. However, 3-*o*-aminophenylthio - 5 - bromo - 7 - isopropyltropolone (XIV) was obtained in addition to XIII when the above mixture was refluxed for 2.5 hr.; XIV was

4) T. Nozoe, Y. Kitahara, K. Yamane and A. Yoshikoshi, *Proc. Japan Acad.*, **27**, 18 (1951).
5) T. Nozoe, K. Kikuchi and T. Ando, ibid., **26 (10)**, 32 (1950).
6) T. Nozoe, Y. Kitahara and T. Ikemi, ibid., **27**, 193 (1951).



VIII



IX R_1=-S-(2-NH_2-phenyl), R_2=H

X R_1=Br, R_2=H

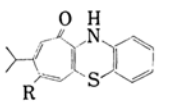
XIII R_1=isoPr, R_2=Br

XV $R_1=R_2$=Br

XVII $R_1=R_2$=Cl

XIX R_1=H, R_2=NO_2

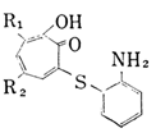
XXII R_1=H, R_2=$NHCOCH_3$



XI R=-S-(2-NH_2-phenyl)

XII R=Br

XX R=NO_2

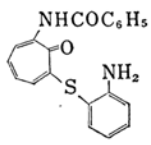


XIV R_1=isoPr, R_2=Br

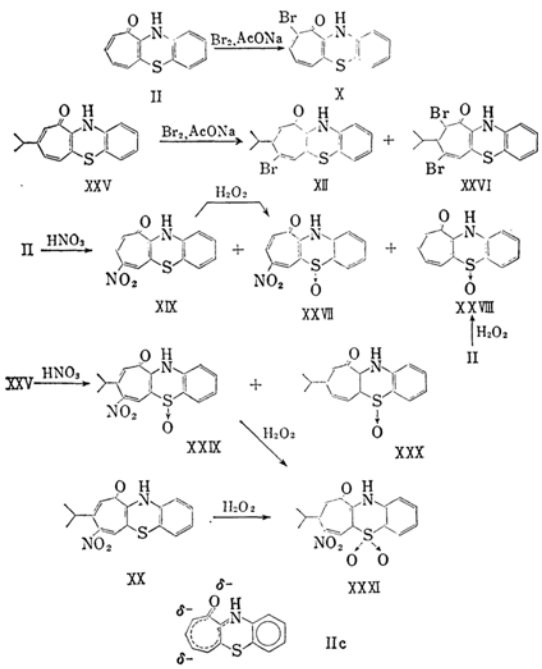
XVI $R_1=R_2$=Br

XVIII $R_1=R_2$=Cl

XXI R_1=H, R_2=NH_2



XXIII



IIc

On refluxing 3, 5, 7-tribromotropolone[7] and III in methanol, the 7,9-dibromo derivative XV was obtained in a good yield. On the other hand, when the reaction mixture was allowed to stand at room temperature, 3-*o*-aminophenylthio-5, 7-dibromotropolone (XVI) was obtained as the main product, in addition to some XV; XVI, on being heated above its melting point, afforded XV. Similar results were obtained in the reaction of 3, 5, 7-trichlorotropolone[8] and III, which afforded the 7, 9-dichloro derivative XVII as well as 3-*o*-aminophenylthio-5, 7-dichlorotropolone (XVIII). XVIII was converted into XVII on being heated above its melting point. When a mixture of 3-bromo-5-nitrotropolone[9] and III in methanol was allowed to stand at room temperature, the 7-nitro derivative of II (XIX) was obtained as black needles.

The nitration of 7-bromohinokitiol afforded two crystalline substances, m. p. 136°C and 111°C, which were considered to be stereoisomers of 7-bromo-5-nitrohinokitiol.[10] However, the latter compound has been shown recently[11] to be a mixture of 7-bromo-5-nitrohinokitiol and a small amount of 7-bromo-3-nitrohinokitiol. The application of III to each of these two substances afforded the same compound, the 7-nitro-8-isopropoyl derivative XX, but the isomeric 9-nitro-8-isopropyl derivative could not be isolated.

When 5-amino-3-bromotropolone[4,12] was allowed to react with III, only 5-amino-3-*o*-aminophenylthiotropolone (XXI) was obtained, even when the reaction mixture was refluxed. The compound XXI did not cyclize when heated above its melting point, and the starting material was recovered, while the *N, N'*-diacetyl derivative was formed when XXI was heated with acetic anhydride. This resistance to cyclization may be attributed to the electron-releasing resonance effect of the amino group in the tropolone nucleus. If this is so, cyclization may be expected to occur when 5-acetamido-3-bromotropolone is used instead of 5-amino-3-bromotropolone. Indeed, both the *N*-acetyl and *N, O*-diacetyl derivatives[4] of 5-amino-3-bromotropolone afforded the 7-acetamido derivative of II (XXII) when they were refluxed with *o*-aminothiophenol (III).

The reactions of 2, 3-, 2, 5- and 2, 7-dibromotropones with III gave no definite compound; only then converted into XIII by refluxing it in acetic acid. The difficulty in the cyclization of XIV is considered to be due to the steric interference and to the electron releasing effect of the isopropyl group.

