3-Phenoxytropolone and 2-Phenoxytropone

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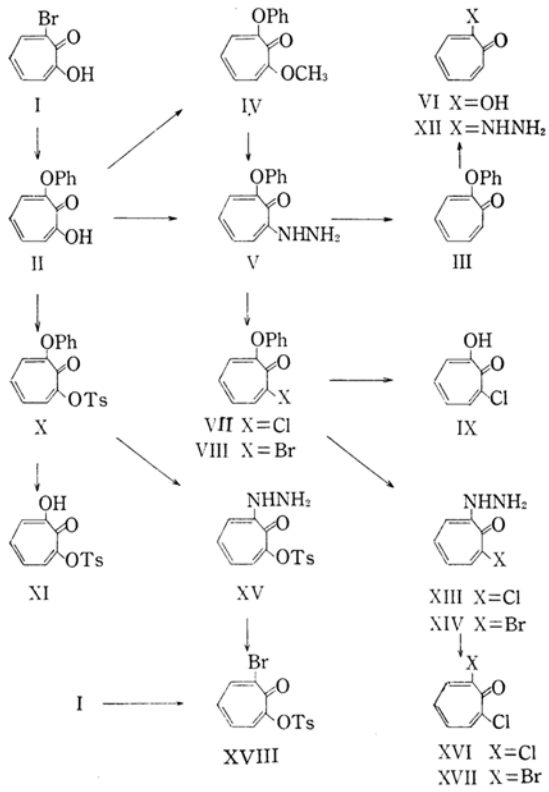
It has been reported[1] that the reaction of 3-bromotropolone (I) and sodium phenoxide affords 3-phenoxytropolone (II) and that its phenoxyl group is not hydrolyzed by heating it with concentrated hydrochloric acid, as in diphenyl ether. In order to make clear the behavior of the phenoxyl group attached to the tropone or tropolone ring, in comparison with diphenyl ether, 2-phenoxytropone (III) and its derivatives were prepared from II and the reactivities of the phenoxyl group in the phenoxytropones toward some nucleophilic reagents, especially dilute alkali and hydrazine, were examined.

The heating of 3-bromotropolone (I) with 2~3 molar equivalents of sodium phenoxide in phenol, in the presence of a catalytical amount of copper acetate, gave 3-phenoxytropolone (II) in a good yield while in the absence of copper acetate the yield of II was low. The reaction did not proceed at all when only one molar equivalent of sodium phenoxide was used. The tropolonic nature of II was shown from the facts that II was soluble in aqueous alkali hydroxide solution, turned red in chloroform with a ferric chloride solution, and formed a pale green copper chelate. The prolonged heating of II which acid or alkali did not produce any change.

The methylation of II with diazomethane gave a crystalline methyl ether (IV), together with an oily substance. When IV was treated with hydrazine, it gave a hydrazinotropone derivative (V), in which the methoxyl was replaced by hydrazine. The oxidative decomposition of V by heating it with copper sulfate in acetic acid afforded phenoxytropone (III), which was easily hydrolyzed by heating it with dilute alkali to give tropolone (VI) and phenol. This result shows that III is 2-phenoxytropone and that IV and V are 7-methoxy- and 7-hydrazino-2-phenoxytropone respectively; consequently, it was concluded that the phenoxyl group of II was located in the 3-position of the tropolone ring. From this evidence, it was clear that the reaction of I and sodium phenoxide under these conditions was not accompanied by an abnormal substitution reaction such as was observed in the case of alkali hydroxide.[1]

1) Y. Kitahara, *Sci. Repts., Tohoku Univ.*, I, 39, 265 (1956).

The oxidative decomposition of V by heating it with copper sulfate in concentrated hydrochloric acid or hydrobromic acid afforded 7-chloro- (VII) or 7-bromo-2-phenoxytropone (VIII), respectively. When VII or VIII was heated with dilute alkali, the phenoxyl group was easily hydrolyzed to give 3-chloro-[2,3] (IX) or 3-bromotropolone (I) respectively. The treatment of II with *p*-toluenesulfonyl chloride afforded a *p*-toluenesulfonate (X), in a quantitative yield; this gave a hydrolyzed product (XI) when heated with dilute alkali. From its reddish coloration with a ferric chloride solution and its ultraviolet absorption spectrum, which was similar to those of tropolones, XI was assumed to be 3-(*p*-tolylsulfonyloxy)tropolone; consequently, X was assumed to be 7-(*p*-tolylsulfonyloxy)-2-phenoxytropone.



