27. Diels-Alder Reaction of Troponoids. III.¹⁾
Reaction of Halogenohinokitiols and Bromotropolone

By Eigai SEBE and Yoshiaki ITSUNO

Department of Pharmacology, Kumamoto Medical College,
Kumamoto, Japan

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Halogen derivatives of hinokitiol react with maleic anhydride in xylene solution yielding normal adduct-anhydrides and the yields of these products vary according to the kind, position, and number of halogen atoms attached to the tropolone nucleus, and the majority of them take endo-cis-configuration with the exception of 5,7-dibromohinokitiol-adduct whose constitution could not be ascertained owing to the poor yield and difficulty of bromination.

7-Bromohinokitiol adduct anhydride (A) comes in lustrous fine colorless needles, m.p. 189–190° (decomp.), soluble in hot acetone; yield, 16–20% (Anal. Calcd. for $C_{14}H_{13}BrO_5$: C, 49.27; H, 3.81. Found: C, 49.15, 49.26; H, 3.69, 3.85).

Free carboxylic acid (B) is obtained from (A) by warming in dilute acetic acid as colorless fine needles m.p. 180–181° (decomp.) (Nozoe and his coworkers reported m.p. as 182–184°²⁾ (decomp.) (Anal. Calcd. for $C_{14}H_{15}BrO_6$: C, 46.80; H, 4.18; Br, 22.28. Found: C, 47.36; H, 3.40, 3.37; Br, 22.19, 22.68. Titration. Calcd. as dibasic: 111.4 c.c. Found: 112.0 c.c.). Dilute acetic acid solution of (B) is treated with calcd. quantity of bromine water, and the bromo-lactone monoacid (C) crystallizes out in a few days, as fine colorless needles, m.p. 199–200° (decomp.) (Anal. Calcd. for $C_{14}H_{14}Br_2O_6$: C, 38.51; H, 2.90; Br, 36.53. Found: C, 39.01; H, 3.28; Br, 35.37. Titration. Calcd. as lactone-monoacid: 45.6 c.c. Found: 46.7 c.c.).

7-Iodo-hinokitiol also reacts in xylene solution forming its adduct-anhydride (D) in 40% yield. During this addition, some part of iodine liberates and colors the solution purple. (D) is obtained as lustrous, colorless long needles, m.p. 178–179° (decomp.), and colors pale yellow by diffused light (Anal. Calcd. for $C_{14}H_{13}IO_5$: C, 43.47; H, 3.39. Found: C, 43.30; H, 3.35). By hydrolysing (D) in dilute acetic acid, free acid (E) crystallizes out as lustrous fine needles, which colors to orange yellow by light and contains one mole of water of crystallization, which is eliminated at 125–130°. (E) decomposes at 176–178° with evolution of iodine vapour (Anal. Calcd. for $C_{14}H_{15}IO_6 \cdot H_2O$: C, 39.65; H, 4.01; I, 29.95. Found: C, 40.00; H, 3.99; I, 28.27. Titration. Calcd. as dibasic: 94.3 c.c. Found: 90.3 c.c.). Bromo-lactone-monoacid (F) is obtained by treating with bromine water as pale yellow fine

needles, m.p. 193–194° (decomp. with evolution of iodine vapour) (Anal. Calcd. for $C_{15}H_{14}BrIO_6$: C, 34.64; H, 2.88; Br + I, 42.68. Found: C, 34.66; H, 2.77; Br + I, 41.91. Titration. Calcd. as lactone-monoacid: 41.3c.c. Found: 42.8c.c.).

3,7-Dibromohinokitiol-adduct anhydride (G) is obtained by the usual method in 85–90% yield, (highest value among the similar reactions examined) as fine colorless needles, m.p. 183–185° (decomp. sinters at 178°) (Anal. Calcd. for $C_{14}H_{12}Br_2O_5$: C, 40.00; H, 2.85; Br, 38.09. Found: C, 40.76, 41.09; H, 2.82, 2.88; Br, 38.72, 37.40). Free acid (H) is formed by the hydrolysis of (G) in dilute acetic acid as lustrous colorless silky needles, m.p. 181–183° (decomp.) (Anal. Calcd. for $C_{14}H_{14}Br_2O_6$: C, 38.25; H, 3.20; Br, 36.53. Found: C, 38.86; H, 3.12; Br, 36.56. Titration. Calcd. as dibasic: 89.3c.c. Found: 93.0c.c.).

