*The Schmidt Reaction in Some Tropolone Derivatives**

By Kozo Doi

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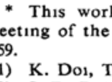
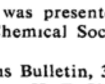
In the preceding paper[1] the author has described the syntheses of 4-aminotropolone (I) and its alkyl derivatives by the extended application of the elimination-addition mechanism involving a benzyne-type intermediate[2] to the tropolone field. As the general method for synthesizing 4-aminotropolones, however, this synthetic method, included amination of 3-iodotropolones with potassium amide in liquid ammonia, appeared to be still unsatisfactory in respect to the yield. Therefore attempts were made for the synthesis of 4-aminotropolones by application of the Schmidt reaction[3] to 4-isopropenyltropolone (β-dolabrin)[4] (II), 4-acetyltropolone[4] (III), and their derivatives.

Addition of both a solution of hydrazoic acid in chloroform and of sodium azide to a cold stirred solution of 4-acetyltropolone (III) in concentrated sulfuric acid resulted in instantaneous reaction to give 4-aminotropolone sulfate, having a composition of $C_7H_7O_2N\cdot1/2\,H_2SO_4\cdot H_2O$, instead of the anticipated acetylaminotropolone (IV). The desired aminotropolone (I) was readily obtained when this product was treated with sodium hydrogen carbonate. The use of excess hydrazoic acid in this reaction did not afford the tetrazole derivative, observed in the reactions with acetone and benzophenone[5]. The fact that 4-acetylaminotropolone (IV), which will be described in the subsequent paper[6], readily forms 4-aminotropolone sulfate on treatment with concentrated sulfuric acid makes it certain that IV arises as an intermediate in the reaction with III.


I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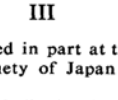
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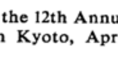
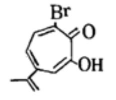

IV

It was reported that bromination of the isopropenyltropolone (II) with *N*-bromosuccinimide yielded 3-bromo-6-isopropenyltropolone[7,8] (V) and its oxidation with hydrogen peroxide in formic acid, followed by that with sodium periodate, afforded 6-acetyl-3-bromotropolone[7] (VI). Application of sodium azide to a concentrated sulfuric acid solution of VI produced the corresponding aminotropolone (VII), in which case the sulfate of VII was not obtained owing to the decreased basicity by the introduction of the bromine atom in the molecule.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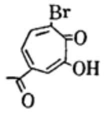
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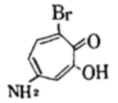
VII

Fig. 1 indicates the ultraviolet absorption of VII, which possesses a maximum at a longer wavelength region than in the case of I[1].

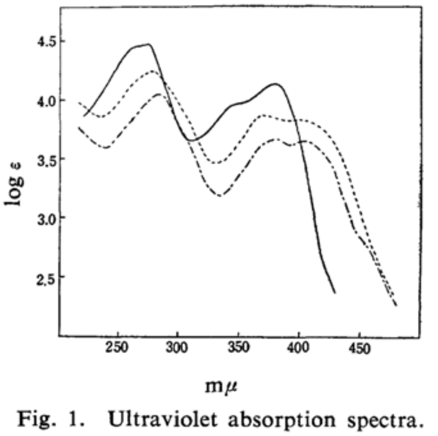

Fig. 1. Ultraviolet absorption spectra.

—— 6-Amino-3-bromotropolone (VII)
---- 4-Amino-5-nitrotropolone (X, log ε +0.2)
-·-·- 6-Amino-3-bromo-5-nitrotropolone (XI, log ε +0.4)

In order to obtain further derivatives of the aminotropolone, nitrations with fuming nitric acid were carried out on the acetyltropolones (III and VI). Thus, 4-acetyl-5-nitrotropolone

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* This work was presented in part at the 12th Annual Meeting of the Chemical Society of Japan Kyoto, April, 1959.

[1] K. Doi, This Bulletin, 34, 497 (1961).

[2] J. D. Roberts, H. E. Simmons, L. A. Carlsmith and C. W. Vaughan, *J. Am. Chem. Soc.*, 75, 3290 (1953); J. D. Roberts, D. A. Semenow, H. E. Simmons and L. A. Carlsmith, ibid., 78, 601 (1956).

[3] A review of the Schmidt reaction is given by H. Wolff, in "Organic Reactions", edited by R. Adams, Vol. III, p. 307, John Wiley and Sons, New York, N. Y. (1946).

[4] T. Nozoe, K. Takase and M. Ogata, *Chem. & Ind.*, 1957, 1070.

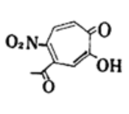
[5] K. F. Schmidt, *Ber.*, 57, 704 (1924).

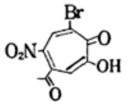
[6] K. Doi, This Bulletin, to be published.

