*2-Phenylthiazolo[4, 5-b]tropones**

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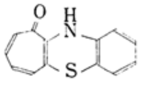
(Received August 8, 1962)

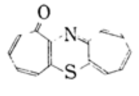
The authors have been reported[1] the synthesis of benzo-1, 4-thiazino [3, 2-b] tropone (cyclohepta [b] benzo-1, 4-thiazin-10(11*H*)-one) (I) and its various derivatives by the reaction of 3-halotropolones and *o*-aminothiophenol. In anticipation of the sythesis of the similar compound II having 7–6–7 ring system, the reaction of 2-amino-3-bromotropones and 2-mercaptotropones was carried out, but in this reaction 2-phenylthiazolo [4, 5-b] tropones, instead of II, were obtained by rearrangement of mercaptotropone nucleus, the results of which will be described herein.

When 2-amino-3-bromotropone (III)[2] and 2-mercaptotropone (2-hydroxytropothione[3]) (IV)[4] was refluxed in ethanol, the starting materials were recovered with a minute amout of disulfide V. However, heating of the mixture of III and IV in ethanol in the presence of sodium ethoxide in a sealed tube at 125°C for 10 hr., which is the same conditon as in the synthesis of 3-alkylthiotropolones from 3-bromotropolone[4], gave yellow prisms (VI), m. p. 183°C, with the correct analytical values for II. In a similar reaction of IV and 2-amino-3-bromo-6-isopropyltropone (VII), which was obtained from 3-bromo-6-isopropyl-2-methoxytropone[5] and liquid ammonia, yellow plates (VIII), m. p. 145°C, were obtained, analysis being agreed with isopropyl derivative of VI.

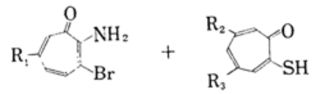
Reaction of III with 6-isopropyl-2-mercaptotropone (IX)[6] or 4-isopropyl-2-mercaptotropone (X)[6] were carried out. Although the reaction of III and IX at 125°C in the presence of sodium ethoxide gave no definite product except disulfide XI and some starting materials, the reaction at 110°C afforded yellow prisms (XII), m. p. 142°C, having the same molecular formula with VIII. X also gave yellow prisms by the reaction with III, but the product proved to be identical with XII. This fact clearly showed that the reactions in both cases underwent a quite different fashion from our anticipation and the product (XII) could not be the homologs of II. These unexpected reaction can be explained by assuming XII is 2(3′-isopropylphenyl)-thiazolo [4, 5-b] tropone produced by rearrangement of the mercaptotropone nucleus to the benzenoid one. Moreover, the similarity of ultraviolet spectra of VI and VIII with that of XII (Fig. 1), implies that VI and VIII, both formed under a similar reaction condition, are not II and its isopropyl derivative but 2-phenylthiazolo [4, 5-b] tropone and its 6-isopropyl derivatives.



I



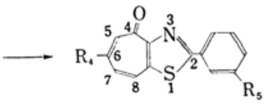
II



III $R_1=H$ IV $R_2=R_3=H$

VII $R_1=iso\text{-Pr}$ IX $R_2=iso\text{-Pr}$, $R_3=H$

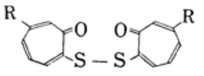
X $R_2=H$, $R_3=iso\text{-Pr}$



VI $R_4=R_5=H$

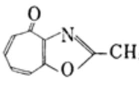
VIII $R_4=iso\text{-Pr}$, $R_5=H$

XII $R_4=H$, $R_5=iso\text{-Pr}$



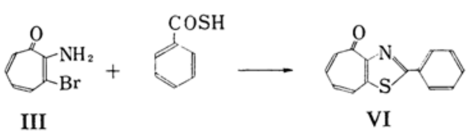
V $R=H$

XI $R=iso\text{-Pr}$



XIII

These hypotheses were confirmed by the formation of VI from the condensation reaction of thiobenzoic acid and III.



III VI

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* Presented at the Local Meeting of the Chemical Society of Japan, Yonezawa, Octorber, 1961.

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

[2] T. Nozoe, S. Seto, H. Takeda, S. Morosawa and K. Matsumoto, *Proc. Japan Acad.*, 27, 556 (1951); *Sci. Repts. Tohoku Univ., First Ser.*, 36, 126 (1952).

[3] T. Nozoe and K. Matsui, This Bulletin, 34, 616 (1961).