By bromination in aqueous solution of (H), bromo-lactone-monoacid (I) is obtained as lustrous colorless fine needles, m.p. 163–164° (decomp.) (Anal. Calcd. for $C_{14}H_{13}Br_3O_6$: C, 32.49; H, 2.51; Br, 46.42. Found: C, 32.00, 32.09; H, 2.67, 2.71; Br, 45.36. Titration. Calcd. as monoacid: 38.6c.c. Found: 39.8c.c.).

As o-bromotropolone does not react with maleic anhydride in xylene solution²³, the authors heated two component substances without a solvent at 145–150° for 6–7 hours and dissolved the reaction products in sodium bicarbonate solution. After filtering once, dark brown filtrate was acidified, then extracted repeatedly with ethyl acetate. Residue from the solution came as viscous crystalline mass and separated into two fractions by cold ethyl acetate, the one less of soluble adduct- α , and the other, adduct- β , easily soluble in the solvent.

o-Bromotropolone-maleic acid adduct- α (J) comes in fine colorless needles m.p. 232–233° (decomp.) insoluble in cold ethyl acetate; yield, 15% (Anal. Calcd. for $C_{11}H_8BrO_6$: C, 41.96; H, 2.84; Br, 25.20. Found: C, 42.02; H, 2.94; Br, 25.33. Titration. Calcd. as dibasic: 126.2c.c. monobasic, 63.2c.c. Found: 77.2c.c.). The analytical data coincide with those for dicarboxylic acid but the constitution of lactol-monoacid may be more preferable from the titration value. By treating (J) with a mixture of acetic anhydride and acetyl chloride, lactol acetate (K) is obtained without formation of anhydride or lactol dehydrate. (K) comes in fine colorless needles, m.p. 220–221° (decomp., sinters at 210°) and contains one mole of water of crystallisation which cannot be removed at 100°, in vacuum (Anal. Calcd. for $C_{11}H_8BrO_5(OAc) \cdot H_2O$: C, 41.38; H, 3.45; Br, 21.22. Found: C, 41.57; H, 3.25; Br, 20.47. Titration. Calcd. as dibasic: 106.1c.c.; as mono basic: 53.1c.c. Found: by NaOH, 83.4c.c.; by Na_2CO_3 , 58.9c.c.). From these data, it is considered that (J) has a lactol ring structure even in aqueous solution

and its acetate (K) is hydrolysed to some extent during neutralization with caustic alkali.

Bromination of (J) by bromine water was much more difficult than that of tropolone-maleic acid-adduct, and even by successive treating, bromine content and the melting point, remained practically unchanged. These facts are quite analogous to the case of tropolone-maleic acid-adduct though the real mechanism can not be elucidated.

o-Bromotropolone-maleic acid-adduct- β (L) crystallizes out from ethyl acetate solution on cooling and evaporating in several days; yield, 25%, as lustrous colorless needles, m.p. 183–184° (decomp.), easily soluble in acetone and ethyl acetate. On drying at room temperature (L) liberates water, changing into its anhydride (Anal. Calcd. for $C_{11}H_7BrO_5$: C, 44.15; H, 2.34; Br, 26.75. Found: C, 44.85, 44.21; H, 2.40, 2.36; Br, 25.83, 25.83. Titration. Calcd. as dibasic: 136.9 c.c. as monobasic: 69.0 c.c. Found: 124.9 c.c.). Namely, it is known that (L) reacts as dibasic acid with dilute alkali differing from adduct- α (J).

An aqueous solution of (L), treated with equimolar amount of bromine water, gives a bromo derivative (M) as fine colorless needles, m.p. 161–162° (decomp.), soluble in water, acetone, and ethyl acetate (Anal. Calcd. for $C_{11}H_8Br_2O_6$: C, 33.33; H, 2.22. Found: C, 34.94; H, 2.36. Titration. Calcd. as lactone-monoacid: 101.0 c.c. Found: 91.5 c.c.). Though these data are not perfectly coincidental, it may be reasonable to consider the configuration of (L) as endo-cis-form.

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References

- 1) Part I and II of this series appeared respectively in *Prcc. Japan Acad.*, **28**, 282 (1952) and *ibid.*, **29**, 107 (1953).
- 2) T. Nozoe, S. Seto, and T. Ikemi: *Proc. Japan Acad.*, **27**, 655 (1951).