7) T. Nozoe, S. Seto, Y. Kitahara, M. Kunori and Y. Nakayama, ibid., **26 (7)**, 38 (1950).
8) W. von E. Doering and L. H. Knox, *J. Am. Chem. Soc.*, **74**, 5683 (1952).
9) T Nozoe, Y. Kitahara, K. Doi and T. Arai, *Bull. Research Inst. Non-Aq. Solns., Thohoku Univ.*, **7**, 13 (1957).
10) T. Nozoe, Y. Kitahara, E. Kunioka and K. Doi, *Proc. Japan Acad.*, **26 (9)**, 38, 40 (1950).
11) L. C. Lin, T. Nozoe, T. Mukai and Y. Kitahara, *Sci. Repts. Tohoku Univ.*, **I, 48**, 96 (1964).
12) T. Nozoe, S. Seto, H. Takeda and T. Sato, ibid., **I, 35**, 274 (1952).

resinous products were obtained. The reactions of 7-amino-, 7-acetamido- and 7-diethylamino-2-bromotropone with III resulted in the complete recovery of the starting materials, whereas 7-benzamido-2-bromotropone yielded 7-benzamido-2-*o*-aminophenylthiotropone (XXIII), which did not afford any cyclization product, even when heated.

The general method utilized for the synthesis of phenothiazines, i. e., the reaction of diphenylamines and sulfur, was applied to 2-toluidinotropone, but the desired product was not obtained; only resinous products were formed.

The bromination of I in acetic acid in the presence of sodium acetate gave a poor yield of compound XXIV, assumed to be the tribromo derivative, in addition to a considerable amount of the recovered starting material. The ultraviolet spectrum*2 of XXIV shows a considerable hypsochromic shift. Furthermore, the 743 cm^{-1} band, due to the out-of-plane deformation of a 1, 2-disubstituted benzene, is present in the infrared spectrum of compound I, but not in the spectrum of XXIV. Therefore, it appears that some substitution must have occurred not only in the seven-membered ring but also in the benzene ring. However, the structure of XXIV could not be established.

The bromination of II afforded a monobromo derivative identical with the 9-bromo derivative X. The bromination of 8-isopropylbenzo-1, 4-thiazino[3, 2-b]tropone (XXV) afforded two products. One of the products was shown to be the 7-bromo derivative XII which had been obtained previously by the reaction of 5, 7-dibromohinokitiol and *o*-aminothiophenol. The structure of the second product, the analyses of which are in accord with those of a dibromo derivative of XXV, was deduced from the facts that its infrared spectrum shows absorption at 750 cm^{-1}, due to an out-of-plane deformation of a 1, 2-disubstituted benzene nucleus, and that its ultraviolet spectrum is similar to those of the 7, 9-dichloro- and the 7, 9-dibromo derivatives of II. This indicates that the compound is the 7, 9-dibromo derivative XXVI.

The nitration of I with fuming nitric acid did not give any definite product except the starting material. However, when II was treated with fuming nitric acid in acetic acid, three compounds were isolated. One of the compounds was found to be identical with the 7-nitro derivative XIX. The other two compounds (XXVII and XXVIII) have molecular formulae of $C_{13}H_9O_2NS$ and $C_{13}H_8O_4N_2S$ respectively, and they exhibit infrared absorption at 1026 and 1027 cm^{-1} respectively, due to a sulfoxide group[13]; therefore, they are considered to be the sulfoxide of II and its mononitro derivative respectively. Actually, XXVIII has also been obtained by the oxidation of II with hydrogen peroxide in acetic acid; this will be described in the following paper. The nitro group in XXVII must be located at the 7-position, since XXVII was also obtained by the oxidation of XIX. The nitration of XXV afforded two products XXIX and XXX. From their analyses and their infrared spectra, it was found that XXIX is the mononitro derivative of the simple sulfoxide XXX. In order to determine the position of the nitro group in XXIX, the authentic 7-nitro compound XX was oxidized with hydrogen peroxide. However, the product was not XXIX, but the sulfone XXXI, which shows absorptions due to a sulfone group[13] at 1295, 1284, 1151 and 1135 cm^{-1} in its infrared spectrum. However, the oxidation of XXIX in the same manner also gave XXXI, thus confirming that XXIX is the 7-nitro derivative of XXX. Similar examples of the oxidation of sulfide by nitric acid have often been observed with the phenothiazines. The oxidation of benzo-1, 4-thiazino[3, 2-b]tropones will be reported in the following paper.

From the results of the above electrophilic substitution reactions, it may be concluded that the ionic structure IIc of II contributes greately to these reactions.

Tropones condensed with some five-membered heterocycles, such as 3-phenylpyrrolo[2, 3-b]-tropone (XXXII)[14] and 2-hydroxyimidazolo-[5, 4-b]tropone (XXXIII)[15] which in part have a structural similarity to benzo-1, 4-thiazino-[3, 2-b]tropones, afforded their chloro derivatives, 8-chloro-3-phenyl-1-azaazulene and 2, 4-dichloro-1, 3-diazaazulene respectively, on treatment with phosphorus oxychloride or thionyl chloride. These reactions are considered to proceed through the enol forms. Although II is considered to exist as its keto form,[1] if II is able to assume the enol form, it may be expected that the 10-chloro derivative of I might be obtained by the reaction of II with some chlorinating reagents. The reaction of II with phosphorus oxychloride in pyridine resulted in the complete recovery of the starting material. However, on being treated with 1.25 molar equivalents of thionyl chloride in dry benzene, II afforded, as violet needles, a product which was not the expected 10-chloro derivative of I, but the 7, 9-dichloro derivative of II (XVII) obtained already by the reaction of 3, 5, 7-trichlorotropolone and *o*-aminothiophenol.