The phenoxyl group in II remains unchanged upon treatment with acid or alkali; this behavior is similar to that of diphenyl ether. On the contrary, as has been mentioned above, the reactivities of the phenoxyl groups in 2-phenoxytropones (III, VII, VIII and X) differ greatly from that in II, and they are easily hydrolyzed with alkali. In order to make clear the different behavior of the phenoxyl group in 2-phenoxytropones and 3-phenoxytropolone, the reaction with hydrazine was examined. 2-Phenoxytropone (III) easily reacted with hydrazine to form 2-hydrazinotropone (XII). The phenoxyl group of VII, VIII and X were also replaced by hydrazine to give 7-chloro- (XIII), 7-bromo- (XIV)[4] and 7-(*p*-tolylsulfonyloxy)-2-hydrazinotropone (XV) respectively. The structure of XIII was confirmed through the formation of the known 2,7-dichloro- (XVI) and 2-bromo-7-chlorotropone (XVII)[3] by oxidative decomposition with copper sulfate in concentrated hydrochloric or hydrobromic acid. The structure of XV, which afforded an acetate and an isopropylidene derivative, was also comfirmed by its derivation, when heated with copper sulfate in concentrated hydrobromic acid, to 2-bromo-7-(*p*-tolylsulfonyloxy)tropone (XVIII), which was also obtained by the tosylation of I.

From the foregoing experiments, it was found that the phenoxyl group of 2-phenoxytropones, rather than the halogen or the *p*-tolylsulfonyloxyl group, was replaced easily by hydrazine, as in the case of alkaline hydrolysis. This bavarior is rather interesting when compared with the behavior of 7-methoxy-2-phenoxytropone (IV) toward hydrazine, in which not the phenoxyl but methoxyl group is replaced. From these findings, the substituents at the 2- (or 7) position of the tropone ring may be arranged in the order of ease (methoxyl, phenoxyl, *p*-tolylsulfonyloxyl and halogen), with which they are replaced by a nucleophile.

When II was heated with hydrazine in ethanol, not the phenoxyl but the hydroxyl group was replaced to give V. This is interesting since tropolones in general do not react with ketonic reagents, and only specific tropolone derivatives, such as, 5-nitroso- and 5-arylazotropolones,[5] which can exist in the tautomeric diketone form, are known to react with ketonic reagents. It is also known that 3-carboxy- and 3-cyanotoropolone react with hydrazine to form 2-hydrazinotropones; this is considered to be due to the electron-attracting nature of the carboxyl or cyano group.[6] 3-Phenoxytropolone (II) cannot take the diketone structure; consequently, the replacement of the hydroxyl group by hydrazine must be due to the electron attraction of the phenoxyl

2) T. Nozoe, S. Seto, S. Ito, M. Sato and T. Katono, *Sci. Repts., Tohoku Univ.*, **I**, 37, 191 (1953).
3) S. Seto, ibid., **I**, 37, 275, 377 (1953).
4) T. Nozoe, S. Seto, H. Takeda, S. Morosawa and K. Matsumoto, *Proc. Japan Acad.*, **28**, 192 (1952); *Sci. Repts., Tohoku Univ.*, **I**, 36, 126 (1952).
5) T. Nozoe, M. Sato and K. Matsui, ibid., **I**, 37, 407 (1953); S. Ito, ibid., **42**, 236 (1958); **43**, 216 (1959); T. Nozoe, S. Ito, S. Suzuki and K. Hiraga, *Proc. Japan Acad.*, **32**, 344 (1956).
6) T. Nozoe, Y. Kitahara, K. Takase and I. Murata, This Bulletin, 37, 1292 (1964).

group, which renders the tropolone ring more liable to the attack of nucleophilic reagents.

