The Mannich Base of Troponoid and its Application. IX. Reaction of 3-Bromo-5-formyl-7-isopropyltropolone

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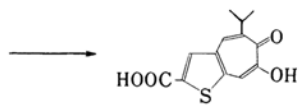
It has been found that alkaline treatment of 3-bromo-7-isopropyltropolon-5-ylmethylenerhodanine (II) obtained by the reaction of 3-bromo-5-formyl-7-isopropyltropolone (I) and rhodanine resulted in the abnormal intramolecular attack of sulfide anion at the 4-position of the tropolone ring with the liberation of the bromide ion from the 3-position to give thieno [2, 3-d] tropolone derivative III[1].

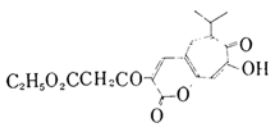
(I) (II)



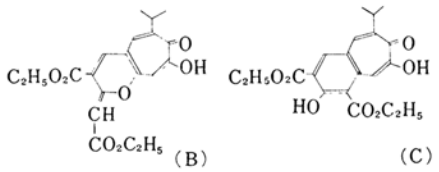
(III)

In order to make further extension of such an abnormal cyclization, some reactions of aldehyde I were studied.

Treatment of I with diethyl acetonedicarboxylate in the presence of piperidine gave colorless needles of m. p. 215°C (IV), corresponding to the molecular formula of $C_{20}H_{22}O_7$. The fact that the bromide ion was liberated in this reaction suggested that IV was not a simple condensation product, but a cyclization product formed by the condensation followed by such an abnormal intramolecular substitution as in the case of thienotropolone derivative III. According to the manner of the intramolecular attack, three structures (A, B and C) are expected for IV, while structure A must be excluded by the analytical values of IV. The ultraviolet absorption spectrum of IV is similar to those of 4, 5-benzotropolone and its derivatives[2], and its infrared spectrum shows absorptions for the hydroxyl group at 3280 cm^{-1} and for the carbonyl group at 1727 and 1680 cm^{-1}. Furthermore it shows absorptions at 1638, 1587, 1538 and 1468 cm^{-1} which agree well with absorption bands of 4, 5-benzotropolone reported by Tarbell et al.[3] These facts show that IV is 1′, 3′-diethoxycarbonyl-2′-hydroxy-3-isopropyl-4, 5-benzotropolone (C). Treatment of IV with alkali gave dicarboxylic acid V, whose ultraviolet spectrum was shown in Fig. 1.



(A)



(B) (C)

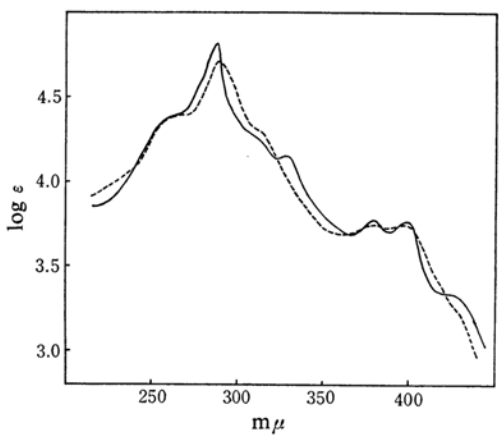
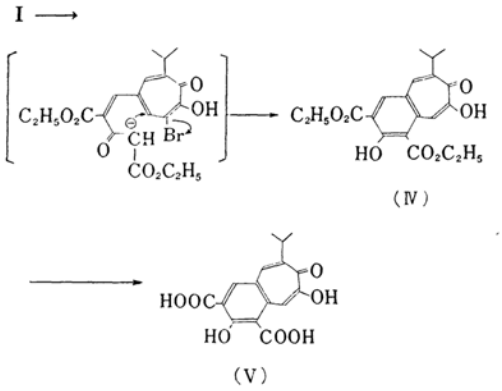


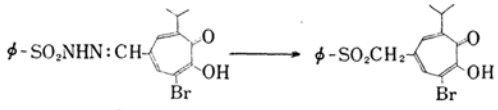
Fig. 1. Ultraviolet spectra of IV (——) and V (·····) in methanol.