The reaction of XXV and thionyl chloride was carried out, and four products were obtained as

*2 See Experimental Section.

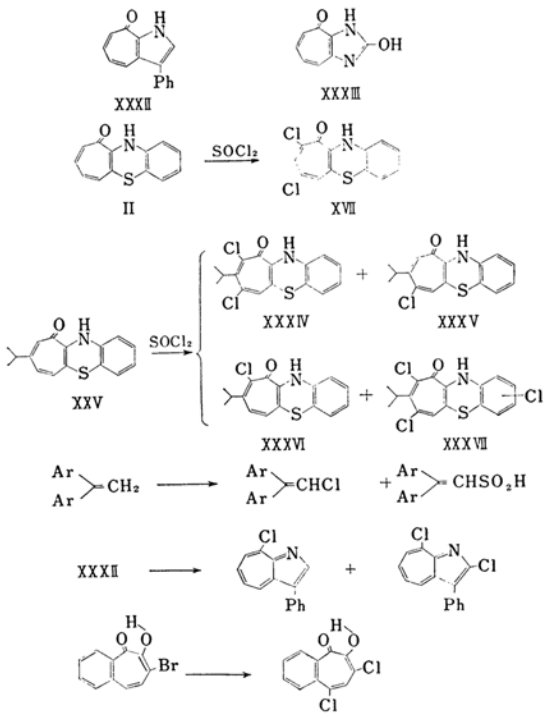
13) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co., London (1958), p. 350.

14) T. Nozoe, Y. Kitahara and J. Shin, to be published.

15) T. Nozoe, T. Mukai and K. Matsumoto, to be published.

follows. By heating XXV with 1.25 molar equivalents of thionyl chloride in dry benzene, red violet prisms (XXXIV), m. p. 156°C, and violet needles (XXXV), m. p. 156°C, were obtained, while from another run of the reaction, red violet plates (XXXVI), m. p. 149°C, were obtained in addition to the compound XXXV. Each of these products showed a depression in its melting point when mixed with any of the others. When XXV was treated with 2.5 molar equivalents of thionyl chloride, it yielded violet needles (XXXVII), m. p. 210°C. The yields of these four products in the crude state were moderate, but their purification proved difficult; consequently, the yields of the pure compounds were fairly low.

The structures of these four products were not determined chemically, but from a consideration of the results of their analyses and their ultraviolet and infrared spectra; the following conclusions were reached. The ultraviolet spectra of these four products show that they have not undergone any skeletal change. The infrared spectra of XXXIV, XXXV and XXXVI show peaks between 741—745 cm^{-1}, due to the out-of-plane deformations of a 1, 2-disubstituted benzene; therefore, it is considered that no substitution has taken place in the benzene rings of these three products. Analyses showed the molecular formulae of XXXIV—XXXVII to be $C_{16}H_{13}ONSCl_2$, $C_{16}H_{14}ONSCl$, $C_{16}H_{14}ONSCl$ and $C_{16}H_{12}ONSCl_3$, respectively. Since the ultraviolet spectrum of XXXIV is similar to those of the 7, 9-dihalo derivatives XV, XVII and XXVI, XXXIV is



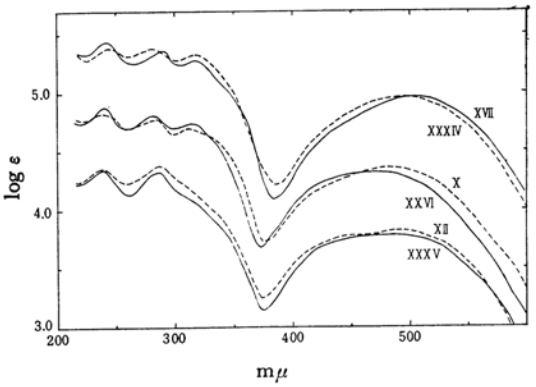


Fig. 3. Ultraviolet absorption spectra of X, XII, XVII, XXXIV, XXXV and XXXVI in MeOH.

assumed to be the 7, 9-dichloro derivative of XXV. The ultraviolet spectra of XXXV and XXXVI are similar to those of XII and X respectively; therefore, it is assumed that they are the 7-chloro and the 9-chloro derivatives of XXV respectively. Two of the three chlorine atoms in XXXVII are considered to be located at the 7- and 9- positions; since its infrared spectrum shows no absorption attributable to a 1, 2-disubstituted benzene, the remaining chlorine atom might be substituted in the benzene ring. However, its position could not be defined.

It is clear from the above that the reactions of benzo-1, 4-thiazino[3, 2-b]tropones with thionyl chloride result in the formation of products chlorinated at the 7- and/or the 9-positions. However, when the compound I was treated with thionly chloride, the reaction resulted in the recovery of the starting material and the formation of a small amount of an undefined, amorphous product.

