The Synthesis and Some Reactions of Polyphenoxytropolones

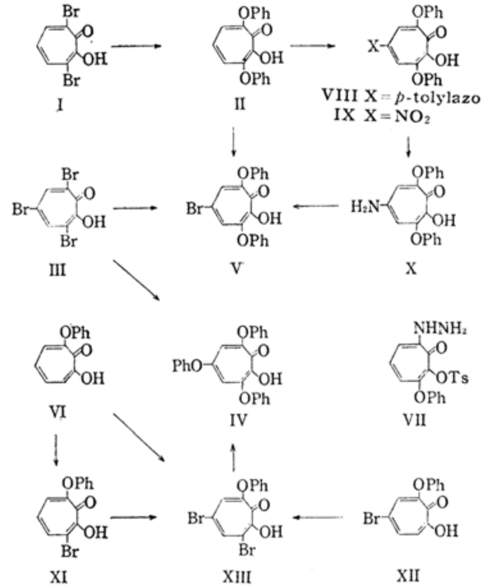
By Kahei Takase

(Received March 24, 1964)

In a previous paper,[1] it was described how the bromine of 3-bromotropolone was easily replaced with a phenoxyl group by heating it with sodium phenoxide, affording 3-phenoxytropolone. This reaction has now been extended to polybromotropolones, such as 3, 7-dibromotropolone and 3, 5, 7-tribromotropolone, in order to obtain polyphenoxytropolones, which are expected to be interesting from the point of view of synthetical studies in troponoid chemistry. In this paper, the synthesis of polyphenoxytropolones and some of their reactions will be reported.

The heating of 3,7-dibromotropolone (I) with an excess of sodium phenoxide in phenol, in the presence of a catalytic amount of copper acetate, gave 3, 7-diphenoxytropolone (II), in which both bromine atoms were replaced with a phenoxyl group. However, even with one or two molar equivalents of sodium phenoxide, no monosubstituted product was obtained. Similarly, when heated with an excess of phenoxide, 3, 5, 7-tribromotropolone (III) afforded 3, 5, 7-triphenoxytropolone (IV), while heated with three molar equivalents of phenoxide, a diphenoxy compound (V) was obtained. By analogy with the formation of 3-phenoxytropolone from 3-bromotropolone,[1] the phenoxyl groups of II and IV are assumed to be located at the 3 : 7 and positions 3 : 5 : 7 respectively. The structure of V was established as 5-bromo-3, 7-diphenoxytropolone from the fact that the bromination of II also afforded V.

These polyphenoxytropolones, like the common tropolones, are soluble in alkali, are colored red in chloroform with a ferric chloride solution, and give methyl ethers with diazomethane and tosylates with *p*-toluenesulfonyl chloride. When heated with hydrazine, II did not give any hydrazinotropone derivative as 3-phenoxytropolone (VI) did,[1] but only hydrazine salt. By heating in acid, the tosylate of II was hydrolyzed to reproduce II, but it gave a resinous substance in alkali. When the tosylate of II was heated with hydrazine, one of the phenoxyl groups was replaced with hydrazine to give a hydrazino derivative (VII). From the similarity of its ultraviolet absorption curve to that of 2-hydrazinotropone, VII may be assumed to be 7-hydrazino-3-phenoxy-2-(*p*-tolylsulfonyloxy)tropone. The methyl ether of II, however, afforded only a resinous product with hydrazine.



The azo-coupling of II with *p*-tolyldiazonium chloride gave a *p*-tolylazo compound VIII in a good yield. The treatment of II with sodium nitrite in acetic acid did not give any nitroso compound, but it did give a nitro compound IX. The catalytic reduction of both VIII and IX gave the same amino compound, X, which then afforded 5-bromo-3, 7-diphenoxytropolone (V) by Sandmeyer reaction. This evidence indicates that VIII, IX and X are 5-(*p*-tolylazo)-, 5-nitro- and 5-amino-3, 7-diphenoxytropolone respectively.

The bromination of 3-phenoxytropolone (VI) in methanol afforded a monobromo derivative (XI), which is different from the 5-bromo-3-phenoxytropolone (XII)[2] obtained from 5-amino-3-phenoxytropolone. On the other hand, the bromination of VI in acetic acid, in the presence of sodium acetate, afforded a dibromo compound XIII, which was also obtained by the bromination of both XI and XII in acetic acid. The treatment of XIII with

---

[1] K. Takase, This Bulletin, 37, 1288 (1964).