Although it was expected that pyrazolotropolone derivative would be obtained by the action of alkali on tosylhydrazone VI, the cyclization did not occur, but 3-bromo-7-isopropyltropolon-5-ylmethyl *p*-tolyl sulfone

1) K. Ogura, This Bulletin, **35**, 808 (1962).
2) H. Fernholz, E. Hartwig and J. C. Salfeld, *Ann.*, **576**, 131 (1952).
3) D. S. Tarbell, G. P. Scott and A. D. Kemp, *J. Am. Chem. Soc.*, **72**, 379 (1950).



(VII) was obtained. It seems to have been formed in the same manner as known in the case of benzaldehyde tosylhydrazone[4].



$\phi = p$-tolyl

Finally for the synthesis of thiazinotropolone derivative the reaction of I with thiourea in the presence of pyridine was examined, and the product corresponding to the molecular formula of $C_{11}H_{12}O_3$ (VIII) was obtained. Its infrared spectrum shows an absorption at 1688 cm^{-1} due to a carbonyl group, and other absorptions expect those in the finger print region agree well with those of I. The ultraviolet spectrum is also similar to that of I. These facts suggest that VIII should be 3-isopropyl-5-formyltropolone formed by debromination of I. In order to make this problem more clear the reaction of 3, 7-dibromotropolone with thiourea in the presence of pyridine was examined, and it was found that the

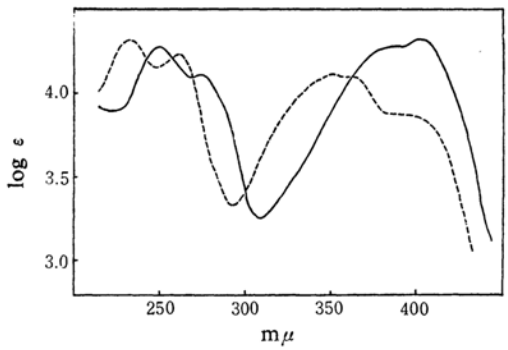
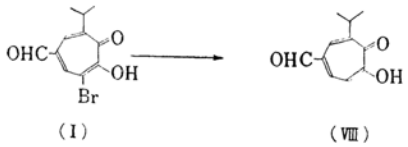


Fig. 2. Ultraviolet spectra of I (——) and VIII (·····) in methanol.

4) W. R. Barmford and T. S. Stevens, *J. Chem. Soc.*, 1952, 4735.



debromination occurred to give 3-bromotropolone in a low yield.

Experimental*

1', 3'-Diethoxycarbonyl-2'-hydroxy-3-isopropyl-4, 5-benzotropolone (IV).—A mixture of I (100 mg.), diethyl acetonedicarboxylate (120 mg.) and piperidine (30 mg.) was refluxed for 7 hr., and then cooled to room temperature. Colorless needles (10 mg.) of IV which precipitated on being cooled were collected. The filtrate was refluxed, with 30 mg. of piperidine further added, for 1 hr., and the solvent was removed to dryness. Addition of a small amount of water and methanol to the resinous residue caused to solidify. The solid thereby formed was collected and recrystallized from ethanol to afford colorless needles of IV (5 mg.), m. p. 213~215°C. λ_{max}^{MeOH} mμ (log ε) : 288 (4.82), 330 (4.16), 380 (3.78), 400 (3.77).

Found : C, 64.15 ; H, 6.19. Calcd. for $C_{20}H_{22}O_7$: C, 64.16 ; H, 5.92%.

