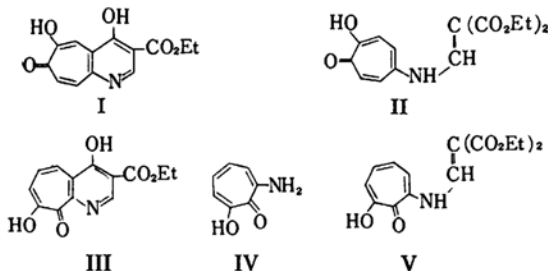


A Ring-Chain Tautomerism in the Reaction Products of 3-Aminotropolone and Some Ethoxymethyleneacetates¹⁾

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(Received April 11, 1960)

Slack and Attridge²⁾ reported the synthesis of a pyridotropolone (I) by application of the Gould-Jacobs' quinoline synthetic method³⁾ involving a process of pyrolysis of 5-(β , β -diethoxycarbonylvinylamino)tropolone (II), a condensation product of 5-aminotropolone and ethyl ethoxymethylenemalonate. This kind of synthetic method of pyridotropolones has also been applied to the other 5-aminotropolone derivatives⁴⁾ and 4-aminotropolone⁵⁾.



In the present series of experiment an attempt was made to prepare a pyridotropolone (III) by application of the similar synthetic method to 3-aminotropolone (IV). Although this objective was not accomplished unfortunately, other interesting observations were made, which are described in this paper.

When 3-aminotropolone (IV) and ethyl ethoxymethylenemalonate were heated, a yellow condensation product of m. p. 138°C was formed in a good yield. Its analytical data agreed with those calculated for the anticipated diethoxycarbonylvinylaminotropolone (V). The ultraviolet absorption spectrum (Fig. 1) of the condensation product seemed to be fairly reasonable for the expected structure V, if the tropolone nucleus and the α , β -unsaturated ester system were to interact through the

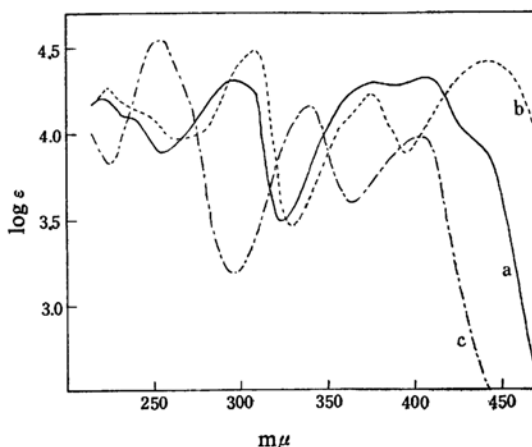


Fig. 1. Ultraviolet absorption spectra.

- a) VIII in methanol
b) VIII in 0.01 N sodium hydroxide
c) IV in methanol

intermediate nitrogen atom.

However, it has been found that pyrolysis of the above condensation product resulted in formation of not the anticipated pyridotropolone (III) but of another curious substances. Thus, on being heated at 250°C without a solvent, the condensation product afforded oxazolo[5:4-b]tropone* (VI) and ethyl malonate. The structure of the former VI was supported from its analytical values, determination of the molecular weight, and the close resemblance of its ultraviolet absorption curve (Fig. 2) to that of the known 2-methyloxazolo[5:4-b]tropone⁶⁾ (VII). Ethyl malonate was identified as its dianilide⁷⁾.

The foregoing finding makes doubtful the assumption that the condensation product of the aminotropolone and ethoxymethylenemalonate may possess a structure like V. Virtually, the condensation product did not show any coloration with alcoholic ferric chloride and was inert to the action of diazomethane, the facts of which do not give

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1) This work in part was presented at the Local Meeting of the Chemical Society of Japan, Yonezawa, June, 1956.

2) R. Slack and C. F. Attridge, *Chem. & Ind.*, 1952, 471.

3) R. G. Gould and W. A. Jacobs, *J. Am. Chem. Soc.*, 61, 2890 (1939).

4) K. Yamane, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, 80, 75 (1959).

5) K. Doi, *Bull. Chem. Research Inst. Non-Aqueous Solns., Tohoku Univ.*, 9, 19 (1959).

6) Y. Kitahara, *Science Repts. Tohoku Univ., Ser. I*, 40, 83 (1956).

* Very recently the same authors have reported the another syntheses and some reactions of the oxazotropone (VI). [*This Bulletin*, 34, 312 (1961)].

7) M. Freund, *Ber.*, 17, 134 (1884).