[2] K. Takase, ibid., 37, 1298 (1964).

sodium phenoxide gave 3, 5, 7-triphenoxytropolone (IV). From this evidence, XI and XIII may be considered to be 7-bromo-3-phenoxytropolone and 5, 7-dibromo-3-phenoxytropolone respectively.

The above-mentioned results show that bromine atoms of bromotropolones are easily replaced by phenoxide and that the chemical natures of polyphenoxytropolones thereby obtained are similar to those of common tropolones. That is, they are acidic, show positive in ferric chloride tests, give ethers or esters, and are capable of the electrophilic substitution reaction at the 3-, 5- and 7-positions. It is interesting that a nitro compound IX was produced in place of a nitroso compound by the action of nitrous acid. This unexpected result is considered to result from the action of nitrogen dioxide, or its equivalent, formed in the reaction medium.

Experimental[3]

3, 7-Diphenoxytropolone (II). — A mixture of 3, 7-dibromotropolone (I) (2.00 g.), dried sodium phenoxide (4.00 g.), copper acetate (50 mg.) and phenol (8 ml.) was heated at 135~140°C for 5 hr. The reaction mixture was then dissolved in a mixture of benzene and water, acidified with 6 N hydrochloric acid, and extracted with benzene. All the benzene extracts were combined, the benzene and phenol were distilled under reduced pressure, and the residue was recrystallized from methanol, affording II (1.95 g.) as colorless prisms, m. p. 138~139°C.

λ_{max}^{MeOH} mμ (log ε); 255 (4.39), 332 (3.95), 375 (3.79), 405 (3.64).

Found: C, 74.46; H, 4.49. Calcd. for $C_{19}H_{14}O_4$; C, 74.45; H, 4.60%.

Hydrazine Salt: M. p. 173°C (decomp.), yellow needles (from ethanol).

Found: C, 67.81; H, 4.87; N, 7.90. Calcd. for $C_{19}H_{18}O_4N_2$: C, 67.44; H, 5.36; N, 8.28%.

Methyl Ether: M. p. 78~79°C, colorless prisms (from benzene - petroleum ether).

λ_{max}^{MeOH} mμ (log ε); 225 (4.39), 325~345 (3.92).

Found: C, 74.90; H, 5.00. Calcd. for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03%.

Tosylate: M. p. 118~119°C, colorless microcrystals (from methanol).

λ_{max}^{MeOH} mμ (log ε); 228 (4.47), 335 (3.91).

Found: C, 67.89; H, 4.37. Calcd. for $C_{26}H_{20}O_6S$: C, 67.82; H, 4.38%.

3, 5, 7-Triphenoxytropolone (IV).—*a) From 3,5,7-Tribromotropolone (III).*—A mixture of III (1.44 g.), dried sodium phenoxide (2.3 g.), copper acetate (10 mg.) and phenol (4 g.) was heated at 135~140°C for 5 hr. The reaction mixture was then treated as described in the above experiment to give IV (1.20 g.), m. p. 155~156°C. Recrystallization from benzene-methanol afforded pale yellow microprisms, m. p. 162~163°C.

λ_{max}^{MeOH} mμ (log ε); 262 (4.49), 337 (4.05), 390 (3.91).

Found: C, 75.14; H, 4.47. Calcd. for $C_{25}H_{18}O_5$: C, 75.37; H, 4.55%.

Methyl Ether: M. p. 96~97°C, pale yellow prisms (from methanol).

λ_{max}^{MeOH} mμ (log ε); 260 (4.48), 347 (4.08).

Found: C, 75.59; H, 4.86. Calcd. for $C_{26}H_{20}O_5$: C, 75.71; H, 4.89%.

Tosylate: M. p. 146~148°C, colorless needles (from methanol).

λ_{max}^{MeOH} mμ (log ε); 230 (4.52), 257 (4.42), 342 (4.33).

Found: C, 69.39; H, 4.28. Calcd. for $C_{32}H_{24}O_7S$: C, 69.56; H, 4.38%.

b) From 5, 7-Dibromo-3-phenoxytropolone (XIII). When a mixture of XIII (370 mg.), dried sodium phenoxide (350 mg.), copper acetate (10 mg.) and phenol (1 g.) was treated as described in a), IV (310 mg.) was obtained as pale yellow microprisms, m. p. 162~163°C.