[7] Y. Kitahara and M. Funamizu, unpublished work.

[8] K. Takase, T. Kusunose and T. Meguro, Abstracts of the 12th Annual Meeting of the Chemical Society of Japan, p. 232 (1959).

(VIII) and 6-acetyl-3-bromo-5-nitrotropolone (IX) were obtained from the respective compound. The positions of the nitro group in VIII and IX are supported from the similarity of their ultraviolet absorption spectra (Fig. 2) to that of 5-nitrotropolone[9]. It has been found that the presence of an alkyl group (especially isopropyl) in the 4-position of a tropolone effects preferential orientation of the nitro group towards the 3- or 7-position instead of the 5-position[10]. In spite of such a fact, nitration of III and VI, possessing a meta-directing acetyl group, has caused substitution of the nitro group into the adjacent position of the acetyl group. This means probably that the acetyl group is not in full conjugation with the tropolone ring. This conclusion is also supported reasonably from the fact that the absorption maximum at 437 mμ (log ε 4.42) in the longest wavelength of the ultraviolet spectrum of VIII is approximately the same value as that of 5-nitrotropolone, 435 mμ (log ε 4.41).


VIII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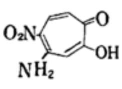
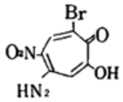

X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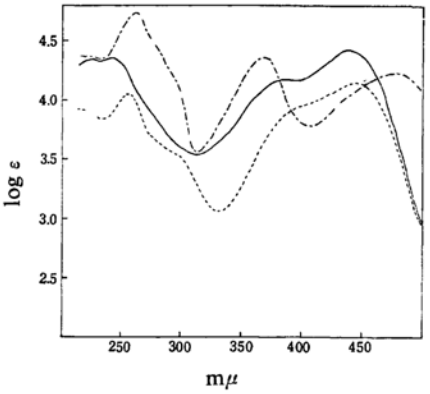
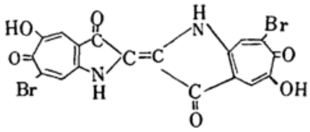


Fig. 2. Ultraviolet absorption spectra.

—— 4-Acetyl-5-nitrotropolone (VIII)
---- 6-Acetyl-3-bromo-5-nitrotropolone (IX, log ε +0.3)
-·- Indigo-type tropolone (XII)

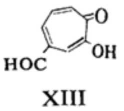
When treated with sodium azide in a concentrated sulfuric acid solution, the above nitroacetyltropolones (VIII and IX) also yielded 4-amino-5-nitrotropolone (X) and 6-amino-3-bromo-5-nitrotropolone (XI), respectively. Their ultraviolet absorptions, indicated in Fig. 1, show that an introduction of a bromine atom in the 3-position of I, VII and IX causes a red shift of the longest wavelength maximum by 13, 8 and 7 mμ respectively, the fact of which is in approximate agreement with the observation of Tsuboi[11].

Catalytic hydrogenation of the bromo-acetyltropolone (IX) over palladized charcoal was found to give instead of the expected debromination product (VIII) an orange red product, which had its ultraviolet maximum in a longer wavelength region than that of the starting compound (cf. Fig. 2). The infrared absorption of this reaction product shows peaks at 3350 (ν_{NH}) and 1648 cm^{-1} ($\nu_{C=O}$). It follows, therefore, that this hydrogenation product of IX is probably an indigo-type tropolone (XII),


XII

the conclusion of which appears to be supported by the fact that 5, 5′-dibromoindigo[12] has infrared peaks at 3300 (ν_{NH}) and 1634 ($\nu_{C=O}$) cm^{-1}.

It was found that the Schmidt reaction was applicable satisfactorily to also 4-formyltropolone (XIII). Thus on being treated with an excess of sodium azide in concentrated sulfuric acid, XIII afforded the aminotropolone (I) and also 4-cyanotropolone (XIV). It has been well known in the reaction with benzaldehyde that the relative yields of the reaction products, benzonitrile and formanilide, vary according to the amount of sulfuric acid used[3], but in the reaction with XIII further detailed examinations could not be made owing to difficulty in preparing the starting material.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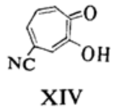
XIV

Some kinds of unsaturated compounds have been reported to react with hydrazoic acid[3]. For instance, amylene forms a Schiff base in high yield, while cyclopentene and camphene undergo ring-enlargement. McEven and Mehta[13] investigated in detail an application of the Schmidt reaction to 1, 1-diphenylethylene and its derivatives. The author's attention

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[9] T. Nozoe, Y. Kitahara, K. Doi and T. Arai, *Bull. Chem. Research Inst. Non-Aqueous Solns. Tohoku Univ.*, **7**, 13 (1957).

