*The Bromination Product of 2-(p-Tolyl)-hinopurpurin**

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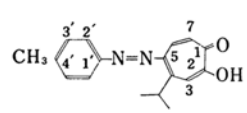
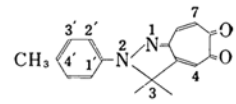
As has been previously reported by Nozoe et al., hinokitiol, i.e., 4-isopropyltropolone, couples with diazotized amines to yield azohinokitiols, which, on heating in an acetic acid solution or in an ethanolic solution in the presence of *p*-benzoquinone, bring about its transformation into so-called hinopurpurins[1]. It has recently been found that 2-phenylhinopurpurin is brominated to yield 2-phenyl-4, 7-dibromohinopurpurin[2]. This paper reports on similar experiment undertaken in order to determine the position of bromine atoms of dibromo-2-(*p*-tolyl)-hinopurpurin (A).

The dibromo compound A was obtained by bromination of 2-(*p*-tolyl)-hinopurpurin (I)[3] and also by bromination of 2-(*p*-tolyl)-7-bromohinopurpurin (II). The ultraviolet spectrum of A was closely analogous to that of I. These facts indicate that A is not a bromine-addition product but a bromine-substitution product of I, and that one of its two bromine atoms is situated at the 7-position in the tropoquinone ring. An ortho directing effect exerted by methyl and nitrogen substituents and an electromeric effect (shown by Ia) suggest that the substitution reaction of I with bromine may take place at the 2′- or 3′-position in the benzene ring, or at the 4- or 7-position in the tropoquinone ring. Accordingly, it can be presumed that A is either a 7, 2′-, 7, 3′- or 4, 7-dibromo derivative of I. An attempt, therefore, was made to synthesize these dibromo derivatives of I as well as some other bromo derivatives of 5-(*p*-tolylazo)-hinokitiol.



5-(*p*-Tolylazo)-hinokitiols

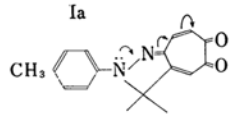
III : 2′-Bromo-
IV : 3′-Bromo-
VII : 7, 2′-Dibromo-
IX : 7, 3′-Dibromo-
XI : 3, 7-Dibromo-



2-(*p*-Tolyl)-hinopurpurins

II : 7-Bromo-
V : 2′-Bromo-
VI : 3′-Bromo-
VIII : 7, 2′-Dibromo-
X : 7, 3′-Dibromo-
XII : 4, 7-Dibromo-
XIII : 4, 7, 2′-Tribromo-
XIV : 4, 7, 3′-Tribromo-

Ia



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1) T. Nozoe, E. Sebe, Y. Kitahara and H. Fujii, *Sci. Repts. Tohoku Univ.*, **136**, 290 (1952); T. Nozoe, T. Ikemi and T. Ozeki, *Proc. Japan Acad.*, **31**, 455 (1955).

2) T. Ikemi, to be published.

3) T. Nozoe, S. Ebine, S. Ito and I. Takasu, *Proc. Japan Acad.*, **27**, 197 (1951).