Experimental[7]

3-Phenoxytropolone (II).—A mixture of 3-bromotropolone (I) (20.1 g.), sodium phenoxide (35 g.) and copper acetate (0.2 g.) in phenol (80 ml.) was heated at 135~140°C for 5 hr. The reaction mixture was then dissolved in a mixture of benzene (100 ml.) and water (100 ml.), acidified with 6 N sulfuric acid, and extracted with benzene. After being dried over sodium sulfate, the solvent was evaporated and the phenol was distilled off under reduced pressure. The residue was recrystallized from methanol to give II (18.3 g.) as colorless prisms, m. p. 106~107°C; reported 105~105.5°C.[1]

Copper Chelate.—M. p. 320°C; pale green crystals.

Found: C, 64.23; H, 3.89. Calcd. for $(C_{13}H_9O_3)_2Cu$: C, 63.73; H, 3.07%.

In this reaction, when copper acetate was not used, 30% of I was recovered and II was formed in a 49% yield after heating for 20 hr.

7-Methoxy-2-phenoxytropone (IV).—Into a cooled suspension of II (1.07 g.) in ether (15 ml.), an ethereal solution of diazomethane (10 ml.) was stirred. After the mixture had been allowed to stand overnight, the crystals which had formed were collected by filtration to give IV (0.41 g.), m. p. 92~95°C. Recrystallization from a mixture of benzene-petroleum ether gave colorless needles, m. p. 95°C.

λ_{max}^{MeOH} mμ (log ε); 242 (4.44), 325 (4.00), 353 (3.99).

Found: C, 73.55; H, 5.58. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30%.

From the mother liquor, an oily substance was obtained. This oil failed to form a picrate and blackened with hydrazine.

7-Hydrazino-2-phenoxytropone (V).—*a) From IV.*—A mixture of IV (200 mg.) and 80% hydrazine hydrate (0.2 ml.) in ethanol (0.2 ml.) was warmed at 80°C for a few minutes to give V (140 mg.), m. p. 198°C (decomp.). Recrystallization from ethanol gave yellow prisms, m. p. 199°C (decomp.).

λ_{max}^{MeOH} mμ (log ε); 250 (4.32), 340 (4.12), 412 (4.04).

Found: C, 68.50; H, 5.17; N, 12.53. Calcd. for $C_{13}H_{12}O_2N_2$: C, 68.41; H, 5.30; N, 12.27%.

Acetate.—M. p. 189~190°C, pale yellow prisms (from methanol).

λ_{max}^{MeOH} mμ (log ε); 252 (4.31), 335 (4.12), 395 (3.99).

Found: C, 66.92; H, 4.77; N, 10.15. Calcd. for $C_{15}H_{14}O_3N_2$: C, 66.65; H, 5.22; N, 10.37%.

Isopropylidene Derivative.—M. p. 156~157°C, yellowish orange prisms (from acetone).

λ_{max}^{MeOH} mμ (log ε); 267 (4.36), 357 (4.33), 418 (4.20).

Found: C, 71.50; H, 5.82; N, 10.48. Calcd. for $C_{16}H_{16}O_2N_2$: C, 71.62; H, 6.01; N, 10.44%.

b) From II.—A mixture of II (1.00 g.) and a 50% ethanolic solution of hydrazine (1.5 ml.) was refluxed for 5 hr. to give V (0.77 g.) as yellow scales, m. p. 197°C. When the reaction period was short, the hydrazine salt of II was obtained as yellow needles m. p. 148°C (decomp.).

Found: C, 63.09; H, 5.65; N, 11.17. Calcd. for $C_{13}H_{14}O_3N_2$: C, 63.40; H, 5.73; N, 11.38%.