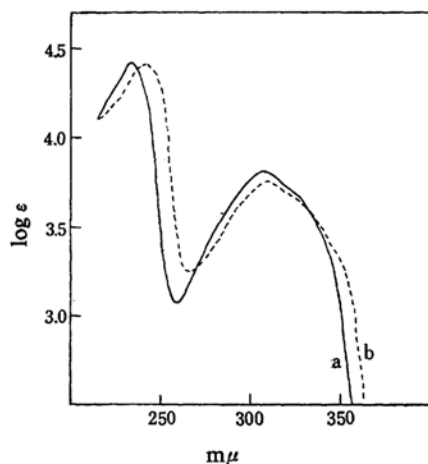
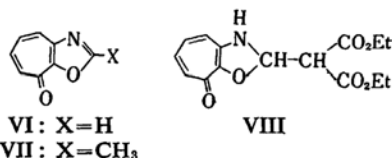


Fig. 2. Ultraviolet absorption spectra.

- a) VI in methanol
b) VII in methanol

enough explanation for the condensation product to be a diethoxycarbonylvinylaminotropolone (V).

From the above facts it seems more reasonable to consider that the condensation product has a dihydro-oxazolotrone structure VIII.

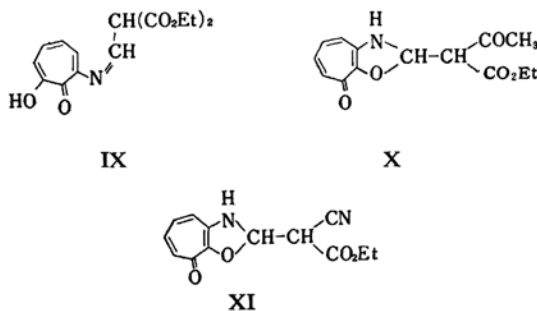


The ultraviolet absorption spectrum of VIII in an alkaline solution shows a red-shift in comparison to that in neutral solution, and this suggests that VIII results in ring-opening to V or IX in an alkaline solution (Fig. 1).

With aid to isolate the chain-isomer V or IX, the condensation product VIII was treated with ethanolic potassium hydroxide, neutralized carefully with dilute mineral acid, and subsequently extracted with chloroform. The fresh extract showed clearly a red coloration with ferric chloride, but the vacuum evaporation of the solvent resulted not in formation of the expected chain-isomer but in recovering of the raw material.

In the condensation reaction of 3-aminotropolone and ethoxymethylenemalonate, it is considered that the anticipated diethoxycarbonylvinylaminotropolone (V) or its isomeric azomethine derivative IX produces at first and spontaneously isomerizes to the ring-isomer VIII. It seems to leave no room for doubt, at any rate, that the condensation product of the aminotropolone and ethoxymethylenemalonate exists in the ring-form of VIII in a neutral state and that it exists in the chain-

form of V or IX in an alkaline medium. That the ultraviolet absorption of VIII in methanol solution has maxima in the comparatively longer wavelength regions indicates probably, though not any evidences have been obtained, that VIII is ring-opening to V or IX at least in the condition of the spectral measurement.



On being heated with ethyl ethoxymethylenecyanoacetate and ethoxymethylenecyanoacetate in place of ethoxymethylenemalonate, 3-aminotropolone (IV) gave readily a condensation product, 2-(*o*-acetyl-*o*-ethoxy-carbonylmethyl)-2,3-dihydrooxazolo[5:4-b]-tropone⁸⁾ (X) and 2-(*o*-ethoxycarbonyl-*o*-cyanomethyl)-2,3-dihydrooxazolo[5:4-b]tropone (XI), respectively. The structures of these compounds were reasonably supported by the similarities of their ultraviolet absorptions (Fig. 3) to that of VIII and by the formation of the oxazolotrone (VI) by their pyrolysis.

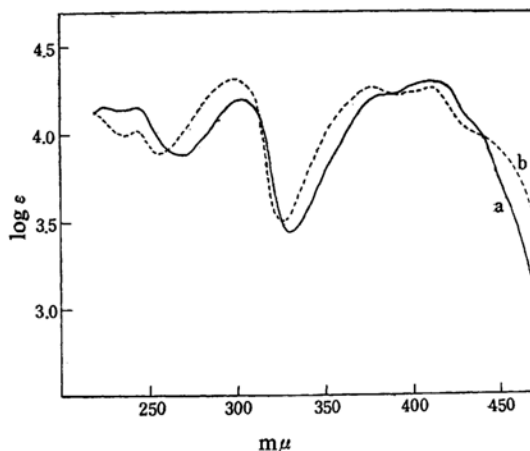


Fig. 3. Ultraviolet absorption spectra.

- a) X in methanol
b) XI in methanol

The authors have found that the condensation products of *o*-aminophenol and the above three ethoxymethyleneacetates are also of the

8) Since the description of this work was completed, K. Yamane, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **81**, 509 (1960), have reported the synthesis of X by the same sequence.

cyclic structures of the corresponding benzoxazolines, the results of which will be described in the following paper.

Experimental

The ultraviolet absorptions were determined in methanol solution, unless otherwise stated, with a Beckman model DU spectrophotometer.

