On Oxazolo[5 : 4-b] tropones[1]

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(Received August 29, 1960)

In the course of trying to prepare a pyridotropolone from 3-aminotropolone (I), it has been found that the condensation product of the aminotropolone and ethyl ethoxymethylenemalonate is not the anticipated vinylaminotropolone (II) but the dihydro-oxazolotropone (III), and that the latter III results in fission to form the oxazolotropone (IV) and ethyl malonate on pyrolysis[2]. An analogous observation has also been found in the

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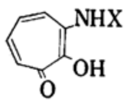
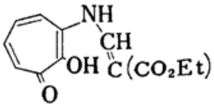
[1] This work in part was presented at the Tohoku Local Meeting of the Chemical Society of Japan, June, 1956.

[2] T. Nozoe, K. Doi and K. Kitahara, This Bulletin, to be published.

condensation product of *o*-aminophenol and ethoxymethylenemalonate³⁾. The structure of the oxazolotropone (IV) was elucidated, at that time, from the similarity of its ultraviolet absorption to that of 2-methyloxazolo[5 : 4-b]-tropone (V) which had been obtained from the reaction of the aminotropolone and acetic anhydride⁴⁾.



I: X=H
VI: X=CHO



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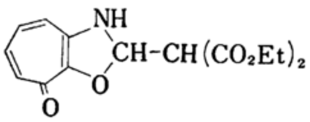
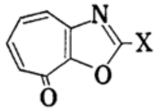


III

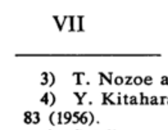


IV: X=H
V: X=CH_3

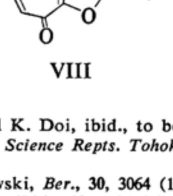
In this communication the present authors will deal with some reactions of the oxazolotropone (IV) and its derivatives, and with the condensation products of the aminotropolone and benzaldehydes in relation to the subject.

Oxazolo [5:4-b] tropone (IV) was also prepared readily by application of methods analogous to those used for the preparations of benzoxazole from *o*-aminophenol to the aminotropolone. Thus, IV was obtained easily on heating the aminotropolone and formamide⁵⁾ and on heating 3-formylaminotropolone (VI) in a sealed tube⁶⁾.

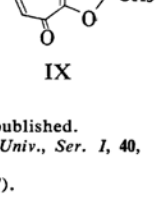
There have been known to date besides IV, the following oxazolotropones: 2-methyloxazolo-[5 : 4-b] tropone⁴⁾ (V) and its bromo derivatives, 2-methyloxazolo [4 : 5-b] tropone⁷⁾ (VII), and 2-methyloxazolo [5:4-b] benzo [d] tropone⁸⁾ (VIII). Recently preparations of 2-methyloxazolo [5 : 4-b] tropones from several diaminotropolones and acetic anhydride have been reported⁹⁾.



VII



VIII



IX

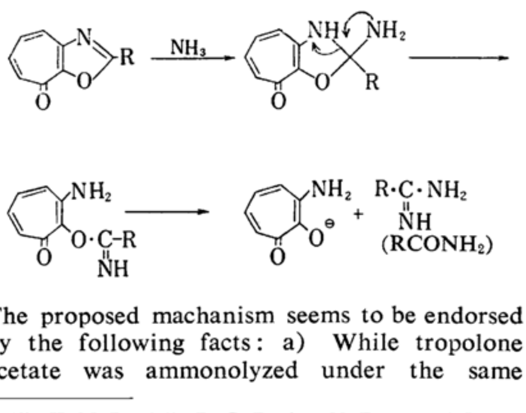
Nicholls and Tarbell⁸⁾ assigned the absorption maxima at 1617 and 1567 cm^{-1} in the infrared spectrum of VIII to the tropone carbonyl and the conjugated C=N stretching vibration, respectively. The oxazolotropone (IV) has maxima at 1635 and 1588 cm^{-1}, and has a further sharp maximum at 3120 cm^{-1}, which is probably considered to originate in the CH vibration of the oxazole ring of IV, because a corresponding absorption is absent in the 2-methyloxazolotropones (V, VII and VIII); benzoxazole has also a maximum at 3125 cm^{-1}, whereas 2-methylbenzoxazole lacks this absorption¹⁰⁾.

It had been reported that 3-amino-4-isopropyltropolone affords a monoacetate of m. p. 70.5~73°C on being heated with acetic anhydride¹¹⁾. This monoacetate, however, was found to be an oxazolotropone (IX) because of the close resemblance of its ultraviolet absorption to that²⁾ of IV.