Such substitutions involving the replacement of a hydrogen atom by the chlorine atom of thionly chloride, without the use of a catalyst, have also been observed in other cases. Patai and Bergmann[16] reported that the reaction of 1, 1-diarylethylene and thionyl chloride afforded mainly 1, 1-diaryl-2-chloroethylene and a small amount of 1, 1-diarylethylenesulfinic acid. Nozoe et al.[14] found that 2, 8-dichloro-3-phenyl-1-azaazulene and 8-chloro-3-phenyl-1-azaazulene were obtained from the reaction of XXXII with thionyl chloride, while Ebine[17] reported that the reaction of 7-bromo-3, 4-benzotropone with thionyl chloride gave an adduct which was converted into 5,7-dichloro-3, 4-benzotropone by recrystallization from ethanol.

Patai et al. has explained the mechanism of the above reaction by assuming that the reaction proceeds through the attack of an SOCl cation at

16) S. Patai and F. Bergmann, *J. Am. Chem. Soc.*, **72**, 1034 (1950).
17) S. Ebine, This Bulletin, **34**, 881 (1961).

a highly negative position, followed by the elimination of SO. Our results are inconsistent with the above mechanistic consideration, since, as has been mentioned previously, the position which undergoes chlorination with thionyl chloride is the same as that which is attacked by electrophilic reagents.

Experimental*3

Benzo-1, 4-thiazino[2, 3-b]tropone (V).—To a solution of 2-chloro-3-methoxytropone (IV) (100 mg.) in methanol (5 ml.), *o*-aminothiophenol (III) (80 mg.) was added; the mixture was then allowed to stand for 6 hr. in an ice box. The crystals which precipitated out were collected by filtration and recrystallized from a large amount of methanol, thus affording 30 mg. of V as black needles, m. p. 286°C (decomp.).

Found: C, 68.89; H, 4.03; N, 6.20. Calcd. for $C_{13}H_9ONS$: C, 68.72; H, 3.99; N, 6.17%.

λ_{max}^{MeOH} mμ (log ε): 230 (4.32), 285 (4.35), 320^{sh} (3.96), 425 (3.71).

$\lambda_{max}^{0.1N\ HCl}$ mμ (log ε): 235 (4.28), 292 (4.41), 334 (3.90), 440 (3.74).

Benzo-1, 4-thiazino[4, 5-b]tropone (VII).—a) To a solution of 2-chloro-5-methoxytropone (VI; R=Me) (200 mg.) in methanol (8 ml.), III (167 mg.) was added; the mixture was then allowed to stand for 48 hr. in an ice box. The solvent was removed, the residue was dissolved in benzene, and the solution was washed with 2 N hydrochloric acid, followed with a 2 N sodium hydroxide solution and water, each three times, dried, and passed through an alumina column. Removing the solvent from the effluent gave 70 mg. of VII as a reddish oil.

Found: C, 68.91; H, 4.38; N, 5.68. Calcd. for $C_{13}H_9ONS$: C, 68.72; H, 3.99; N, 6.17%.

λ_{max}^{MeOH} mμ (log ε): 225 (4.24), 275 (4.25), 330 (3.69), 418 (3.70).

$\lambda_{max}^{0.1N\ HCl}$ mμ (log ε): 238 (4.20), 288 (4.13), 358 (3.95), 460—470 (3.46).

b) A solution of 2-chloro-5-hydroxytropone (VI; R=H) (110 mg.) and III (91.5 mg.) in methanol (15 ml.) was refluxed for one hour. The black resinous substance obtained by removing the solvent was dissolved in chloroform and passed through an alumina column; a reddish oily substance was thus obtained. Its infrared and ultraviolet spectra were superimposable upon those of VII obtained by procedure a).

The Reaction of 3, 7-Dibromotropolone with *o*-Aminothiophenol (III).—When a solution of 3, 7-dibromotropolone (280 mg.) and III (260 mg.) in methanol (8 ml.) was refluxed for 2.5 hr., 240 mg. of crude crystals were obtained. The crystals were separated into a soluble part A and an insoluble part B in benzene, and B was recrystallized from pyridine-ethanol, thus yielding VIII as deep violet plates, m. p. 175—176°C.

Found: C, 68.33; H, 3.42; N, 8.52. Calcd. for $C_{19}H_{12}N_2S_2$: C, 68.67; H, 3.64; N, 8.43%.

λ_{max}^{MeOH} mμ (log ε): 282 (4.51), 490—500 (4.00). In A, an insoluble part in methanol was recrystallized from pyridine, thus affording IX as reddish prisms, m. p. 251—252°C.

Found: C, 64.98; H, 3.80; N, 7.76. Calcd. for $C_{19}H_{14}ON_2S_2$: C, 65.15; H, 4.03; N, 8.00%.

λ_{max}^{MeOH} mμ (log ε): 245 (4.26), 280 (4.16), 355 (4.34), 470 (3.76). The part in A soluble in methanol was recrystallized from pyridine-methanol to give X as violet plates, m. p. 221—222°C.

Found: C, 50.93; H, 2.51; N, 4.62. Calcd. for $C_{13}H_8ONSBr$: C, 51.16; H, 2.31; N, 4.59%.

λ_{max}^{MeOH} mμ (log ε): 242 (4.32), 287 (4.28), 313 (4.19), 485 (3.86).

The Reaction of 5, 7-Dibromohinokitiol with III.—A solution of 5, 7-dibromohinokitiol (300 mg.) and III (124 mg.) in methanol (5 ml.) was refluxed for 2 hr. The solvent was removed, and the residue was dissolved in benzene, washed with water, and evaporated to leave a dark reddish oily substance. The crystals which were precipitated out by adding ether to the oil were filtered and recrystallized from ethanol to give 80 mg. of XI as reddish needles, m. p. 205°C.