2-Phenoxytropone (III).—To a hot solution of V (500 mg.) in a mixture of glacial acetic acid (7.5 ml.) and water (3.5 ml.), a hot solution of copper sulfate (1.2 g.) in water (3 ml.) was added in one lot. After being heated for 5 min., the mixture was cooled, diluted with water (30 ml.), and extracted with chloroform. The solvent was then evaporated and the residue passed through a short alumina column, as with the benzene solution. The eluted substance was distilled under reduced pressure at 150°C to give III (320 mg.) as a colorless oil, which solidified on being allowed to stand, forming colorless crystals, m. p. 43~45°C.

λ_{max}^{MeOH} mμ (log ε); 228 (4.41), 322 (3.98).

Found: C, 79.19; H, 5.17. Calcd. for $C_{13}H_{10}O_2$: C, 78.77; H, 5.09%.

The Hydrolysis of III.—A mixture of III (100 mg.), ethanol (2 ml.) and a 2 N potassium hydroxide solution (2 ml.) was refluxed for 5 hr. and then acidified with 6 N hydrochloric acid and extracted with benzene. The benzene extract was shaken with 2 N sodium carbonate solution, and the aqueous layer was acidified and extracted with benzene. The evaporation of the solvent from the extract left crystals (60 mg.), m. p. 45~49°C; these crystals and its picrate, m. p. 81~83°C, shown no depression of melting point on admixture with tropolone (VI), m. p. 50°C, and its picrate, m. p. 83°C respectively.

7-Chloro-2-phenoxytropone (VII).—To a heated suspension of V (500 mg.) in concentrated hydrochloric acid (10 ml.), a hot solution of copper sulfate (3 g.) in water (7 ml.) was added in one lot. After it had been heated for 5 min., the mixture was cooled, diluted with water, and extracted with benzene. The benzene extract was passed through a short alumina column to give VII (480 mg.), m. p. 137~140°C. Recrystallization from cyclohexane afforded colorless prisms, m. p. 141~142°C.

λ_{max}^{MeOH} mμ (log ε); 242 (4.44), 328 (3.99), 355 (3.91).

Found: C, 67.33; H, 4.13. Calcd. for $C_{13}H_9O_2Cl$: C, 67.11; H, 3.90%.

7-Bromo-2-phenoxytropone (VIII).—When heated suspension of V (500 mg.) in concentrated hydrobromic acid (10 ml.) was treated with an aqueous copper sulfate solution as in the above experiment, VIII (320 mg.), m. p. 139~142°C, was obtained. Recrystallization from cyclohexane afforded colorless prisms, m. p. 142~143°C.

λ_{max}^{MeOH} mμ (log ε); 252 (4.33), 330 (3.98), 355 (3.91).

Found: C, 56.61; H, 3.37. Calcd. fo $C_{13}H_9O_2Br$: C, 56.34; H, 3.27%

3-Chlorotropolone (IX): The Hydrolysis of VII.—When VII (200 mg.) was treated with a 2 N potassium hydroxide solution, as in the experiment concerning the hydrolysis of III, it afforded crystals

7) All melting poins are uncorrected.

(80 mg.), m. p. 98~103°C, Sublimation at reduced pressure and recrystallization from ethanol gave colorless prisms, m. p. 103~104°C, this melting point was undepressed on admixture with an authentic specimen.[3]

λ_{max}^{MeOH} mμ (log ε); 248 (4.51), 324 (3.89), 379 (3.76), 398 (3.38).

3-Bromotropolone (I): The hydrolysis of VIII. —The treatment VIII (100 mg.) as in above experiment afforded I (40 mg.), m. p. 106~107°C.

7-(*p*-Tolylsulfonyloxy)-2-phenoxytropone (X).—Into a cooled solution of II (630 mg.) in pyridine (1.5 ml.), *p*-toluenesulfonyl chloride (600 mg.) was stirred; the mixture was then stirred for an additional hour and allowed to stand overnight. Water (20 ml.) was added, and the crystals (1.05 g.), m. p. 119~123°C, thereby obtained were recrystallized from methanol to give X (980 mg.), m. p. 114~116°C. Further recrystallization from methanol gave colorless prisms, m. p. 127~128°C.

λ_{max}^{MeOH} mμ (log ε); 228 (4.52), 325 (3.95), 350 (3.90).