Oxazolotropone (IV), similarly to benzoxazole, was readily hydrolyzed by dilute acid or alkali to form 3-aminotropolone (I). In either case, the formylaminotropolone (V) was not isolated as the intermediate of the reaction.

It has been known that tropolone methyl ethers react with liquid ammonia to give 2-aminotropones. Oxazolotropone (IV) is also regarded as a methyl ether analogue of tropolone and an examination, therefore, was directed to find a possibility of formation of 1, 3-diazaazulene derivative from IV.

When oxazolotropone (IV) was allowed to stand in liquid ammonia overnight, there was obtained the aminotropolone (I) as an ammonolysis product. The 2-methyloxazolotropone (V) resulted in formation of I and additional acetamide on being treated in the same way as the above. The reaction mechanism is probably interpreted as follows:



The proposed machanism seems to be endorsed by the following facts: a) While tropolone acetate was ammonolyzed under the same

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[3] T. Nozoe and K. Doi, ibid., to be published.

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

[5] S. Niementowski, *Ber.*, **30**, 3064 (1897).

[6] A. Ladenburg, ibid., **10**, 1124 (1877).

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

[8] C. A. Nicholls and D. S. Tarbell, *J. Am. Chem. Soc.*, **74**, 4935 (1951).

[9] T. Nozoe, Y. Kitahara, K. Doi and M. Takahashi, *Bull. Chem. Research Inst. Non-Aqueous Solns.*, Tohoku Univ., **9**, 7 (1959).

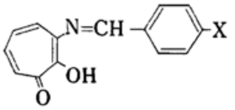
[10] H. M. Randall, R. G. Fowler, N. Fuson and J. R. Dangl, "Infrared Determination of Organic Molecules", Van Nostrand, New York (1949), p. 214.

[11] T. Nozoe, Y. Kitahare, E. Kunioka and K. Doi, *Proc. Japan Acad.*, 26, 38 (1950).

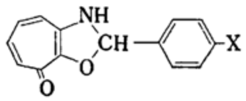
condition to give tropolone and acetamide, 3-acetylaminotropolone was recovered unreacted. b) While the dibenzoyl compound of the aminotropolone was also ammonolyzed readily to give the *N*-benzoylaminotropolone and benzamide under the same condition, the former was recovered likewise in an unreacted state. These facts suggest that the formation of *O*-acylated compound as an intermediate occurs in the respective reaction of the oxazolotropone and liquid ammonia. The cleavage of this kind of oxazole ring recalls the reaction of imino ethers and ammonia resulting in the formation of the corresponding alcohol and amidine[12].

In the subsequent papers[2,3], the authors are to discuss a ring-chain tautomerism between aromatic vinylamines possessing a hydroxyl group in the ortho position and oxazoline derivatives. According to Sachs and Brunetti[13], the reaction product of *o*-aminophenol and 2,4-dinitrobenzaldehyde exists in the form of 2-(2,4-dinitrophenyl)benzoxazoline in place of the expected 2,4-dinitrobenzylidene-*o*-aminophenol. It seems to be very interesting to find whether such a fact would also be applicable to the condensation products of the aminotropolone (I) and benzaldehydes.

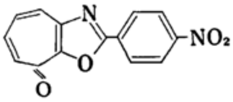
Unlike 5-aminotropolone[14], 3-aminotropolone (I) did not give any reaction product when heated with benzaldehyde. Even on being heated with more reactive *p*-nitrobenzaldehyde at 150°C for one hour, a condensation product was not obtained. This difficulty, however, was overcome easily by the use of caustic alkali in the reaction. When an equimolar mixture of the aminotropolone, respective benzaldehyde and sodium hydroxide was heated in methanol, the azomethine derivative (X, XI and XII) could be readily prepared. These products showed red coloration with ferric chloride test and hydrolyzed readily to form the aminotropolone (I) with water or aqueous alcohol. These facts mean that they do not exist in the form of their ring-tautomers of XIII. The same reaction of the aminotropolone and *p*-nitrobenzaldehyde afforded 2-(*p*-nitrophenyl)oxazolotropone (XIV), the structure of which was assumed from the fact that it agreed with a reaction product of the aminotropolone and *p*-nitrobenzoyl chloride.