Found: C, 66.99; H, 5.09; N, 7.12. Calcd. for $C_{22}H_{20}ON_2S_2$: C, 67.33; H, 5.14; N, 7.14%.

λ_{max}^{MeOH} mμ (log ε): 239 (4.64), 290 (4.34), 323 (4.22), 490 (3.86). The solvent of the filtrate was removed, and the residue was dissolved in benzene, washed with 6 N hydrochloric acid and a 10% sodium carbonate solution, and passed through an alumina column. From the effluent, XII was obtained as violet needles, m. p. 198—199°C.

Found: N, 4.46. Calcd. for $C_{16}H_{14}ONSBr$: N, 4.02%.

λ_{max}^{MeOH} mμ (log ε): 240 (4.26), 287 (4.27), 486—492 (3.73).

The Reaction of 5, 7-Dibromo-α-thujaplicine with III.—a) To a solution of 5, 7-dibromo-α-thujaplicine (1.66 g.) in methanol (20 ml.), III (1.33 g.) was added and the mixture was refluxed for 5 hr. The solvent was removed, leaving a reddish residue which was then dissolved in benzene. The solution was washed with a 2 N sodium hydroxide solution, followed by 2 N hydrochloric acid and water. The benzene solution was passed through an alumina column and eluted with benzene. 700 mg. of a reddish oil was obtained, it was then crystallized with ether. Recrystallization from methanol afforded XIII as reddish plates, m. p. 84—85°C.

Found: C, 55.44; H, 3.97; N, 3.98. Calcd. for $C_{16}H_{14}ONSBr$: C, 55.18; H, 4.05; N, 4.02%.

λ_{max}^{MeOH} mμ (log ε): 238 (4.38), 286 (4.28), 470—480 (3.86).

b) A solution of 5, 7-dibromo-α-thujaplicine (500 mg.) and III (404 mg.) in methanol (6 ml.) was refluxed for 2 hr. The crystals which separated out on cooling were filtered and recrystallized from methanol, yielding 230 mg. of XIV as pale yellow needles, m. p. 165°C. An ethanolic solution of XIV turned green when treated with ferric chloride.

Found: C, 52.48; H, 4.29; N, 4.24. Calcd. for $C_{16}H_{16}O_2NSBr$: C, 52.46; H, 4.40; N, 3.83%.

From the mother liquor, 264 mg. of hydrobromide of III and 80 mg. of XIII were obtained.

The Cyclization of XIV to XIII.—A solution of XIV (20 mg.) in acetic acid (3 ml.) was refluxed for 2.5 hr. The solvent was then distilled off in vacuo,

*3 All melting points are uncorrected.

the residue was dissolved in benzene, and the solution was washed with a 2 N sodium hydroxide solution, 2 N hydrochloric acid and water. By removing the solvent, 15 mg. of a reddish, oily substance was obtained. The ultraviolet and infrared spectra of this oil were superimposable upon those of XIII.

The Reaction of 3, 5, 7-Tribromotropolone with III.—To a solution of 3, 5, 7-tribromotropolone (360 mg.) in methanol (15 ml.), III (140 mg.) was added; when the solution was then allowed to stand for 2 hr. at room temperature, 170 mg. of crystals (A) were obtained. By letting the filtrate stand, 200 mg. of violet crystals (B), m. p. 228—230°C, were obtained. These crystals A were dissolved in chloroform and shaken with a 10% sodium carbonate solution; yellow sodium salt was thus obtained. From the chloroform layer, 50 mg. of violet crystals (C) were obtained. When the sodium salt was dissolved in water and acidified with 2 N hydrochloric acid, 85 mg. of yellow crystals were obtained. Recrystallization from chloroform-methanol afforded XVI as yellow prisms, m. p. 176°C.

Found: C, 38.44; H, 2.58; N, 3.29. Calcd. for $C_{13}H_9O_2NSBr_2$: C, 38.73; H, 2.25; N, 3.48%.

The combined crystals of B and C were recrystallized from chloroform, giving XV as reddish violet needles, m. p. 237—238°C.

Found: C, 40.62; H, 1.56; N, 3.29. Calcd. for $C_{13}H_7ONSBr_2$: C, 40.53; H, 1.83; N, 3.64%.

λ_{max}^{MeOH} mμ (log ε): 252 (4.30), 275 (4.31), 320 (4.18), 510—520(3.92). The heating of XVI over its melting point gave XV quantitatively.

The Reaction of 3, 5, 7-Trichlorotropolone with III.—To a solution of 3, 5, 7-trichlorotropolone (240 mg.) in methanol (4.5 ml.), III (150 mg.) was added; the solution was then allowed to stand at room temperature. After 2 hr. 110 mg. of yellow crystals were obtained by filtration. Recrystallization from chloroform-ethanol gave XVIII as orange yellow prisms, m. p. 178—179°C.

Found: C, 49.24; H, 2.84; N, 4.49. Calcd. for $C_{13}H_9O_2NSCl_2$: C, 49.99; H, 2.90; N, 4.48%.