Found: C, 64.96; H, 4.54. Calcd. for $C_{20}H_{15}O_5S$: C, 65.22; H, 4.26%.

3-(*p*-Tolylsulfonyloxy)tropolone (XI).—A mixture of X (370 mg.), ethanol (1 ml.) and a 2 N potassium hydroxide solution (1 ml.) was heated for 10 min. and then acidified. The crystals (240 mg.), m. p. 83~115°C, so obtained were recrystallized twice from benzene to give XI (70 mg.) as colorless needles, m. p. 169~170°C.

λ_{max}^{MeOH} mμ (log ε); 232 (4.43), 328 (3.85), 375 (3.76), 400 (3.54).

Found: C, 57.68; H, 4.10. Calcd. for $C_{14}H_{12}O_5S$: C, 57.54; H, 4.14%.

2-Hydrazinotropone (XII): The Reaction of III with Hydrazine. — A mixture of III (100 mg.), ethanol (0.5 ml.) and 80% hydrazine hydrate (0.05 ml.) was heated for 2 min., diluted with water, and extracted with chloroform. The chloroform extract was washed with a 2 N sodium hydroxide solution and evaporated to dryness, leaving crystals (60 mg.), m. p. 90~93°C, which were then recrystallized from benzene to give XII as yellow needles, m. p. 92~93°C.

λ_{max}^{MeOH} mμ (log ε); 247 (4.37), 238 (4.09), 406 (4.05).

7-Chloro-2-hydrazinotropone (XIII).—To a suspension of VII (230 mg.) in ethanol (1 ml.), 80% hydrazine hydrate (0.06 ml.) was added, and the mixture was heated for 2 min., affording XIII (160 mg.) as yellow needles, m. p. 165°C (decomp.), after recrystallization from ethanol.

λ_{max}^{MeOH} mμ (log ε); 255 (4.35), 342 (4.07), 416 (4.05).

Found: C, 49.43; H, 4.28; N, 16.32. Calcd. for $C_7H_7ON_2Cl$: C, 49.28; H, 4.14; N, 16.42%.

Acetate.—M. p. 205°C (decomp.), yellow needles (from ethanol).

λ_{max}^{MeOH} mμ (log ε); 255 (4.40), 338 (4.08), 404 (4.07).

Found: C, 50.89; H, 4.39; N, 13.02. Calcd. for $C_9H_9O_2N_2Cl$: C, 50.83; H, 4.27; N, 13.18%.

7-Bromo-2-hydrazinotropone (XIV). — To a suspension of VIII (140 mg.) in ethanol (0.5 ml.), 80% hydrazine hydrate (0.03 ml.) was added, and the mixture was heated for 1 min. to give XIV (100 mg.), m. p. 150°C. Recrystallization from ethanol afforded yellow needles, m. p. 156°C (decomp.).

λ_{max}^{MeOH} mμ (log ε); 253 (4.26), 345 (4.03), 418 (4.07).

Found: C, 38.99; H, 3.17; N, 12.84. Calcd. for $C_7H_7ON_2Br$: C, 39.10; H, 3.28; N, 13.02%.

Acetate. — M. p. 196°C (decomp.), pale yellow, silky needles (from ethanol).

λ_{max}^{MeOH} mμ (log ε); 258 (4.35), 3.40 (4.04), 406 (4.07).

Found: C, 41.42; H, 3.47; N, 10.58. Calcd. for $C_9H_9O_2N_2Br$: C, 42.04; H, 3.53; N, 10.90%.

Isopropylidene Derivative.—M. p. 101~103°C, pale orange prisms (from ethanol).

λ_{max}^{MeOH} mμ (log ε); 272 (4.38), 358 (4.23), 428 (4.31).

Found: C, 47.44; H, 4.39; N, 10.83. Calcd. for $C_{10}H_{11}ON_2Br$: C, 47.08; H, 4.35; N, 10.98%.