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

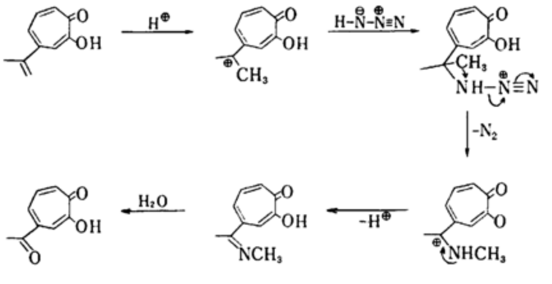
[11] M. Tsuboi, This Bulletin, **25**, 369 (1952).

[12] J. Weinstein and G. M. Wymann, *J. Am. Chem. Soc.*, **78**, 2387 (1956).

[13] W. E. McEven and N. B. Mehta, ibid., **74**, 526 (1952).

was directed to examine this reaction in 4-isopropenyltropolones (II and V), since there is no example of application of the Schmidt reaction to asymmetrically 1, 1-disubstituted ethylenes.

On being treated with one equivalent of hydrazoic acid in concentrated sulfuric acid solution, II afforded the acetyltropolone (III) in a fairly good yield, whereas on being treated with an excess of the reagent II yielded the aminotropolone (I). A similar phenomenon was recognized also in the reaction with the bromo derivative V. A Schiff base XV, as shown in the following mechanism, is expected to form as an intermediate in these reactions, but has not been isolated, since it is probably too hydrolyzable to be isolated under the reaction conditions.



XV

It has been elucidated from the above description that the Schmidt reaction can be satisfactorily applied to the acetyl, isopropyl, and formyl derivatives of tropolone. On the other hand, it has been found that not only 4-carboxytropolone but also 3- and 5-carboxytropolones are entirely inert to the same reaction, and that neither use of trifluoroacetic acid[14] instead of sulfuric acid nor the application of the method for preparing amines by the action of hydroxylamine sulfate with carboxylic acids[15] produce aminotropolones from the carboxytropolones.

Experimental

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

Reaction of 4-Acetyltropolone (III).—To a stirred solution of III (16.4 g.) and concentrated sulfuric acid (50 ml.), was added a solution of chloroform (200 ml.) and hydrazoic acid, prepared from sodium azide (13 g.), during 1 hr. at room temperature. After 1 hr's stirring, the acid layer was diluted with ice water (200 ml.) and the colorless solid thereby separated was crystallized from methanol to give 4-aminotropolone sulfate as colorless needles, m. p. 146∼147°C (decomp.).

Found: C, 41.16; H, 4.89; N, 6.83; water of crystallization, 8.64. Calcd. for $(C_7H_7O_2N)_2 \cdot H_2SO_4 \cdot 2H_2O$: C, 41.17; H, 4.94; N, 6.86; water of crystallization, 8.82%.

The sulfate was digested with saturated sodium carbonate solution to an alkaline point, acidified with acetic acid, and the deposited solid was crystallized from methanol to afford 4-aminotropolone (I, 11.8 g.), m. p. 187∼188°C, undepressed on admixture with an authentic specimen[1].

Reaction of 6-Acetyl-3-bromotropolone (VI).—To a stirred mixture of VI[7] (0.24 g.), concentrated sulfuric acid (1 ml.) and chloroform (6 ml.), was added sodium azide (0.2 g.) for 5 min. at room temperature. After 1 hr., the acid layer was diluted with water (5 ml.), the precipitated solid was collected, and crystallized from methanol to form 6-amino-3-bromotropolone (VII) as pale yellow needles, m. p. 214∼215°C.

Found: N, 6.19. Calcd. for $C_7H_6O_2NBr$: N, 6.48%. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 273 (4.48), 380 (4.14).

4-Acetyl-5-nitrotropolone (VIII). — To a stirred mixture of III (1.64 g.) and acetic acid (2 ml.), was added dropwise a solution of fuming nitric acid (d=1.8, 0.7 g.) and acetic acid (2 ml.) at room temperature, and resulting deep red solution was diluted with water (25 ml.). The precipitated solid was collected and recrystallized from a mixture of acetic acid and methanol to yield 4-acetyl-5-nitrotropolone (VIII, 0.14 g.) as yellow prisms, m. p. 213°C (decomp.).

Found: C, 51.68; H, 3.37; N, 6.70. Calcd. for $C_9H_7O_5N$: C, 51.92; H, 3.27; N, 6.68%. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 225 (4.33), 245 (4.34), 385 (4.17), 437 (4.42).

