The Reaction of Tropoids and Quinone Derivatives. III. Reaction of Several Tropolones and o-Benzoquinone Dibenzimide

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(Received November 22, 1961)

In earlier papers of this series, reaction of several tropolones with *p*-benzoquinone-dibenzenesulfonimide⁽¹⁾ and *p*-benzoquinone⁽²⁾ was reported. The present paper describes the structure of the reaction products of tropolone and its bromo derivatives with *o*-benzoquinone-dibenzimide (I)⁽³⁾.

A solution of tropolone and I dissolved in a mixture of methanol and chloroform, added with a small quantity of triethylamine, affords colorless crystals (II) when allowed to stand at room temperature. Analytical values of II correspond to the formula $C_{27}H_{20}O_4N_2$ and the presence of a tropolone ring in II is certain from its ultraviolet absorption spectrum and coloration to ferric chloride. II is also obtained by the use of diethylamine in place of triethylamine in the foregoing reaction, and also by the same reaction carried out in an aqueous solution with addition of alkali, though in a poor yield. Heating of II in a sealed tube with concentrated hydrochloric acid gives 2-phenylbenzimidazole derivative III and phenylenediamine derivative IV. Although the latter was not isolated in a pure state, its formation seemed certain from the facile formation of a triazole derivative V by application of sodium nitrite to the mother liquor left after separation of III. III is also obtained on treatment of II with alcoholic potassium hydroxide. Oxidation of III with alkaline potassium permanganate affords 2-phenylbenzimidazole and

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1) S. Seto, H. Yamazaki and Y. Nishiyama, This Bulletin, 33, 1081 (1960).
2) S. Seto and H. Sato, ibid., 35, 349 (1962).
3) R. Adams and J. W. Way, *J. Am. Chem. Soc.*, 76, 2763 (1954).

this fact suggests that 2-phenylbenzimidazole and tropolone are bonded through the nitrogen in the imidazole ring in III.

In order to make further confirmation of the structure of III, rearrangement of the tropolone ring in III into benzoic acid was attempted.

Application of diazomethane to III afforded only one kind of methyl ether VI, suggesting that 2-phenylbenzimidazole is bonded to 5-position of the tropolone ring in III. The methyl ether VI was converted into 2-chlorotropone derivative VIII through the hydrazino derivative VII[4].

2-Chlorotropone derivative VIII easily underwent conversion to a benzoic acid derivative when heated with alkali and this derivative was changed to a methyl ester IX with diazomethane. According to the afore-mentioned assumption, this methyl ester IX should be 1-(4′-methoxycarbonylphenyl)-2-phenylbenzimidazole and structurally apparent IX was synthesized by the following route.

2-Amino-4′-methyldiphenylamine[5] was treated with benzoyl chloride in pyridine and the monobenzoyl derivative so formed was treated with acetic anhydride to effect cyclization to 1-(4′-methylphenyl)-2-phenylbenzimidazole, which was oxidized with potassium permanganate to form the benzoic acid derivative.

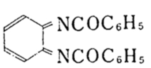
The methyl ester obtained from this acid derivative has the structure of 1-(4′-methoxycarbonylphenyl)-2-phenylbenzimidazole and this was found to be identical with the foregoing IX through mixed fusion test and by comparison of ultraviolet and infrared spectra. The foregoing facts have proved that III is 1-(tropolon-5′-yl)-2-phenylbenzimidazole and II is *N*-(tropolon-5-yl)-*N*, *N*′-dibenzoyl-*o*-phenylenediamine.

3-Bromotropolone also undergoes reaction with I to form a monobromo derivative X, whose structure was determined from its analytical values and formation of II by hydrogenolysis.

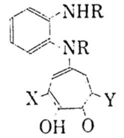
X is also obtained by monobromination of II.

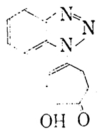
3, 7-Dibromotropolone also affords a dibromo derivative XI by the reaction with I and the structure of XI was also determined from its analytical values and formation of II by hydrogenolysis.

From the similarity of tropolone and phenol, reaction of I with phenol is of interest and examination of this reaction revealed that the product in this case is *N*-(4-hydroxyphenyl)-*N*, *N*′-dibenzoyl-*o*-phenylenediamine, analogous to II in the case of tropolone[6].