Neither the acetate nor the isopropylidene derivative of XIV showed any depression of the melting point on admixture with the respective derivative prepared from authentic 7-bromo-2-hydrazinotropone.[4]

7-(*p*-Tolylsulfonyloxy)-2-hydrazinotropone (XV). —To a suspension of X (630 mg.) in ethanol (4 ml.), 80% hydrazine hydrate (0.4 ml.) was added, and the mixture was heated for 2 min. to give XV (520 mg.) as yellow microneedles, m. p. 204°C.

λ_{max}^{MeOH} mμ (log ε); 230 (4.37), 250 (4.31), 340 (4.05), 412 (4.10).

Found: C, 55.44; H, 4.35; N, 9.30. Calcd. for $C_{14}H_{14}O_4N_2S$: C, 54.89; H, 4.61; N, 9.15%.

Acetate.—M. p. 187~188°C (decomp.), pale yellow prisms (from ethanol).

λ_{max}^{MeOH} mμ (log ε); 230 (4.38), 335 (4.00), 402 (4.09).

Found: C, 55.52; H, 4.86; N, 8.29. Calcd. for $C_{16}H_{16}O_5N_2S$: C, 55.16; H, 4.63; N, 8.04%.

Isopropylidene Derivative. — M. p. 165~166°C, yellow prisms (from ethanol).

λ_{max}^{MeOH} mμ (log ε); 227 (4.37), 267 (4.34), 353 (4.19), 422 (4.29).

Found: C, 58.94; H, 5.23; N, 8.09. Calcd. for $C_{17}H_{18}O_4N_2S$: C, 58.90; H, 4.93; N, 8.19%.

2,7-Dichlorotropone (XVI).—To a hot solution of XIII (100 mg.) in concentrated hydrochloric acid (2 ml.), a 25% aqueous copper sulfate solution (2 ml.) was added; the mixture was then heated for 2 min. Water was added and the crystals thereby obtained were collected and sublimed at reduced pressure to give XVI (90 mg.), m. p. 127~129°C. Recrystallization from benzene-cyclohexane afforded colorless needles, m. p. 130~131°C.

λ_{max}^{MeOH} mμ (log ε); 248 (4.46), 328 (3.92).

Found: C, 48.29; H, 2.53. Calcd. for $C_7H_4OCl_2$: C, 48.04; H, 2.30%.

2-Bromo-7-chlorotropone (XVII). — When a suspension of XIII (100 mg.) in concentrated hydrobromic acid (2 ml.) was treated with a copper sulfate solution as in the foregoing experiment, XVII

(100 mg.), m. p. 148~150°C, was obtained. Recrystallization from benzene-cyclohexane afforded pale yellow plates, m. p. 150~151°C.

λ_{max}^{MeOH} mμ (log ε) ; 220 (4.04), 253 (4.29), 337 (3.87).

Found : C, 38.65 ; H, 2.05. Calcd. for $C_7H_4OBr\cdot Cl$: C, 38.73 ; H, 1.79%.

2-Bromo-7-(*p*-tolylsulfonyloxy)tropone (XVIII). — *a) From XV.* — To a hot solution of XV (460 mg.) in concentrated hydrobromic acid (10 ml.), a 30% aqueous copper sulfate solution (10 ml.) was added ; the mixture was then heated for 1 min. The reaction mixture was diluted with water and extracted with chloroform. When the residue obtained after the evaporation of the solvent was passed through a short alumina column, as with the benzene solution, XVIII (250 mg.), m. p. 114~116°C, was obtained. Recrystallization from methanol afforded colorless needles, m. p. 117~118°C.

λ_{max}^{MeOH} mμ (log ε) ; 227 (4.35), 248 (4.27), 325 (3.87).

Found : C, 47.30 ; H, 3.03. Calcd. for $C_{14}H_{11}\cdot O_4SBr$: C, 47.33 ; H, 3.12%.

b) From 3-Bromotropolone (I). — Into a cooled solution of I (200 mg.) in pyridine (1 ml.), *p*-toluenesulfonyl chloride (200 mg.) was stirred. The mixture was then stirred for 3 hr., diluted with water (20 ml.), and allowed to stand, thus giving XVIII (150 mg.), m. p. 113~115°C. Recrystallization from methanol afforded colorless needles, m. p. 117~118°C.

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