Reaction of 4-Acetyl-5-nitrotropolone (VIII).—Sodium azide (0.1 g.) was added at room temperature to a stirred mixture of VIII (0.1 g.), concentrated sulfuric acid (0.5 ml.) and chloroform (3 ml.). The initial red color of the acid layer changed gradually to yellow with progress of the reaction. The acid layer, after dilution with water (5 ml.), filtration of the resulting solid and subsequent crystallization from acetic acid, gave 4-amino-5-nitrotropolone (X, 0.07 g.) as yellow needles, which turned black at around 270°C and did not melt up to 300°C.

Found: C, 46.24; H, 3.38; N, 15.36. Calcd. for $C_7H_6O_4N_2$: C, 46.16; H, 3.32; N, 15.38%. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 275 (4.45), 370 (4.09), 397 (4.04).

6-Acetyl-3-bromo-5-nitrotropolone (IX). — Nitration of VI (2.2 g.), which was carried out essentially as described in the case of III, resulted in formation of IX (1.0 g.) as yellow needles from acetic acid, m. p. 164∼165°C.

Found: C, 37.85; H, 2.07; N, 4.92. Calcd. for $C_9H_6O_5NBr$: C, 37.67; H, 2.10; N, 4.92%. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 255 (4.35), 445 (4.46).

Reaction of 6-Acetyl-3-bromo-5-nitrotropolone (IX).—To a stirred mixture of IX (0.15 g.), concentrated sulfuric acid (1 ml.) and chloroform (4

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[14] K. G. Rutherford and M. S. Newman, ibid., **79**, 213 (1957).

[15] H. R. Snyder, C. T. Elston and D. B. Kellom, ibid., **75**, 2014 (1953).

ml.) was added sodium azide (0.1 g.). The followed procedure was carried out as described in the preceding Schmidt reaction, and then 6-amino-3-bromo-5-nitrotropolone (XI) was obtained as yellow prisms (from dimethylformamide), having m. p. 250°C (decomp.).

Found: N, 10.57. Calcd. for $C_7H_5O_4N_2Br$: N, 10.73%. λ_{max}^{MeOH} mμ (log ε): 284 (4.46), 380 (4.08), 404 (4.06).

Hydrogenation of IX.—A mixture of IX (0.29 g.), sodium acetate trihydrate (0.14 g.), 5% palladium-on-charcoal (0.04 g.), and methanol (15 ml.) was shaken in hydrogen atmosphere until 30 ml. of hydrogen was absorbed at room temperature. The catalyst was removed by filtration, the solvent was evaporated from the filtrate, and the residue, after washing with dilute hydrochloric acid, was recrystallized from methanol to afford an indigo-type tropolone (XII) as orange red needles, m. p. 209°C (decomp.).

Found: C, 42.37; H, 1.41; N, 5.48. Calcd. for $C_{18}H_8O_6N_2Br_2$: C, 42.54; H, 1.59; N, 5.51%. λ_{max}^{MeOH} mμ (log ε): 260 (4.72), 370 (4.36), 480 (4.23).

Reaction of 4-Formyltropolone (XIII).—To a stirred mixture of XIII[16] (0.15 g.), concentrated sulfuric acid (0.5 ml.) and chloroform (5 ml.) was added sodium azide (0.08 g.) at room temperature. After 2 hr's stirring, the acid layer was diluted with water (3 ml.), neutralized to pH 7 with sodium carbonate, and the resulting solid was collected. Fractional recrystallization of the solid from methanol afforded 4-cyanotropolone (XIV, 0.03 g.), m. p. and mixed[17] m. p. 194∼195°C. from the less soluble portion, and 4-aminotropolone (I, 0.08 g.), m. p. and mixed[1] m. p. 187∼188°C, from the more soluble portion.

Reaction of 4-Isopropenyltropolone (II).—Sodium azide (0.97 g.) was added to a stirred mixture of II[4] (1.62 g.), concentrated sulfuric acid (5 ml.) and chloroform (5 ml.) at room temperature, and then the mixture was stirred at 40∼50°C for 3 hr. The acid layer was diluted with water (20 ml.) and the resulting acetyltropolone (III, 1.0 g.), m. p. 129°C, undepressed on admixture with an authentic specimen[4], was collected. The use of excess of sodium azide gave 4-aminotropolone (I) in this reaction.

Reaction of 3-Bromo-6-isopropenyltropolone (V).—The Schmidt reaction with V[7,8] (0.24 g.) was carried out essentially as described in the preceding experiment. As the reaction product 3-bromo-6-acetyltropolone (VI, 0.13 g.), m. p. and mixed[7] m. p. 132∼133°C, was obtained. The use of excess of sodium azide in this reaction yielded 6-amino-3-bromotropolone (VII), similarly in the case of II.

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[16] R. D. Haworth and J. D. Hobson, *J. Chem. Soc.*, **1951**, 561.

[17] K. Doi, This Bulletin, to be published.