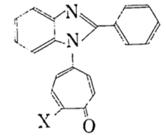
I



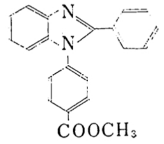


V

II; R=COC_6H_5, X=Y=H
IV; R=X=Y=H
X; R=COC_6H_5, X=Br, Y=H
XI; R=COC_6H_5, X=Y=Br



III; X=OH
VI; X=OCH_3
VII; X=$NHNH_2$
VIII; X=Cl



IX

Experimental[7]

***N*-(Tropolon-5-yl)-*N*, *N*′-dibenzoyl-*o*-phenylenediamine (II).**—a) A solution of 1 g. of *o*-benzoquinone-dibenzimide (I) and 770 mg. of tropolone dissolved in 65 ml. of a mixture (3 : 1 by volume) of methanol and chloroform, added with 3 drops of triethylamine, was allowed to stand at room temperature for 4 days. Evaporation of the solvent in a reduced pressure precipitated crystals. The first crop of 470 mg. of crystals melted at 212∼213°C. Its mother liquor was further concentrated, the residue was treated with dilute hydrochloric acid, and washed with petroleum ether, affording a second crop of 780 mg. of crystals melting at 199∼203°C. The two crops of crystals were combined and recrystallized from a chloroform-ethanol mixture to give 970 mg. of colorless crystals (II), m. p. 220∼221°C.

Found: C, 73.55; H, 4.74; N, 6.87. Calcd. for $C_{27}H_{20}O_4N_2$: C, 74.30; H, 4.62; N, 6.42%. λ_{max}^{MeOH} mμ (log ε): 230 (4.62), 352 (4.20).

The petroleum ether layer left after separation of the second crop of crystals was evaporated and the residue was sublimed at 60°C (bath temperature) at 1 mmHg, affording 200 mg. of the recovered tropolone.

Addition of an aqueous solution of ferric chloride to a solution of II in ethyl acetate resulted in coloration of the aqueous layer to green and organic layer, red.

b) A solution of 100 mg. of I and 100 mg. of tropolone dissolved in 16 ml. of a mixture (3 : 1 by volume) of methanol and benzene, added with 3 drops of diethylamine, was allowed to stand for

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[4] S. Seto, *Sci. Repts. Tohoku Univ.*, **37**, 292 (1953).

[5] W. Borsche and M. Feise, *Ber.*, **40**, 383 (1907).

[6] S. Seto and Y. Nishiyama, *J. Pharm. Soc. Japan* (*Yakugaku Zasshi*,) **82**, 590 (1962).

[7] All melting points are uncorrected. Microanalyses were carried out by Misses Yôko Endô and Yukiko Endô of this Institute. Measurements of ultraviolet spectra were made by a Hitachi EPU-2A type spectrophotometer.

7 days at room temperature. Evaporation of the solvent in a reduced pressure left 40 mg. of crystals, m. p. 217~222°C, which were recrystallized from an ethanol-chloroform mixture to 35 mg. of colorless crystals, m. p. 225°C, undepressed on admixture with the product obtained by the foregoing method a).

c) A mixture of 100 mg. of I with 100 mg. of tropolone, 100 mg. of potassium hydroxide, and 5 ml. of water was stirred for 15 hr. under ice cooling, and *o*-phenylenedibenzamide (40 mg.) that separated from the reaction mixture was filtered off. The filtrate was acidified with dilute hydrochloric acid, the solid that precipitated, was collected, and recrystallized from an ethanol-chloroform mixture to 5 mg. of colorless crystals. This product was found to be identical with the product obtained by the foregoing methods a) and b). The filtrate left after separation of the solid was extracted with chloroform and the extract was sublimed on a water bath at 60°C 1 mmHg, affording 50 mg. of recovered tropolone.

Reaction of II and Concentrated Hydrochloric Acid.—A mixture of II (432 mg.) and concentrated hydrochloric acid (8.8 ml.) was heated in a sealed tube at 120°C for 3 hr. When cooled, the tube was opened and the reaction mixture was extracted with benzene. The benzene extract afforded benzoic acid. Concentration of the aqueous layer in a reduced pressure gave 100 mg. of colorless crystals, m. p. 248~250°C (decomp.), which is the hydrochloride of 1-(tropolone-5′-yl)-2-phenylbenzimidazole (III).