5-Bromo-3,7-diphenoxytropolone (V).—*a) From 3, 5, 7-Tribromotropolone (III).*—A mixture of III (720 mg.), dried sodium phenoxide (720 mg.), copper acetate (10 mg.) and phenol (2 g.) was heated at 135~140°C for 5 hr. The reaction mixture was treated as described in the above experiment, and V (370 mg.), m. p. 138~139°C was obtained. Recrystallization from methanol afforded pale yellow prisms, m. p. 140~141°C.

λ_{max}^{MeOH} mμ (log ε); 258 (4.40), 350 (4.06), 425 (3.81).

Found: C, 59.22; H, 3.45. Calcd. for $C_{19}H_{13}O_4Br$: C, 59.24; H, 3.40%.

b) The Bromination of 3, 7-Diphenoxytropolone (II).—To a suspension of II (30 mg.) and sodium acetate (140 mg.) in glacial acetic acid, a solution of bromine (160 mg.) in the same solvent (0.5 ml.) was added; the mixture was then stirred under cooling for 4 hr. The reaction mixture was diluted with water and extracted with chloroform. After the solvent had been removed from the extract, the residual oil was solidified by the addition of methanol, affording V (220 mg.) as pale yellow prisms, m. p. 140~141°C.

c) The Sandmeyer Reaction of 5-Amino-3, 7-diphenoxytropolone (X).—A solution of X (110 mg.) in dioxane (1 ml.) containing 6 N sulfuric acid (0.3 ml.) was diazotized by the addition of a solution of sodium nitrite (30 mg.) in water (0.3 ml.) at 0~5°C over a 40 min. period. This diazotized mixture was then stirred into a solution of cuprous bromide (200 mg.) in concentrated hydrobromic acid (2 ml.) at room temperature. After being stirred for a further 2 hr., the mixture was diluted with water, and the copper chelate thereby formed was collected and dried. Into a suspension of this copper chelate in chloroform, hydrogen sulfide gas was passed, and the copper sulfide thereby formed was filtered off. The removal of the solvent from the filtrate and the recrystallization of the residue from methanol gave V (80 mg.) as pale yellow prisms, m. p. 140~141°C.

7-Hydrazino-3-phenoxy - 2 -(*p* - tolylsulfonyloxy)-tropone (VII).—A mixture of the tosylate of II

---

[3] All melting points are uncorrected.

(100 mg.), 80% hydrazine hydrate (0.2 ml.) and ethanol (2 ml.) was heated for 1 min., affording VII (80 mg.) as yellow micro-needles, m. p. 194°C (decomp.).

λ_{max}^{MeOH} mμ (log ε); 228 (4.34), 260 (4.41), 343 (3.95), 404 (4.13).

Found: C, 60.32; H, 4.60; N, 6.81%. Calcd. for $C_{20}H_{18}O_5N_2S$: C, 60.30; H, 4.55; N, 7.03%.

5-(*p*-Tolylazo)-3, 7-diphenoxytropolone (VIII).—A *p*-tolyldiazonium chloride solution prepared from *p*-toluidine (110 mg.), 6 N hydrochloric acid (0.5 ml.) and sodium nitrite (80 mg.) was stirred into a solution of II (300 mg.) in pyridine (4 ml.). After it had stirred for 2 hr., water was added, and the crystals thereby formed were collected and washed with methanol to give VIII (400 mg.), m. p. 194∼197°C. Recrystallization from ethyl acetate afforded orange silky needles, m. p. 200∼201°C.

λ_{max}^{MeOH} mμ (log ε); 307 (4.22), 414 (4.36), 462 (4.30).

Found: C, 73.37; H, 4.49; N, 6.92. Calcd. for $C_{26}H_{20}O_4N_2$: C, 73.57; H, 4.75; N, 6.60%.

5-Nitro-3, 7-diphenoxytropolone (IX). — Into a cooling suspension of II (200 mg.) in glacial acetic acid (3 ml.), a solution of sodium nitrite (150 mg.) in water (0.5 ml.) was stirred. After it had been stirred for a further 3 hr., the mixture was diluted with water, giving yellow crystals (120 mg), m. p. 172°C (decomp.). Recrystallization from methanol gave IX (80 mg.) as yellow silky needles, (m. p. 188°C (decomp.).

λ_{max}^{MeOH} mμ (log ε); 220 (4.38), 404 (4.23).