[4] T. Nozoe, M. Sato and K. Matsui, *Proc. Japan Acad.*, 28, 407 (1952); *Sci. Repts. Tohoku Univ., First Ser.*, 37, 211 (1953).

[5] S. Seto, ibid., 37, 297 (1953).

[6] K. Matsui, This Bulletin, 33, 1448 (1960).

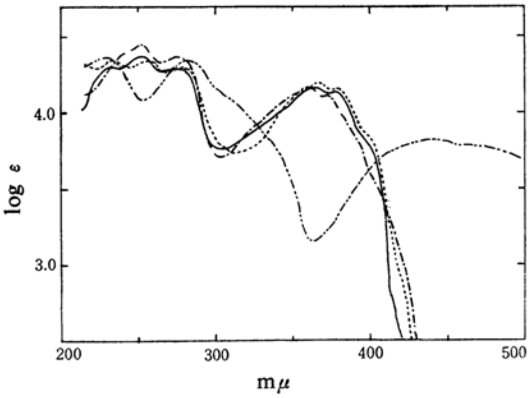
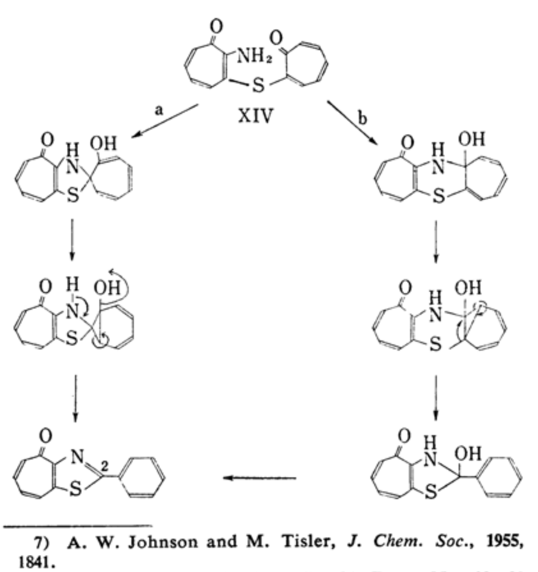


Fig. 1. Ultraviolet absorption spectra of I (—··—··), VI (———), VIII (—·—·) and XII (·········) in methanol.

Ultraviolet spectra of these thiazolotropones show considerable hypsochromic shift compared with I and rather resemble that of 2-methyloxazolo[4, 5-b]tropone (XIII)[7]. While, in their infrared spectra, absorption band of N–H or O–H do not appear and C=O stretching bands appear at 1627 cm^{-1} in VI and 1622 cm^{-1} in VIII, and these values seem to be reasonably corresponding to the C=O band of tropones[8] VI, VIII and XII are very stable toward heat, acid or alkali and do not give any molecular compound such as picrate. However, they give 2, 4-dinitrophenylhydrazones, m. p. 251, 259 and 218°C, respectively.

Since it was found that 2-mercaptotropone was stable under the condition employed in these condensation reactions, the reaction path to these 2-phenylthiazolo[4, 5-b]tropones involves the initial formation of thio ether XIV which undergoes rearrangement by one of the following routes.

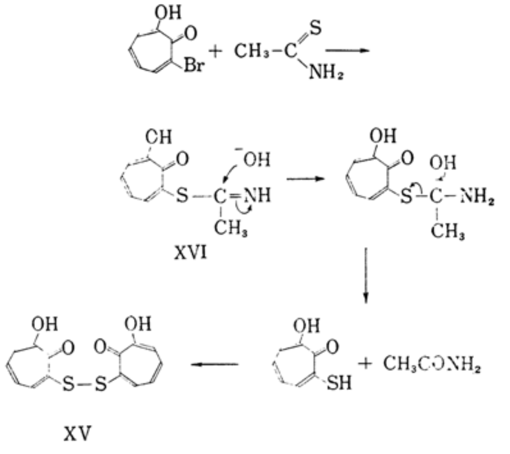


In path a, carbon at 2-position in the product, thiazolotropone, is originated from carbon-2 of mercaptotropone, while the same carbon in the product is carbonyl carbon if path b has been followed. It is considered that b is the more favorable path than a, since the aromatization of 2-substituted tropones is accepted to be initiated by attack of bases on the carbonyl-carbon, a similar attack on carbon-2 resulting in the replacement of the substituent at the same carbon[9]. A more detailed examination would, however, be desirable before any difinite conclusion is drawn.