X : X=H
XI : X=Cl
XII : X=OCH$_3$



XIII



XIV

While the reaction of the aminotropolone and benzoyl chloride in pyridine produced a mixture of the dibenzoylated and *N*-benzoylated compounds, the reaction of the aminotropolone and *p*-nitrobenzoyl chloride under the same condition resulted in the formation of the oxazolotropone (XIV), which showed no coloration with ferric chloride. An oxazole ring formation in the reaction with benzaldehydes or benzoyl chlorides seems to be more rapid in the case of the aminotropolone (I) than in the case of *o*-aminophenol[15].

Experimental

The ultraviolet absorptions were measured in methanol solution with a Beckman model DU spectrophotometer. The infrared absorption was measured on potassium bromide disk with a Perkin-Elmer model 21 infrared spectrometer, using a rock salt prism.

Oxazolo[5:4-b]tropone (IV).—a) 3-Aminotropolone (I, 0.28 g.) and formamide (1 ml.) was heated under reflux at 220°C. Benzene (2 ml.) was added to the reaction mixture at room temperature and the residual solid was collected. It gave IV (0.1 g.), m. p. and mixed m. p.[2] 150~151°C, after sublimation in vacuo following recrystallization from benzene. b) A mixture of the aminotropolone (I, 1.4 g.) and 80% formic acid (30 ml.) was heated under reflux for 3 hr. The evaporated residue of the solvent was crystallized from ethanol to give 3-formylaminotropolone (VI, 1.2 g.) as yellow prisms, m. p. 167~168°C (reported[4] m. p. 168~169°C). When VI (0.3 g.) in a sealed tube was heated on an oil bath of 250°C for 30 min., the oxazolotropone (IV, 0.1 g.) was obtained.

Hydrolysis of the Oxazolotropone (IV).—A mixture of IV (30 mg.) and 3 N hydrochloric acid (1 ml.) or 2 N sodium hydroxide (1 ml.) was heated at 50°C for 30 min. Neutralization of the reaction mixture gave 3-aminotropolone (I), m. p. and mixed[4] m. p. 97~98°C.

2-Methyl-4-isopropyloxazolo[5:4-b]tropone (IX).—A mixture of 3-amino-4-isopropyltropolone[11] (30 mg.) and acetic anhydride (1 ml.) was heated under reflux for one hour. The evaporated residue of the solvent, after sublimation in vacuo following crystallization from petroleum ether (b. p. 40~60°C), gave the oxazolotropone (IX) as colorless prisms, undepressed on admixture with an authentic sample which had been reported[11] to be a monoacetate of the aminotropolone.

Found: C, 69.82; H, 6.21; N, 7.35. Calcd. for $C_{11}H_{11}O_2N$: C, 69.82; H, 5.86; N, 7.40%. $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 245 (4.51), 320 (3.91)

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[12] J. Houben et al., *J. prakt. Chem.*, **105**, 12 (1922).

[13] F. Sachs and W. Brunetti, *Ber.*, **40**, 3230 (1907).

[14] T. Nozoe, S. Seto et al., *Proc. Japan Acad.*, **27**, 426 (1951).

[15] R. D. Desai, *J. Chem. Soc.*, **1934**, 1186.

Ammonolysis of the Oxazolotropone (IV).—A solution of IV (0.7 g.) in liquid ammonia (50 ml.) was allowed to stand in a pressure bottle for 24 hr. at room temperature. Ammonia was allowed to evaporate, the residue was washed out with methanol (50 ml.), and the evaporated residue of the solvent was crystallized from benzene to give the aminotropolone (I, 0.53 g.).

Ammonolysis of the 2-Methyloxazolotropone(V).—A solution of V (0.5 g.) in liquid ammonia (50 ml.) was allowed to stand for 3 days at room temperature. The residual solid of evaporation of ammonia, afer recrystallization from dilute methanol, afforded the aminotropolone (I, 0.3 g.). The evaporated residue of the mother-liquor, after chromatographic purification (alumina—benzene) following crystallization from petroleum ether (b. p. 40~60°C), gave acetamide (50 mg.) of m. p. 80~81°C.

Ammonolysis of Tropolone Acetate.—A solution of tropolone acetate (0.4 g.), which prepared according to Doering's description[16], in liquid ammonia (40 ml.) was allowed to stand overnight at room temperature. The evaporated residue of ammonia was dissolved in water, the residual solution was acidified with dilute hydrochloric acid, and extracted with chloroform (20 ml.). The extract, after re-extraction with dilute alkali followed by evaporation in vacuo, gave acetamide (50 mg.). The alkaline extract, after acidification with dilute hydrochloric acid, and after being extracted with chloroform and subsequent evaporation of the solvent, gave tropolone (0.27 g.). The result similar to the above has been recently reported by Sato[17]. An experiment on ammonolysis of 3-acetylaminotropolone under the same condition ended in the recovery of unreacted material.