Hinokitiol was coupled with diazotized 2- and 3-bromo-4-methylanilines to yield 5-(2′-bromo-4′-methylphenylazo)- and 5-(3′-bromo-4′-methylphenylazo)-hinokitiols (III and IV), which, on heating with *p*-benzoquinone in an ethanolic solution, were then transformed into the corresponding 2-(2′-bromo-4′-methylphenyl)- and 2-(3′-bromo-4′-methylphenyl)-hinopurpurins (V and VI) respectively. The bromination of V and VI gave 2-(2′-bromo-4′-methylphenyl)- and 2-(3′-bromo-4′-methylphenyl)-*x*,*x*-dibromohinopurpurins. The coupling of 7-bromohinokitiol with diazotized 2-bromo-4-methylaniline afforded 5-(2′-bromo-4′-methylphenylazo)-7-bromohinokitiol (VII), which was subsequently transformed into 2-(2′-bromo-4′-methylphenyl)-7-bromohinopurpurin (VIII). Although 5-(*p*-tolylazo)-hinokitiol is brominated to its 7-bromo derivative[3], bromination of III did not give VII but, rather, yielded a tribromo hinopurpurin identical with a bromination product of V. The coupling of 7-bromohinokitiol with diazotized 3-bromo-4-methylaniline afforded 5-(3′-bromo-4′-methylphenylazo)-7-bromohinokitiol (IX), which was also prepared by bromination of IV. The transformation of IX into 2-(3′-bromo-4′-methylphenyl)-7-bromohinopurpurin (X) was effected in the usual manner. Neither of the dibromohinopurpurins, VIII or X, was identical with A. The coupling of 3, 7-dibromohinokitiol with diazotized *p*-toluidine failed to occur in an alkaline solution, but it did take place in a pyridine solution to yield 5-(*p*-tolylazo)-3, 7-dibromohinokitiol (XI). XI was somewhat stable towards hinopurpurin-transformation and recovered unchanged when its acetic acid solution was heated on a water bath for 3 hr. However, when heated with *p*-benzoquinone in an ethanolic solution under reflux for 5 hr., XI underwent transformation, accompanied by the elimination of one of its bromine atoms, to yield II. Thus it was impossible to prepare 2-(*p*-tolyl)-4, 7-dibromohinopurpurin (XII) from XI, which had its bromine atoms at known positions. Nevertheless, it has now become evident that XII is the only possible structure for A because neither VIII nor X proved to be identical with A, as has been described above. Therefore, it is furthermore presumed that the above-mentioned bromination products of V and VI are 2-(2′-bromo-4′-methylphenyl)- and 2-(3′-bromo-4′-methylphenyl)-4, 7-dibromohinopurpurins (XIII and XIV) respectively.

It is of interest to note that 2′-brominated 2-(*p*-tolyl)-hinopurpurins, such as V, VIII and XIII, are light red-colored compounds, while all other hinopurpurins are dark purple or deep blue. The light color of 2′-brominated 2-(*p*-tolyl)-hinopurpurins may be ascribed to the steric hindrance of the 2′-bromine atoms which rotate the benzene rings, out of the plane of the hinopurpurin molecules.

Experimental

Monobromo-5-(*p*-tolylazo)-hinokitiols.—*5-(2′-Bromo-4′-methylphenylazo)-hinokitiol (III).*—2-Bromo-4-methylaniline hydrochloride (1.5 g.), dissolved in 8 ml. of 1.2 N hydrochloric acid, was diazotized with a solution of 0.42 g. of sodium nitrite in 4 ml. of water. The diazotized solution was added drop by drop to a solution of 1 g. of hinokitiol and 1.2 g. of potassium hydroxide in 30 ml. of water. The product which separated out on acidification with dilute hydrochloric acid was collected, washed with water, dried and crystallized from benzene to yield 1.65 g. (75%) of III, in the form of orange needles, m. p. 147.5°C.

Found: C, 56.47; H, 4.94; N, 7.85. Calcd. for $C_{17}H_{17}O_2N_2Br$: C, 56.52; H, 4.74; N, 7.75%.

5-(3′-Bromo-4′-methylphenylazo)-hinokitiol (IV).—This was prepared by the coupling of hionkitiol with diazotized 3-bromo-4-methylaniline in the same way as described above. Yield, 77% in the form of reddish orange needles (from benzene), m. p. 147°C.

Found: C, 56.28; H, 4.96; N, 7.88. Calcd. for $C_{17}H_{17}O_2N_2Br$: C, 56.52; H, 4.74; N, 7.75%.

Dibromo-5-(*p*-tolylazo)-hinokitiols.—*5-(2′-Bromo-4′-methylphenylazo)-7-bromohinokitiol (VII).*—A solution of 0.5 g. of 7-bromohinokitiol[4] and 0.4 g. of potassium hydroxide in 50 ml. of water was coupled with a diazotized solution prepared from 0.5 g. of 2-bromo-4-methylaniline hydrochloride, 0.14 g. of sodium nitrite and 2.7 ml. of 1.2 N hydrochloric acid. The crude product obtained was crystallized from acetone to yield 0.6 g. (66%) of VII, as reddish orange needles, m. p. 132.5°C.

Found: C, 46.53; H, 3.55; N, 6.65. Calcd. for $C_{17}H_{16}O_2N_2Br_2$: C, 46.39; H, 3.66; N, 6.35%.