From the filtrate obtained from the reaction mixture, 120 mg. of violet crystals were obtained. Recrystallization from chloroform gave XVII as violet needles, m. p. 237—238°C.

Found: C, 53.34; H, 2.09; N, 4.46. Calcd. for $C_{13}H_7ONSCl_2$: C, 53.06; H, 2.40; N, 4.76%.

λ_{max}^{MeOH} mμ (log ε): 242 (4.43), 290 (4.35), 315 (4.25), 500—510 (3.95). The heating of XVIII over its melting point gave XVII quantitatively.

7-Nitrobenzo-1, 4-thiazino[3, 2-b]tropone (XIX).—By allowing a solution of 3-bromo-5-nitrotropolone (322 mg.) and III (170 mg.) in methanol (8 ml.) to stand, 132 mg. of crystals were obtained. Recrystallization from acetone afforded XIX as black needles, m. p. 260°C (decomp.).

Found: C, 56.98; H, 3.11. Calcd. for $C_{13}H_8O_3N_2S$: C, 57.36; H, 2.96%.

λ_{max}^{MeOH} mμ (log ε): 232 (3.14), 295 (4.11), 366 (4.00), 553 (3.78).

8-Isopropyl-7-nitrobenzo-1, 4-thiazino [3, 2-b] tropone (XX).—*a) From 7-Bromo-5-nitrohinokitiol with a m. p. of 135°C.*—By allowing a solution of 7-bromo-5-nitrohinokitiol (410 mg.) and III (185 mg.) in methanol (9 ml.) to stand at room temperature for 10 hr., 150 mg. of crystals were obtained. Recrystallization from acetone gave 90 mg. of XX as black needles, m. p. 230°C.

Found: C, 61.00; H, 4.56; N, 8.79. Calcd. for $C_{16}H_{14}O_3N_2S$: C, 61.14; H, 4.49; N, 8.91%.

λ_{max}^{MeOH} mμ (log ε): 238 (4.36), 290 (4.32), 438—450 (3.74), 515 (3.79).

b) From 7-Bromo-5-nitrohinokitiol with a m. p. of 111°C.—The reaction of 7-bromo-5-nitrohinokitiol (170 mg.) and III (95 mg.) according to a method similar to that described above resulted in 54 mg. of XX, m. p. 230°C, which showed no depression of melting point on admixture with the sample obtained from the procedure a); moreover, the ultraviolet and infrared spectra of these two samples were superimposable upon one another.

5-Amino-3-(*o*-aminophenylthio)tropolone (XXI).—A solution of 5-amino-3-bromotropolone (300 mg.) and III (190 mg.) in ethanol (25 ml.) was refluxed for 2 hr. The reddish oil obtained by removing the solvent was dissolved in water, neutralized with sodium hydrogen carbonate, and extracted with ethyl acetate. From the extract, 320 mg. of crystals, m. p. 215—218°C, were obtained. Recrystallization from ethanol gave XXI as brown prisms, m. p. 218—219°C.

Found: C, 59.92; H, 4.56; N, 10.73. Calcd. for $C_{13}H_{12}O_2N_2S$: C, 59.99; H, 4.65; N, 10.77%.

Diacetate: pale brown crystals, m. p. 253—254°C.

Found: C, 59.20; H, 5.02; N, 8.00. Calcd. for $C_{17}H_{16}O_4N_2S$: C, 59.30; H, 4.68; N, 8.14%.

7-Acetamidobenzo-1, 4-thiazino[3, 2-b]tropone (XXII).—The reaction of 5-acetamido-3-bromotropolone (44 mg.) and III (27 mg.) in methanol gave 40 mg. of XXII, m. p. 251°C (from ethanol).

Found: C, 63.10; H, 4.39; N, 9.48. Calcd. for $C_{15}H_{12}O_2N_2S$: C, 63.38; H, 4.26; N, 9.86%.

λ_{max}^{MeOH} mμ (log ε): 235 (4.31), 286 (4.23), 318 (4.19), 477 (3.84). The compound XXII was also obtained from 5-acetamido-2-acetoxy-7-bromotropone and III by the method described above.

2-Benzamido-7-(*o*-aminophenylthio) tropone (XXIII).—A solution of 2-bromo-7-benzamidotropone (150 mg.) and III (70 mg.) in methanol (5 ml.) and benzene (1 ml.) was refluxed for 5 hr. The crystals which precipitated out were recrystallized from methanol, thus yielding XXIII as pale yellow crystals, m. p. 185—186°C.

Found: C, 68.78; H, 4.73; N, 7.86. Calcd. for $C_{20}H_{16}O_2N_2S$: C, 68.96; H, 4.63; N, 8.04%.

The Bromination of Benzo[b]tropothiazine (I).—To a solution of I (500 mg.) and sodium acetate (214 mg.) in acetic acid (25 ml.), bromine (470 mg.) in acetic acid (1 ml.) was added drop by drop at room temperature, and then the mixture was stirred for 1 hr. The precipitate was removed by filtration, the filtrate was concentrated, water was added, and the precipitate formed was filtered. A solution of the crude product in benzene was chromatographed on alumina and eluted with benzene. The crystals were recrystallized from ethanol to afford 60 mg. of XXIV as orange needles, m. p. 156.5°C.

Found: C, 35.17; H, 1.47; N, 2.88. Calcd. for $C_{13}H_6NSBr_3$: C, 34.81; H, 1.35; N, 3.12%.