Attempted synthesis of other thiazolotropones will be described in the following. Attempted reaction of III and thioacetic acid gave an oily substance, whose ultraviolet spectrum is similar to that of VI. However, the closer investigation on the structure was interrupted by minuteness of the yield.

It has been known that the reaction of 3-bromotropolone and thioacetamide gave an undifined compound[10]. This reaction was duplicated in various condions. The compound, m. p. 236°C, was obtained which was identical with the one previously obtained. However, it became clear that this compound is, in fact, 3, 3′-ditropolonyl disulfide (XV)[4]. It is considered that this reaction proceeds through the initial formation of thio ether XVI followed by its decomposition to acetamide and 3-mercaptotropolone, which is oxidized to XV as is depicted below[11].

The reaction of thiourea with isomeric methyl



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[7] A. W. Johnson and M. Tisler, *J. Chem. Soc.*, **1955**, 1841.

[8] Cf. Y. Ikegami, *Kagaku-no-Ryoiki, Extra*, No. **38**, 33 (1959).

[9] Cf. T. Nozoe, "Non-Benzenoid Aromatic Compounds", Ed. by D. Ginsburg, Interscience Publishers, Inc., New York (1959), p. 339.

[10] K. Matsui, *Sci. Repts. Tohoku Univ., First Ser.*, **43**, 223 (1959).

[11] 3-Mercaptotropolone has not been obtained due to its facile oxidation to give the corresponding disulfide under neutral or acidic conditions (cf. Ref. 4).

ethers obtained from 3-bromotropolone was attempted. Heating of 2-bromo-7-methoxytropone with thiourea in ethanol gave yellow needles (XVII), m. p. 152°C. By the same way, pale yellow needles (XVIII), m. p. 108°C, were obtained from 3-bromo-2-methoxytropone. From the fact that original bromomethoxytropones were obtained by treatment of these products with silver nitrate and their ultraviolet spectra resemble those of original tropones, together with their analyses, it is concluded that XVII is a molecular compound of 2-bromo-7-methoxytropone and thiourea with a ratio of 2 : 1, and XVIII is 1 : 1 molecular compound of 3-bromo-2-methoxytropone and thiourea. These molecular compounds are quite stable and always only products obtained from the above-menthioned reactions under more severe conditions.

Experimental*

2-Phenylthiazolo[4, 5-b]tropone (VI).—a) To a sodium ethoxide solution prepared from sodium (51.7 mg.) and anhydrous ethanol (15 ml.), 2-mercaptotropone (IV) (310 mg.) and 2-amino-3-bromotropone (III) (300 mg.) were added, and the mixture was heated in a sealed tube at 125°C for 10 hr. After cooling, the precipitate was filtered off, the solvent was removed from the filtrate in vacuo. To the dark oily residue, water (50 ml.) was added, adjusted to slightly alkaline and extracted with chloroform. Recrystallization from benzene of the crude crystals (159 mg.) obtained from the extract afforded yellow prisms (VI), m. p. 182∼183°C.

Found: C, 70.02; H, 3.77; N, 5.56. Calcd. for $C_{14}H_9ONS$: C, 70.29; H, 3.79; N, 5.86%.

UV: $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 233 (4.29), 252 (4.37), 273 (4.29), 363 (4.16), 380 (4.13).

2,4-Dinitrophenylhydrazone; violet needles, m. p. 251°C.

Found: C, 57.18; H, 2.87; N, 16.37. Calcd. for $C_{20}H_{13}O_4N_5S$: C, 57.28; H, 3.12; N, 16.70%.

b) To a solution of sodium (26 mg.) in anhydrous ethanol (10 ml.), III (150 mg.) and thiobenzoic acid (155 mg.) were added and the mixture was treated in the same way as in a). Sixty milligrams of yellow prisms obtained showed no depression of the melting point on admixture with VI obtained by method a) and their ultraviolet and infrared spectra were identical.

2 (3′-Isopropylphenyl)-thiazolo [4, 5-b] tropone (XII).—a) Heating of a solution of III (300 mg.) and 6-isopropyl-2-mercaptotropone (IX) (405 mg.) in a sodium ethoxide solution prepared from 57 mg. of sodium and 15 ml. of ethanol in a sealed tube at 110°C for 10 hr., followed by the same procedure described in the preceeding section yielded 227 mg. of yellow prisms (XII) (from acetone), m. p. 141∼142°C.