Condensation of 3-Aminotropolone (I) and Benzaldehydes.—To a solution of I (0.28 g.), respective benzaldehyde (0.02 mol.) and methanol (5 ml.), was added a solution of sodium hydroxide (80 mg.) in water (0.5 ml.), and the mixture was heated under reflux for 30 min. Then the reaction mixture was diluted with water (10 ml.), neutralized with acetic acid, and extracted with chloroform (30 ml.). The evaporated residue of the solvent was crystallized from a suitable solvent to give:

3-Benzylideneaminotropolone (X): yellow leaflets (chloroform), m. p. 142~143°C,

Found: N, 6.19. Calcd. for $C_{14}H_{11}O_2N$: N, 6.22%.

3-p-Chlorobenzylideneaminotropolone (XI): yellow prisms (chloroform), m. p. 124~125°C,

Found: N, 5.68. Calcd. for $C_{14}H_{10}O_2NCl$: N, 5.40%.

3-Anisylideneaminotropolone (XII): yellow prisms (benzene), m. p. 110~111°C.

Found: N, 5.34. Calcd. for $C_{15}H_{13}O_3N$: N, 5.49%.

All of the three reaction products showed red coloration with alcoholic ferric chloride and hydrolyzed easily to form the aminotropolone (I) on being shaken with water or aqueous alcohol.

2-*p*-Nitrophenyloxazolo[5 : 4-b]tropone (XIV).—a) A solution of sodium hydroxide (0.1 g.) in water (0.5 ml.) was added to a solution of the aminotropolone (I, 0.35 g.), *p*-nitrobenzaldehyde (0.4 g.) and methanol (5 ml.), and heated under reflux for 30 min. The reaction mixture, treated as above, afforded the oxazolotropone (XIV, 0.2 g.) as yellow needles, m. p. 251~252°C. It did not show any coloration with ferric chloride.

Found: C, 62.69; H, 3.01; N, 10.45. Calcd. for $C_{14}H_8O_4N_2$: C, 62.69; H, 3.12; N, 10.51%. $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 265 (4.44), 374 (4.06).

b) A mixture of the aminotropolone (0.14 g.), *p*-nitrobenzoyl chloride (0.19 g.), and pyridine (4 ml.) was stirred for one hour at room temperature. It was then diluted with water (10 ml.) and the residual solid was collected. Recrystallization of it from nitrobenzene gave the above XIV, m. p. and mixed m. p. 251~252°C.

Benzoylation of 3-Aminotropolone (I).—A solution of I (0.14 g.), benzoyl chloride (0.14 g.) and pyridine (2 ml.) was stirred for 20 min. at room temperature, then diluted with water (10 ml.), and the residual solid (0.19 g.) of m. p. 150~152°C, was collected. Its fractional recrystallization from a mixture of benzene and methanol afforded 3-benzoylaminotropolone benzoate from the less soluble portion, and 3-benzoylaminotropolone from the more soluble portion,

3-Benzoylaminotropolone Benzoate: pale yellow leaflets, m. p. 174°C, which showed no coloration with ferric chloride.

Found: C, 73.29; H, 4.40; N, 4.07. Calcd. for $C_{21}H_{15}O_4N$: C, 73.29; H, 4.38; N, 4.06%.

3-Benzoylaminotropolone: pale yellow needles, m.p. 146°C, which showed red coloration with ferric chloride.

Found: C, 69.62; H, 4.72; N, 6.00. Calcd. for $C_{14}H_{11}O_3N$: C, 69.70; H, 4.59; N, 5.80%.

When a mixture of the dibenzoylated compound (0.5 g.) and liquid ammonia (60 ml.) was allowed to stand for 7 days at room temperature, 3-benzoylaminotropolone and benzamide were obtained by treatment similar to the above description.

The authors express their gratitude to Messrs. K. Kato, S. Ohyama, A. Iwanaga and S. Azumi for microanalyses, and to Mr. Y. Ikegami for the infrared spectral measurement.

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[16] W. von E. Doering and L. H. Knox, *J. Am. Chem. Soc.*, **73**, 828 (1951).

[17] T. Sato, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **80**, 1058 (1959).