Found: C, 68.08; H, 4.38; N, 7.81. Calcd. for $C_{20}H_{15}O_2N_2Cl$: C, 68.45; H, 4.31; N, 7.99%.

A solution of sodium nitrite (50 mg.) in water (0.5 ml.) was added to the filtrate left after separation of the foregoing crystals and the crystals that separated immediately were recrystallized from an ethanol-chloroform mixture to 10 mg. of 1-(tropolon-5′-yl)-benztriazole (V) as crystals of m. p. 225°C.

Found: C, 64.91; H, 3.75; N, 18.13. Calcd. for $C_{13}H_9O_2N_3$: C, 65.26; H, 3.76; N, 17.57%. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 288 (4.41), 345 (4.25).

Reaction of II and Potassium Hydroxide. — A solution of II (1 g.), potassium hydroxide (3 g.), water (10 ml.), and ethanol (15 ml.) was heated at 120°C for 4 hr. and then evaporated to dryness. A small amount of water was added to the residue, insoluble matter was collected, and suspended in water. The mixture was adjusted to pH 4 with acetic acid, the solid (530 mg.) that remained was collected, and recrystallized from an ethanol-chloroform mixture to 340 mg. of 1-(tropolon-5′-yl)-2-phenylbenzimidazole (III) as colorless crystals, m. p. 247~248°C.

Found: C, 75.99; H, 4.03; N, 9.03. Calcd. for $C_{20}H_{14}O_2N_2$: C, 76.42; H, 4.49; N, 8.91%. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 227 (4.55), 289 (4.24), 341 (4.19), 405 (3.70).

Oxidation of III with Potassium Permanganate. — A solution of VII (100 mg.) dissolved in 2 N potassium hydroxide (2 ml.), added to 1 ml. of 5% aqueous solution of potassium permanganate and 2 ml. of pyridine, was heated on a water bath for 30 min., cooled, and filtered to remove manganese dioxide. Evaporation of the filtrate left 30 mg. of colorless crystals, m. p. 293°C, undepressed on admixture with an authentic specimen of 2-phenylbenzimidazole.

1-(2′-Methoxytropon-5′-yl)-2-phenylbenzimidazole (VI). — An ether solution of diazomethane was added to a suspension of III (50 mg.) in methanol (10 ml.) and the mixture was allowed to stand over night. The solvent was evaporated from the reaction mixture in a reduced pressure and the residue was recrystallized from ethanol to 20 mg. of colorless crystals, m. p. 161~162°C.

Found: C, 74.67; H, 4.51; N, 8.42. Calcd. for $C_{21}H_{16}O_2N_2$: C, 76.81; H, 4.91; N, 8.53%. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 289 (4.29), 325 (4.11).

1-(2′-Hydrazinotropon-5′-yl)-2-phenylbenzimidazole (VII). — A solution of the 2-methoxytropone derivative (VI) (100 mg.) dissolved in methanol (1 ml.), added with 80% hydrazine (20 mg.), was allowed to stand for one hour, during which yellow crystals began to precipitate after a few minutes. The crystals were collected by filtration and 90 mg. of yellow crystals, m. p. 233~235°C (decomp.), was obtained.

Found: C, 71.96; H, 4.26; N, 16.29. Calcd. for $C_{20}H_{16}ON_4$: C, 73.15; H, 4.91; N, 17.06%. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 230 (4.47), 255 (4.45), 352 (4.23), 415 (3.98).

1-(2′-Chlorotropon-5′-yl)-2-phenylbenzimidazole (VIII). — A solution of cupric sulfate crystals (1 g.) dissolved in water (1.6 ml.) with warming was maintained at 120°C and a mixture of VII (110 mg.) and concentrated hydrochloric acid (1 ml.) was added with stirring, by which a vigorous evolution of nitrogen was observed. After being maintained at 120°C, the solution was cooled, adjusted to pH 4 by addition of water (10 ml.) and sodium hydrogencarbonate, and shaken thoroughly with chloroform. The mixture was filtered, the chloroform layer was separated from the filtrate, and dried over anhydrous sodium sulfate. The solution was purified through an alumina column and evaporation of the solvent from its effluent afforded 95 mg. of colorless crystals, m. p. 185~186°C.