2-(ω , ω -Diethoxycarbonylmethyl)-2, 3-dihydro-oxazolo[5:4-b]tropone (VIII).—A mixture of 3-aminotropolone (IV, 1.0 g.) and ethyl ethoxymethylenemalonate (1.7 g.) was heated on an oil bath at 130°C for 30 min. After being cooled at room temperature, the residual solid was recrystallized from ethanol to give the dihydrooxazolotrope (VIII) as yellow leaflets, m. p. 138°C, in nearly quantitative yield.

Found: C, 58.60; H, 5.67; N, 5.05. Calcd. for $C_{15}H_{17}O_5N$: C, 58.63; H, 5.58; N, 4.56%. $\lambda_{\max}^{\text{m}\mu}(\log \epsilon)$: in methanol, 220 (4.33), 295 (4.44), 381 (4.45), 408 (4.45); in 0.01 N sodium hydroxide, 225 (4.34), 310 (4.56), 377 (4.31), 442 (4.49).

The condensation product VIII did not show any coloration with alcoholic ferric chloride and remained inert to the action of diazomethane.

A mixture of VIII (0.3 g.), methanol (10 ml.), sodium hydroxide (0.4 g.) and water (5 ml.) was heated on a water bath at 50°C for 30 min. The orange solution so formed was cooled, neutralized cautiously with dilute hydrochloric acid, and then extracted with chloroform. The extract showed red coloration with ferric chloride, but its evaporation of the solvent under reduced pressure left only starting material VIII.

Oxazolo[5:4-b]tropone (VI).—VIII (1.45 g.) was placed in a Claisen flask of small capacity and heated on an oil bath at 230°C for 30 min. Colorless liquid (0.1 g.), which distilled out at 197–199°C and smelled like ethyl malonate, was collected. On being heated at 150°C with excess of aniline, it gave malonic dianilide, m. p. 275°C, undepressed on admixture with an authentic specimen⁹. The distilled residue, after extraction with warm benzene and subsequent evaporation of the solvent, crystallized from cyclohexane to give oxazolotrope (VI, 0.6 g.) as pale yellow prisms, m. p. 151–152°C.

Found: C, 65.60; H, 3.90; N, 9.40; mol. wt.

(Rast), 146. Calcd. for $C_8H_5O_2N$: C, 65.30; H, 3.43; N, 9.52%; mol. wt., 147. $\lambda_{\max}^{\text{MeOH}} \text{m}\mu(\log \epsilon)$: 235 (4.42), 305 (3.80).

2-(ω -Acetyl- ω -ethoxycarbonylmethyl)-2,3-dihydro-oxazolo[5:4-b]tropone (X).—A mixture of the aminotropolone (0.7 g.) and ethyl ethoxymethylenacetate⁹ (0.9 g.) was heated at 130°C for 30 min. and the residual solid was crystallized from ethanol to give dihydrooxazolotrope (X) as yellow prisms, m. p. 136°C, in a nearly quantitative yield.

Found: C, 60.69; H, 5.42; N, 5.34. Calcd. for $C_{13}H_{15}O_5N$: C, 60.64; H, 5.45; N, 5.05%. $\lambda_{\max}^{\text{MeOH}} \text{m}\mu(\log \epsilon)$: 245 (4.30), 303 (4.35), 415 (4.45).

Pyrolysis of the product (X, 0.54 g.) at 250°C for 30 min. afforded the oxazolotrope (VI, 0.15 g.) and ethyl acetoacetate (50 mg.), identified as its anilide¹⁰.

2-(ω -Ethoxycarbonyl- ω -cyanomethyl)-2,3-dihydro-oxazolo[5:4-b]tropone (XI).—A mixture of the aminotropolone (140 mg.) and ethyl ethoxymethylenecyanoacetate¹¹ (170 mg.) was heated at 130°C for 30 min. and the residual solid was crystallized from methanol to give the condensation product (XI) as yellow needles, m. p. 182°C, in nearly quantitative yield.

Found: C, 60.06; H, 4.87; N, 10.86. Calcd. for $C_{13}H_{12}O_4N_2$: C, 59.99; H, 4.64; N, 10.77%. $\lambda_{\max}^{\text{MeOH}} \text{m}\mu(\log \epsilon)$: 245 (4.11), 300 (4.41), 378 (4.35), 410 (4.35).

Pyrolysis of XI (0.54 g.) as above described afforded also the oxazolotrope (VI, 0.2 g.) and ethyl cyanoacetate (50 mg.), identified as its amide¹².

The authors express their gratitude to Messrs. S. Ohyama, K. Kato, A. Iwanaga and S. Azumi for microanalyses.

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9) L. Claisen, *Ann.*, **297**, 16 (1897).

10) L. Knorr, *ibid.*, **236**, 75 (1886).

11) M. E. G. deBollefont, *Bull. soc. chim. France*, [3] **25**, 20 (1901).

12) B. B. Corson, R. W. Scott and C. E. Vose, "Organic Syntheses," Coll. Vol. I, 173 (1932).