Found: C, 72.51; H, 5.09; N, 4.85. Calcd. for $C_{17}H_{15}ONS$: C, 72.58; H, 5.37; N, 4.98%.

UV: $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 235 (4.35), 256 (4.35), 275 (4.29), 365 (4.19), 380 (4.15).

2, 4-Dinitrophenylhydrazone; violet needles, m. p. 218°C.

Found: C, 60.15; H, 3.93; N, 15.02. Calcd. for $C_{23}H_{19}O_4N_5S$: C, 59.87; H, 4.15; N, 15.18%.

b) The reaction of III (300 mg.) and 4-isopropyl-2-mercaptotropone (X) (405 mg.) according to the above mentioned procedure afforded 265 mg. of yellow prisms, m. p. 142°C, which is identical with XII (mixed melting point, and ultraviolet and infrared spectra).

6-Isopropyl-2-phenylthiazolo[4,5-b]tropone (VIII).—The reaction of IV (857 mg.) and 2-amino-3-bromo-6-isopropyltropone (VII) (752 mg.) in ethanol contained 143 mg. of sodium followed by the above-mentioned procedure resulted in 300 mg. of yellow plates (XIII), m. p. 144∼145°C.

Found: C, 72.89; H, 5.59; N, 4.82. Calcd. for $C_{17}H_{15}ONS$: C, 72.58; H, 5.37; N, 4.98%.

UV: $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 253 (4.45), 275 (4.38), 359 (4.16), 375 (4.10).

2, 4-Dinitrophenylhydrazone; violet needles, m. p. 259°C.

Found: C, 59.61; H, 3.95; N, 15.14. Calcd. for $C_{23}H_{19}O_4N_5S$: C, 59.87; H, 4.15; N, 15.18%.

2-Amino-3-bromo-6-isopropyltropone (VII).—After a solution of 3-bromo-6-isopropyl-2-methoxytropone (1.16 g.) in liquid ammonia (20 ml.) was allowed to stand at room temperature for 3 days, ammonia was evaporated, the residual yellow oil was dissolved in chloroform, washed with water, dried (sodium sulfate) and passed through an alumina column, and 812 mg. of yellow oil was obtained, which was crystallized by adding ethanol. Recrystallization from ethanol gave yellow crystals, m. p. about 35°C.

Found: C, 48.80; H, 4.69; N, 5.99. Calcd. for $C_{10}H_{12}ONBr$: C, 49.60; H, 4.99; N, 5.79%.

Reaction of 3-Bromotropolone with Thioacetamide.—a) A solution of 3-bromotropolone (600 mg.) and thioacetamide (600 mg.) in pyridine (12 ml.) was refluxed for 3.5 hr. To the residue left after removal of pyridine, water was added and the precipitate (484 mg.) was recrystallized from ethanol affording 3, 3′-ditropolonyl disulfide, m. p. 235°C, which was identified by the mixed melting point with authentic sample[4]).

b) A solution of sodium salt (300 mg.) of 3-bromotropolone and thioacetamide (250 mg.) in anhydrous pyridine (8 ml.) was heated in a sealed tube at 120°C for 3 hr., from which 127 mg. of 3, 3′-ditropolonyl disulfide was obtained.

Molecular Compounds (XVII and XVIII) of 3-Bromotropolone Methyl Ethers and Thiourea.—a) A solution of 2-bromo-7-methoxytropone (500 mg.) and thiourea (266 mg.) in ethanol (13 ml.) was refluxed for 1 hr. By cooling the mixture, yellow needles (432 mg.) were obtained and recrystallized from methanol giving yellow needles (XVII), m. p. 152°C.

Found: C, 40.27; H, 3.56; N, 5.58. Calcd. for $C_{17}H_{18}O_4N_2SBr_2$: C, 40.33; H, 3.66; N, 5.54%.

b) Heating of a solution of 3-bromo-2-methoxytropone (600 mg.) and thiourea (213 mg.) in ethanol

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* All melting points were not corrected.

(15 ml.) afforded XVIII (213 mg.) pale yellow needles, m. p. 108°C.

Found: C, 36.69; H, 3.71; N, 9.56. Calcd. for $C_9H_{11}O_2N_2SBr$: C, 37.13; H, 3.81; N, 9.63%.

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