Found: C, 72.09; H, 3.86; N, 8.36. Calcd. for $C_{20}H_{13}ON_2Cl$: C, 72.18; H, 3.94; N, 8.42%. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 237 (4.50), 290 (4.29), 336 (3.97).

Rearrangement Reaction of VIII with Alkali.— A mixture of the chlorotropone derivative (VIII) (90 mg.), 50% methanol (4 ml.), and sodium hydroxide (200 mg.) was heated on a water bath for 30 min., methanol was evaporated, and the solid that separated was collected. This solid was suspended in water and acidified with acetic acid by which 1-(4′-carboxyphenyl)-2-phenylbenzimidazole separated as colorless crystals (50 mg.), m. p. 330°C (decomp.).

Found: C, 74.78; H, 4.00; N, 9.04. Calcd. for $C_{20}H_{14}O_2N_2$: C, 76.42; H, 4.49; N, 8.91%. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 272 (4.25).

The carboxylic acid (40 mg.) thereby obtained was suspended in methanol (3 ml.), ether solution of diazomethane was added, and the mixture was allowed to stand over night. The solvent was evaporated to dryness, the residue was dissolved in ether, and the solution was passed through an alumina column for purification. Evaporation of the solvent from the effluent afforded 20 mg. of the methyl ester as colorless crystals, m. p. 115°C.

Found: C, 74.84; H, 4.61; N, 8.09. Calcd. for $C_{21}H_{16}O_2N_2\cdot 1/2H_2O$: C, 74.76; H, 5.08; N, 8.30%. λ_{max}^{MeOH} mμ (log ε): 276 (4.31).

This methyl ester showed no depression of the melting point on admixture with 1-(4′-methoxycarbonylphenyl)-2-phenylbenzimidazole (IX), prepared by the method to be described below. The ultraviolet and infrared spectra of the two were also identical.

1-(4′-Methoxycarbonylphenyl)-2-phenylbenzimidazole (IX).—Benzoyl chloride (0.9 ml.) was added to a solution of 2-amino-4′-methyldiphenylamine (1 g.) dissolved in pyridine (5 ml.) while cooling with ice, the mixture was allowed to stand at room temperature for 30 min., and heated at 90°C for 30 min. Ice water was added to the reaction mixture, crystals that precipitated were collected, and recrystallized from ethanol to 1.2 g. of 2-benzamido-4′-methyldiphenylamine, m. p. 145~146°C.

Found: C, 79.63; H, 4.18; N, 9.18. Calcd. for $C_{20}H_{18}O_2N_2$: C, 79.44; H, 6.00; N, 9.27%. λ_{max}^{MeOH} mμ (log ε): 270 (4.23).

A mixture of the diphenylamine derivative (500 mg.) obtained as above and acetic anhydride (4 ml.) was heated at 140°C for 6 hr. Acetic anhydride was evaporated in a reduced pressure from the reaction mixture, water (2 ml.) was added to the residue, and the mixture was allowed to stand to over night. This was extracted with ether, the extract was dried over anhydrous sodium sulfate, and passed through a column of alumina.

Evaporation of ether from the effluent afforded 430 mg. of 1-(4′-methylphenyl)-2-phenylbenzimidazole, m. p. 91~92°C.

Found: C, 83.93; H, 5.34; N, 9.70. Calcd. for $C_{20}H_{16}N_2$: C, 84.48; H, 5.67; N, 9.85%. λ_{max}^{MeOH} mμ (log ε): 289 (4.22).

The benzimidazole derivative (400 mg.) so obtained was dissolved in pyridine (3 ml.), added to a solution of potassium permanganate (450 mg.) in water (6 ml.), and the mixture was heated on a water bath for 1 hr. After cooling, manganese dioxide that separated out was filtered off, a small amount of water was added to the filtrate, and extracted with ether to remove neutral substances. Acidification of the aqueous layer with acetic acid afforded 120 mg. of 1-(4′-carboxyphenyl)-2-phenylbenzimidazole as crystals of m. p. 340°C (decomp.).

The carboxylic acid (110 mg.) thereby obtained was suspended in methanol (6 ml.), ether solution of diazomethane was added to it to effect methylation, and the solvent was evaporated. The residue was dissolved in ether, the solution was passed through a column of alumina, and the solvent was evaporated from the effluent, affording 1-(4′-methoxycarbonylphenyl)-2-phenylbenzimidazole (IX) (60 mg.) as colorless crystals, m. p. 115°C.