5-(3′-Bromo-4′-methylphenylazo)-7-bromohinokitiol (IX).—a) It was prepared by the coupling of 7-bromohinokitiol with diazotized 3-bromo-4-methylaniline in the same way as cited above. b) To a solution of 0.5 g. of IV in 70 ml. of acetic acid was added, drop by drop, 0.35 g. of bromine dissolved in 3.5 ml. of acetic acid. After the mixture had been left standing for 30 min., the precipitate was collected by filtration. The product obtained was an addition compound which, on crystallization from acetone, regenerated IV with the liberation of bromine. The addition compound was dissolved in pyridine, and the solution was warmed at 80°C for 10 min., and diluted with water. The precipitate formed was recrystallized from acetone to yield 0.32 g. (52%) of IX, in the form of orange needles, m. p. 168~169°C.

Found: C, 46.58; H, 3.75; N, 6.55. Calcd. for $C_{17}H_{16}O_2N_2Br_2$: C, 46.39; H, 3.66; N, 6.35%.

5-(p-Tolylazo)-3,7-dibromohinokitiol (XI).—3, 7-Dibromohinokitiol[4] (500 mg.) dissolved in 50 ml. of pyridine was coupled with a diazotized solution prepared from 185 mg. of *p*-toluidine, 107 mg. of

4) T. Nozoe, E. Sebe, S. Mayama and S. Iwamoto, *Sci. Repts. Tohoku Univ.*, I, 36, 184 (1952).

sodium nitrite and 3.4 ml. of 1.2 N hydrochloric acid. After the mixture had been left standing overnight in an ice-chest, the pyridine was removed in vacuo below 30°C and the residue was treated with boiling ligroin. The ligroin solution gave a crystalline precipitate on cooling, which precipitate was collected and recrystallized from methanol or acetone to yield 110 mg. (16%) of XI, as orange needles, m. p. 167°C.

Found: C, 46.26; H, 3.56; N, 6.14. Calcd. for $C_{17}H_{16}O_2N_2Br_2$: C, 46.39; H, 3.66; N, 6.35%.

Monobromo-2-(*p*-tolyl)-hinopurpurins.—An ethanolic solution consisting of monobromo-5-(*p*-tolylazo)-hinokitiols and of a 1 mol. equiv. of *p*-benzoquinone was refluxed for 5 hr. The ethanol was then evaporated, and the residue was recrystallized from ethanol or acetic acid to yield the corresponding hinopurpurins.

2-(2'-Bromo-4'-methylphenyl)-hinopurpurin (V).—A solution of 200 mg. of III and 60 mg. of *p*-benzoquinone in 10 ml. of ethanol was refluxed for 5 hr. to yield 150 mg. (75%) of V, in the form of orange, prismatic needles, m. p. 222~223°C.

Found: C, 56.79; H, 4.31; N, 7.91. Calcd. for $C_{17}H_{15}O_2N_2Br$: C, 56.84; H, 4.21; N, 7.80%.

2-(3'-Bromo-4'-methylphenyl)-hinopurpurin (VI).—IV (200 mg.) and 60 mg. of *p*-benzoquinone dissolved in 10 ml. of ethanol gave 140 mg. (70%) of VI, as dark blue crystals with a greenish luster, m. p. 241°C.

Found: C, 57.12; H, 4.38; N, 7.55. Calcd. for $C_{17}H_{15}O_2N_2Br$: C, 56.84; H, 4.21; N, 7.80%.

2-(p-Tolyl)-7-bromohinopurpurin (II).—A solution of 200 mg. of XI and 60 mg. of *p*-benzoquinone in 80 ml. of ethanol was refluxed for 5 hr. to give 100 mg. (61%) of II, in the form of steel-blue prisms, m. p. 222°C (Found: C, 57.18; H, 4.01; N, 7.86. Calcd. for $C_{17}H_{15}O_2N_2Br$: C, 56.84; H, 4.21; N, 7.80%), the melting point of which was not depressed on admixture with an authentic sample[5] prepared by the transformation of 5-(*p*-tolylazo)-7-bromohinokitiol.

The same tranformation was effected when an acetic acid solution of XI was refluxed for 5 hr. Dilution of the reaction mixture with water gave II in a 55% yield, and an addition of silver nitrate to the filtrate caused the precipitation of a quantitative amount of silver bromide.