λ_{max}^{MeOH} mμ (log ε): 225 (4.34), 255 (4.41), 355 (3.88).

The Bromination of Benzo-1, 4-thiazino[3, 2-b]-tropone (II).—To a stirred solution of II (500 mg.)

and sodium acetate (180 mg.) in acetic acid (25 ml.), these was added a solution of bromine (353 mg.) in acetic acid (0.5 ml.) under cooling with ice. The mixture was then stirred for a further 30 min. and allowed to stand overnight in an ice box. The crystals which separated out were filtered and purified by alumina chromatography, followed by recrystallization from pyridine, to give 190 mg. of reddish violet needles, m. p. 226—227°C; undepressed on admixture with a compound X prepared by the reaction of 3, 7-dibromotropolone with *o*-aminothiophenol.

The Bromination of 8-Isopropylbenzo - 1, 4-thiazino[3, 2-b]tropone (XXV).—To a stirred solution of XXV (500 mg.) and sodium acetate (169 mg.) in acetic acid (30 ml.), these was added, drop by drop, a solution of bromine (365 mg.) in acetic acid (1 ml.) under cooling with ice. After this addition, the solution was stirred for 2 hr., and the solid thus precipitated was filtered and washed with methanol. Repeated recrystallizations of the more insoluble part of the solid from chloroform-methanol afforded 140 mg. of XXVI as reddish needles, m. p. 205—207°C.

Found: C, 45.28; H, 3.07; N, 3.22. Calcd. for $C_{16}H_{13}ONSBr_2$: C, 45.00; H, 3.07; N, 3.28%.

λ_{max}^{MeOH} mμ (log ε): 246 (4.31), 279 (4.27), 295 (4.27), 315(4.23), 470(3.80). The mother liquor of the recrystallization was evaporated to a small volume, water was added, and the solution was extracted with benzene. The dried benzene solution was then passed through an alumina column and eluted with benzene. The crystals (80 mg.) obtained from the effluent were recrystallized from methanol to give violet needles, m. p. 198°C. The ultraviolet and infrared spectra of these crystals were identical with those of XII, the 7-bromo derivative of XXV, obtained by the reaction of 5, 7-dibromohinokitiol with *o*-aminothiophenol.

The Nitration of Benzo-1, 4-thiazino[3, 2-b]tropone (II).—To a stirred solution of II (2.0 g.) in acetic acid (20 ml.), a solution of fuming nitric acid (0.6 ml.) in acetic acid (2 ml.) was added dropwise at 5—7°C over a period of 1.5 hr. After this addition, the reaction mixture was allowed to stand at room temperature for 4 hr. and then in an ice box overnight. Black crystals (720 mg.) were obtained by filtration. The crystals were chromatographed on an alumina column using chloroform and recrystallized from chloroform to give black needles, m. p. 262°C (decomp.). The ultraviolet and infrared spectra of these crystals are superimposable upon those of 7-nitrobenzo-1, 4-thiazino[3, 2-b]-tropone (XIX). The filtrate from the reaction mixture was diluted with water and extracted with chloroform, the solvent was removed, and the residue was washed with ether and then crystallized by the addition of chloroform. The crystals were filtered and recrystallized from acetic acid to give XXVII as yellow prisms (210 mg.), m. p. 273°C.

Found: C, 53.53; H, 2.93; N, 9.22. Calcd. for $C_{13}H_8O_4N_2S$: C, 54.17; H, 2.80; N, 9.72%.

λ_{max}^{MeOH} mμ (log ε): 234 (4.29), 435 (4.28). The above filtrate from the chloroform solution was then concentrated and passed through an alumina column. The crystals obtained from the first effluent by chloroform were recrystallized from benzene and then from dilute ethanol to afford 240 mg. of XXVIII as yellow prisms, m. p. 207°C.

Found: C, 64.27; H, 3.60; N, 5.65. Calcd. for $C_{13}H_9O_2NS$: C, 64.20; H, 3.73; N, 5.76%.

λ_{max}^{MeOH} mμ (log ε): 234 (4.42), 365 (4.22), 380 (4.22).

The Nitration of 8-Isopropylbenzo-1, 4-thiazino-[3, 2-b]tropone (XXV).—To a stirred solution of XXV (600 mg.) in acetic acid (6 ml.), a solution of nitric acid (144 mg.) in acetic acid (1 ml.) was added drop by drop under cooling with ice. After being allowed to stand at room temperature for 4 hr., the reaction mixture was diluted with water and extracted with chloroform. The extract was concentrated to a small volume, passed through an alumina column, and eluted with chloroform. The crystals obtained from the first effluent were recrystallized from methanol to afford 210 mg. of XXX as yellow prisms, m. p. 174°C.

Found: C, 67.21; H, 4.89; N, 4.89. Calcd. for $C_{16}H_{15}O_2NS$: C, 67.36; H, 5.30; N, 4.91%.

λ_{max}^{MeOH} mμ (log ε): 237 (4.43), 363 (4.20), 382 (4.23). The crystals obtained from the later effluent were recrystallized from methanol to give 32 mg. of XXIX as yellow prisms, m. p. 263°C.

Found: C, 58.21; H, 4.00; N, 8.26. Calcd. for $C_{16}H_{14}O_4N_2S$: C, 58.18; H, 4.27; N, 8.48%.