***N*-(3-Bromotropolon-5-yl)-*N*, *N*′-dibenzoyl-*o*-phenylenediamine (X).** — A solution of 3-bromotropolone (35 mg.) and I dissolved in a mixture (3 : 1 by volume) of ethanol and chloroform, added with 1 drop of triethylamine, was allowed to stand at room temperature for 3 days. The crystals that separated were collected. Concentration of the filtrate in a reduced pressure afforded a second crop of crystals. The two crops of crystals were combined and recrystallized from an ethanol-chloroform mixture to give pale yellow crystals (30 mg.), m. p. 242~243°C (decomp.).

Found: C, 63.19; H, 3.83; N, 5.36. Calcd. for $C_{27}H_{19}O_4N_2Br$: C, 62.90; H, 3.72; N, 5.44%. λ_{max}^{MeOH} mμ (log ε): 230 (4.54), 240 (4.53), 250 (4.53), 355 (4.23), 420 (3.86).

***N*-(3, 7-Dibromotropolon-5-yl)-*N*, *N*′-dibenzoyl-*o*-phenylenediamine (XI).** — By the same procedure as above, 250 mg. of 3,7-dibromotropolone and 150 mg. of I afforded 75 mg. of yellow crystals, m. p. 230~231°C (decomp.)

Found: C, 54.35; H, 3.19; N, 4.72. Calcd. for $C_{27}H_{18}O_4N_2Br_2$: C, 54.55; H, 3.05; N, 4.72%. λ_{max}^{MeOH} mμ (log ε): 265 (4.49), 275 (4.49), 360 (4.16), 430 (3.86), 440 (3.87).

Hydrogenolysis of X.—A solution of the monobromo derivative X (90 mg.) dissolved in a solution of potassium hydroxide (20 mg.) in water (1 ml.), to which was added palladium-carbon (50 mg.), was shaken in a hydrogen stream at room temperature. When the absorption of hydrogen had ceased, the catalyst was filtered off, the filtrate was acidified, and the precipitate that appeared was collected. Its recrystallization from an ethanol-chloroform mixture afforded 30 mg. of colorless crystals, m. p. 218~220°C, undepressed on admixture with II. The ultraviolet spectra of the two were identical.

Bromination of II.—A chloroform (1 ml.) solution of bromine (15 mg.) was added to the tropolonyl-*o*-phenylenediamine derivative II (20 mg.) suspended in chloroform (2 ml.) and the mixture was allowed to stand over night at room temperature, by which a resinous substance precipitated. The chloroform layer was separated by decantation, a small quantity of methanol was added to the resinous precipitate, and the crystallized solid was recrystallized from an ethanol-chloroform mixture to 5 mg. of crystals, m. p. 237~240°C undepressed on admixture with X. The ultraviolet spectra of these two substances were identical.

Hydrogenolysis of XI. — A solution of the dibromo derivative XI (200 mg.) in water (20 ml.) and ethanol (10 ml.) containing potassium hydroxide (600 mg.), added with palladium-carbon (400 mg.), was shaken in a hydrogen stream at room temperature. When the absorption of hydrogen had ceased, the catalyst was filtered off, the ethanol was evaporated from the filtrate at a reduced pressure, and the residual solution was acidified with 6 N sulfuric acid. This was extracted with ethyl acetate, the solvent was evaporated from the extract, and the residue was washed with benzene. The benzene-insoluble residue was recrystallized from an ethanol-chloroform mixture to 10 mg. of colorless crystals, m. p. 218~220°C, undepressed on admixture with II. The ultraviolet spectra of these two substances were identical.

Summary

Reaction of tropolone and *o*-benzoquinone dibenzimide was carried out and the structure of its product was determined by deriving it to a 2-phenylbenzimidazole derivative. This revealed that the product is *N*-(tropolon-5-yl)-*N*, *N*′-dibenzoyl-*o*-phenylenediamine. 3-Bromotropolone and 3, 7-dibromotropolone also underwent the same reaction to afford the corresponding bromo derivatives. For the sake of identification, 1-(4′-methoxycarbonylphenyl)-2-phenylbenzimidazole was synthesized from 2-amino-4′-methyldiphenylamine.

A part of the expenses for the present work was supported by a fund from the Sankyo Co., Ltd., which is gratefully acknowledged.

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