Dibromo-2-(*p*-tolyl)-hinopurpurins.—*2-(p-Tolyl)-4,7-dibromohinopurpurin (XII).*—a) To a solution of 200 mg. of I in 160 ml. of acetic acid was added 250 mg. (2.2 mol. equiv.) of bromine dissolved in 3 ml. of acetic acid. A crystalline product began to separate immediately. After the solution had been left standing for 30 min., the product was collected and recrystallized from acetic acid to yield 220 mg. (70%) of XII, m. p. 227°C. XII dissolves in boiling acetic acid, forming a deep purple solution, from which on cooling it separates in the form of golden yellow scales with a metallic luster. XII showed a marked melting point depression on admixture with VIII and X, as is described below.

Found: C, 46.32; H, 3.56; N, 6.58. Calcd. for $C_{17}H_{14}O_2N_2Br_2$: C, 46.60; H, 3.22; N, 6.39%. Treatment of I with a 1 mol. equiv. of bromine again gave XII, the corresponding monobromo derivative not being formed. b) Bromination of 100 mg. of II with 75 mg. of bromine in 110 ml. of acetic acid gave 90 mg. (74%) of XII.

2-(2'-Bromo-4'-methylphenyl)-7-bromohinopurpurin (VIII).—A solution of 70 mg. of VII and 35 mg. of *p*-benzoquinone in 30 ml. of ethanol was refluxed for 3 hr.; the ethanol was then evaporated, and the residue was recrystallized from ethanol to give 45 mg. (64%) of VIII, in the form of reddish orange crystals, m. p. 207.5~208°C.

Found: C, 46.39; H, 3.20; N, 6.20. Calcd. for $C_{17}H_{14}O_2N_2Br_2$: C, 46.60; H, 3.22; N, 6.39%.

2-(3'-Bromo-4'-methylphenyl)-7-bromohinopurpurin (X).—A solution of 100 mg. of IX in 5 ml. of acetic acid was heated at 100°C for 3 hr. The product which separated on cooling was crystallized from acetic acid to afford 55 mg. (55%) of X, as dark violet prisms, m. p. 248~249°C.

Found: C, 46.58; H, 3.33; N, 6.15. Calcd. for $C_{17}H_{14}O_2N_2Br_2$: C, 46.60; H, 3.22; N, 6.39%.

Tribromo-2-(*p*-tolyl)-hinopurpurins.—*2-(2'-Bromo-4'-methylphenyl)-4,7-dibromohinopurpurin (XIII).*—To a solution of 100 mg. of III in 15 ml. of acetic acid at 60°C was added 100 mg. of bromine. The solution was allowed to stand for 30 min. at the same temperature. Dilution with 5 ml. of water gave a precipitate, which was collected and crystallized from ethanol. Yield, 85 mg. (59%), in the form of reddish orange prisms, m. p. 179°C.

Found: C, 39.65; H, 2.72; N, 5.25. Calcd. for $C_{17}H_{13}O_2N_2Br_3$: C, 39.49; H, 2.54; N, 5.42%.

XIII was reduced with alkaline hydrosulfite to a leuco compound which regained its original red color on exposure to air and which gave a quinoxaline derivative of red plates melting at 189°C.

Found: C, 47.19; H, 2.86; N, 9.18. Calcd. for $C_{23}H_{17}N_4Br_3$: C, 46.89; H, 2.91; N, 9.51%.

2-(3'-Bromo-4'-methylphenyl)-4,7-dibromohinopurpurin (XIV).—Bromine (200 mg.) dissolved in 2 ml. of acetic acid was added to a solution of 100 mg. of VI in 300 ml. of acetic acid; the resulting solution was allowed to stand for 30 min. Dilution with water gave the product, which was collected and recrystallized from acetic acid. Yield, 90 mg. (62%) in the form of scales with a golden metallic luster, m. p. 246°C.

Found: C, 39.22; H, 2.67; N, 5.70. Calcd. for $C_{17}H_{13}O_2N_2Br_3$: C, 39.49; H, 2.54; N, 5.42%.

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5) T. Nozoe, E. Sebe and S. Ebine, *Proc. Japan Acad.*, 26(8), 24 (1950).