Found: C, 64.77, 64.91; H, 3.52, 3.90; N, 3.64. Calcd. for $C_{19}H_{13}O_6N$: C, 64.96; H, 3.73; N, 3.99%.

5-Amino-3, 7-diphenoxytropolone (X). — *a) The Hydrogenolysis of VIII.* — A suspension of VIII (200 mg.) in methanol (5 ml.) was shaken with hydrogen in the presence of platinum oxide (5 mg.); 27 ml. of hydrogen gas was absorbed in a period of 1.5 hr. The catalyst was then filtered off, and the filtrate was concentrated to a small volume to give X (110 mg.), m. p. 235∼239°C. Recrystallization from methanol afforded yellow plates, m. p. 240∼241°C.

λ_{max}^{MeOH} mμ (log ε); 258 (4.45), 353 (4.15), 410 (3.94).

Found: C, 70.82; H, 4.63; N, 4.41. Calcd. for $C_{19}H_{15}O_4N$: C, 71.02; H, 4.71; N, 4.36%.

N-Acetate: M. p. 216∼217°C, pale yellow micro-needles (from ethanol.)

λ_{max}^{MeOH} mμ (log ε); 465 (4.42), 348 (4.11).

Found: C, 68.68; H, 4.39; N, 3.91. Calcd. for $C_{21}H_{17}O_5N$: C, 69.41; H, 4.72; N, 3.86%.

b) The Hydrogenolysis of IX.—A suspension of IX (90 mg.) in methanol (3 ml.) was skaken with hydrogen in the presence of platinum oxide (5 mg.); 23 ml. of hydrogen gas was absorbed in a period of 1 hr. After the removal of the catalyst and the solvent, the residue was recrystallized from methanol, affording X (60 mg.) as yellow plates, m. p. 240∼241°C.

7-Bromo-3-phenoxytropolone (XI).—Into a cooling suspension of 3-phenoxytropolone (VI) (640 mg.) in methanol (10 ml.), a solution of bromine (530 mg.) in methanol (1 ml.) was stirred. After the mixture had been stirred for 1 hr., the removal of the solvent gave an oily material, which was chromatographed through a column of silica gel as a solution in benzene. From the second effluent, the evaporation of the solvent gave crystals (220 mg.), m. p. 91∼94°C, which were then recrystallized from cyclohexane, affording XI as pale yellow needles, m. p. 98∼99°C.

λ_{max}^{MeOH} mμ (log ε); 260 (4.45), 335 (3.96), 415 (3.89).

Found: C, 53.32; H, 3.23. Calcd. for $C_{13}H_9O_3Br$: C, 53.26; H, 3.10%.

5, 7-Dibromo-3-phenoxytropolone (XIII).—*a) The Bromination of 3-Phenoxytropolone (VI).*—To a suspension of VI (210 mg.) and sodium acetate (240 mg.) in glacial acetic acid (1 ml.), bromine (320 mg.) was added. After the mixture had been stirred for 2 hr., water was added and the crystals thereby formed were collected to give XIII (340 mg.), m. p. 136∼138°C. Recrystallization from methanol afforded pale yellow needles, m. p. 140∼141°C.

λ_{max}^{MeOH} mμ (log ε); 262 (4.50), 350 (4.14), 435 (3.97).

Found: C, 42.17; H, 2.29. Calcd. for $C_{13}H_8O_3Br_2$: C, 41.99; H, 2.17%.

b) The Bromination of 7-Bromo-3-phenoxytropolone (XI).—To a suspension of XI (30 mg.) and sodium acetate (10 mg.) in glacial acetic acid (0.5 ml.), bromine (20 mg.) was added. After it had been stirred for 2 hr., the mixture was treated as described in a) and XIII (30 mg.) was obtained as pale yellow needles, m. p. 140∼141°C.

c) The Bromination of 5-Bromo-3-phenoxytropolone (XII).—When XII (60 mg.) was brominated as in a), XIII (40 mg.) was obtained, m. p. 140∼141°C.

The author wishes to take this opportunity to express his sincere gratitude to Professor Tetsuo Nozoe for his kind guidance throughout the course of this work, and to Professor Shuichi Seto and Professor Yoshio Kitahara for much helpful advice. Thanks are also due to Miss Kuni Kato and Miss Ayako Iwanaga for their elementary analyses.

Department of Chemistry
Faculty of Science
Tohoku University
Katahira-cho, Sendai