λ_{max}^{MeOH} mμ (log ε): 240 (4.40), 400 (4.26).

The Oxidation of 7-Nitrobenzo-1, 4-thiazino-[3, 2-b]tropone (XIX).—To a suspended solution of XIX (80 mg.) in acetic acid (1 ml.) 35% hydrogen peroxide (0.04 ml.) was added; the mixture was then allowed to stand at room temperature for a week, during which time it was occasionally stirred. Yellow brown crystals were filtered out, treated with charcoal in acetic acid, and recrystallized from the same solvent to give 50 mg. of yellow prisms, m. p. 273°C (decomp.). The ultraviolet and infrared spectra of this crystals were superimposable upon those of XXVII.

8-Isopropyl-7-nitrobenzo-1, 4 - thiazino[3, 2-b]tropone 5, 5-Dioxide (XXXI).—a) A mixture of XX (80 mg.) and 35% hydrogen peroxide (0.1 ml.) in acetic acid (1 ml.) was allowed to stand at room temperature for 2 weeks. The crystals which precipitated out were then filtered and recrystallized from acetic acid affording XXXI as yellow needles, m. p. 295°C (decomp.).

Found: C, 56.90; H, 4.18; N, 7.15. Calcd. for $C_{16}H_{14}O_5N_2S$: C, 55.49; H, 4.08; N, 8.09%.

b) A mixture of XXIX (34 mg.) and 35% hydrogen peroxide (0.05 ml.) in acetic acid (1 ml.) was allowed to stand at room temperature for a week. The crystals which separated out were recrystallized from acetic acid to give yellow needles, m. p. 295°C (decomp.) which were identical with the XXXI obtained from XX.

The Reaction of Benzo-1, 4-thiazino[3, 2-b]tropone (II) with Thionyl Chloride.—After a solution of II (200 mg.) and thionyl chloride (130 mg.) in dry benzene (25 ml.) had been allowed to stand at room temperature for 30 min., the solution was refluxed for 3 hr.; then the solvent and excess of thionyl chloride were distilled off. The residue was washed with 2 N sodium hydroxide and water each three times, the benzene solution was dried over sodium sulfate, and the solvent was removed to give 150 mg. of a crude product. A benzene solution of the product was then passed through an alumina column, and the crystals obtained from the elute were recrystallized from benzene to yield violet needles, m. p. 223°C. This product was

identified as 7, 9-dichlorobenzo-1, 4-thiazino[3, 2-b]-tropone (XVII) by a mixed melting point determination and by a comparison of the ultraviolet and infrared spectra.

The Reaction of 8-Isopropylbenzo-1, 4-thiazino-[3, 2-b]tropone (XXV) with Thionyl Chloride.—a) A solution of XXV (500 mg.) and thionyl chloride (270 mg.) in dry benzene (30 ml.) was refluxed for 3 hr. After the evaporation of the solvent, the residue was dissolved in benzene, washed with water, dried, and passed through an alumina column. The crystals obtained from the first effluent were recrystallized from acetone, thus affording 20 mg. of XXXIV as violet prisms, m. p. 154—156°C.

Found: C, 55.55; H, 3.45; N, 4.11. Calcd. for $C_{16}H_{13}ONSCl_2$: C, 56.82; H, 3.87; N, 4.14%.

λ_{max}^{MeOH} mμ (log ε): 245 (4.35), 278 (4.35), 320 (4.32), 495 (3.90). The crystals obtained from the second effluent were recrystallized from acetone to give 60 mg. of XXXV as violet needles, m. p. 155—156°C, which showed a marked depression of melting point on admixture with another compound XXXIV.

Found: C, 62.84; H, 4.42; N, 4.89. Calcd. for $C_{16}H_{14}ONSCl$: C, 63.28; H, 4.65; N, 4.61%.

λ_{max}^{MeOH} mμ (log ε): 240 (4.38), 287 (4.36), 495 (3.81).

b) A solution of XXV (500 mg.) and thionyl chloride (270 mg.) in dry benzene (40 ml.) was allowed to stand for 4 hr. at room temperature, and then it was refluxed for 5 hr. After a work-up such as that described above, 30 mg. of XXXVI as reddish violet plates, m. p. 149°C (from acetone) were obtained from the first fraction of the chromatograph.

Found: C, 62.31; H, 4.18; N, 4.69. Calcd. for $C_{16}H_{14}ONSCl$: C, 63.21; H, 4.65; N, 4.61%.

λ_{max}^{MeOH} mμ (log ε): 240 (4.39), 280 (4.30), 313 (4.25), 470 (3.83). The crystals obtained from the second fraction were recrystallized from acetone to give 80 mg. of violet needles, m. p. 156°C; undepressed on admixture with XXXV.

c) A solution of XXV (2.0 g.) and thionyl chloride (2.2 g.) in dry benzene (20 ml.) was refluxed for 10 hr. The solvent was then distilled off, and the residue was recrystallized from benzene, thus yielding 410 mg. of XXXVII as violet needles, m. p. 208—210°C.

Found: C, 51.36; H, 3.31; N, 3.85. Calcd. for $C_{16}H_{12}ONSCl_3$: C, 51.60; H, 3.25; N, 3.78%.

λ_{max}^{MeOH} mμ (log ε): 250 (4.29), 265 (4.88), 320 (4.25), 490—500 (3.84).

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