1', 3'-Dicarboxy-2'-hydroxy-3-isopropyl-4, 5-benzotropolone (V).—After IV (30 mg.) was heated in aqueous potassium hydroxide solution (potassium hydroxide, 15 mg. ; water, 0.2 ml.) in a water bath for 1 hr., the solution was neutralized with hydrochloric acid (pH, 3~4). The mixture was extracted by ether. The evaporation of the ether from the extract left pale yellow powder, which was collected, washed with water and recrystallized from methanol to afford colorless crystals, m. p. 270~275°C (decomp.). Yield, 10 mg. λ_{max}^{MeOH} mμ (log ε) : 290 (4.72), 380 (3.75), 398 (3.75).

Found : C, 59.39 ; H, 4.71. Calcd. for $C_{16}H_{14}O_7$: C, 60.38 ; H, 4.43%.

3-Bromo-5-formyl-7-isopropyltropolone *p*-Tosylhydrazone (VI).—A solution of I (100 mg.) and *p*-tolylsulfonylhydrazide (60 mg.) in methanol (1 ml.) was refluxed for 15 min., and then cooled to room temperature. Yellow crystals that separated were collected and recrystallized from ethanol to give yellow granular crystals, m. p. 165~166°C. Yield, 120 mg.

Found : C, 47.36 ; H, 4.31 ; N, 6.32. Calcd. for $C_{18}H_{19}O_4N_2$ $SBr \cdot H_2O$: C, 47.28 ; H, 4.63 ; N, 6.13%.

3-Bromo-7-isopropyltropolon-5-ylmethyl *p*-Tolyl Sulfone (VII).—A solution of VI (100 mg.) and piperidine (30 mg.) in ethanol (1.5 ml.) was refluxed for 4 hr. The evaporation of the ethanol left yellow oily residue, which was solidified by addition of a few drops of 6 N hydrochloric acid and 1 ml. of methanol. The solid was collected and recrystallized from methanol to afford colorless needles,

* All melting points are uncorrected. The microanalyses were carried out by Miss Yoko Endo and Miss Yukiko Endo of this Institute, to whom the present author wishes to express his gratitude.

m. p. 162~164°C. Yield, 20 mg. λ_{max}^{MeOH} mμ (log ε): 277 (4.23), 265 (4.50), 345 (4.00), 413 (3.76).

Found: C, 52.52; H, 4.69. Calcd. for $C_{18}H_{19}O_4SBr$: C, 52.57; H, 4.66%.

3-Isopropyl-5-formyltropolone (VIII).—A mixture of I (130 mg.) and thiourea (40 mg.) in pyridine (1 ml.) was warmed in a water bath for 1.5 hr., by which the whole dissolved to form a black solution. After the removal of pyridine dilute hydrochloric acid was added to the residue and the precipitate was collected, washed with water and recrystallized from benzene to form pale yellow granular crystals, which was further purified by sublimation in reduced pressure, m. p. 107~109°C. Yield, 20 mg. λ_{max}^{MeOH} mμ (log ε): 233 (4.31), 262 (4.23), 351 (4.10), 390 (3.88).

Found: C, 66.55; H, 5.92. Calcd. for $C_{11}H_{12}O_3 \cdot 1/2H_2O$: C, 66.65; H, 6.32%.

Reaction of 3, 7-Dibromotropolone and Thiourea.—A mixture of 3, 7-dibromotropolone (100 mg.) and thiourea (30 mg.) in pyridine (1 ml.) was heated in a water bath for 2 hr., by which the whole dissolved to form a dark red solution. The pyridine was evaporated, 6 N hydrochloric acid (0.5 ml.) was added to the residue, and the brown precipitate so formed was collected. The solid was warmed in benzene and the mixture was filtered. The evaporation of the benzene left pale yellow powder, whose sublimation in reduced pressure afforded a trace of 3-bromotropolone.

The author wishes to express his deep gratitude to Professor Shuichi Seto for his kind guidance and encouragement throughout this work, and to Dr. Yusaku Ikegami and Dr. Shingo Matsumura for their helpful advice. 3-Isopropyltropolone was graciously furnished by the Takasago Perfumery Co., Ltd., and a part of the expenses was defrayed by Sankyo Co., Ltd., to whom the author is deeply indebted.

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