14. *Reaction of Some Chromens and Naphthopyrans with Bromine. Part II.*[1]

By R. Livingstone.

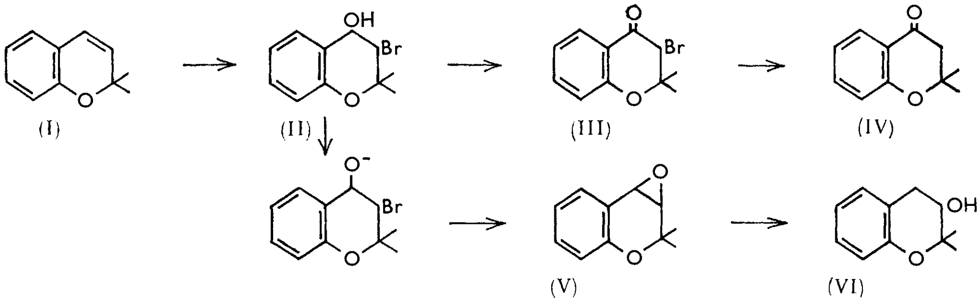
The orientation of the bromohydrins discussed in Part I [1] was based on the reduction with sodium amalgam in ethanol to give alcohols different from those obtained by the reduction of the 4-chromanone and the 4-pyrone. Recently the author was informed by Professor P. Yates, University of Toronto, that chromanones gave different products on reduction with lithium aluminium hydride and sodium amalgam in ethanol. Consequently the orientation of these bromohydins has been re-investigated.

The bromohydrin (II) [1] formed from 2,2-dimethylchromen (I) and hypobromous acid and previously reported as 4-bromo-2,2-dimethylchroman-3-ol gave, on oxidation with chromium trioxide in acetic acid, 3-bromo-2,2-dimethylchroman-4-one (III). Treatment with zinc dust and acetic acid converted the bromo-ketone (III) into 2,2-dimethylchroman-4-one (IV). Reduction of the bromohydrin (II) in ethanol with sodium amalgam besides removing the bromine atom also caused migration of the hydroxyl group from the 4- to the 3-position (VI) *via* the epoxide (V), some of which reacted with the ethanol to give 3-ethoxy-2,2-dimethylchroman-4-ol (VIIa). The same products were obtained following reduction of 3,4-epoxy-2,2-dimethylchroman (V), formed by reaction of the bromohydrin (II) in ether with powdered potassium hydroxide. The epoxide (V) on

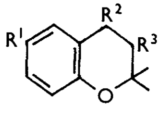
---

[1] Part I, Livingstone, Miller, and Morris, *J.*, 1960, 3094.

reduction in methanol afforded 3-methoxy-2,2-dimethylchroman-4-ol (VIId), and 2,2-dimethylchroman-3-ol (VI). When boiled with ethanol or methanol the epoxide (V) gave 3-ethoxy-2,2-dimethylchroman-4-ol (VIIa) or 3-methoxy-2,2-dimethylchroman-4-ol (VIId), respectively. When the ethanol contained a drop of concentrated sulphuric acid a small amount of material, $C_{22}H_{24}O_4$, m. p. 194—195°, was obtained.



Evidence for the formation of the epoxide (V) as an intermediate during the reduction of 3-bromo-2,2-dimethylchroman-4-ol was obtained on treating the bromohydrin with sodium ethoxide. The epoxide thus formed was converted by boiling ethanol into the ethoxy-alcohol (VIIa).



(VII)

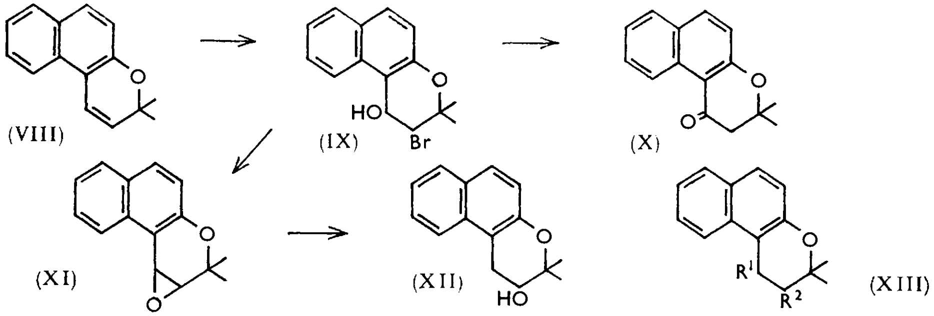
(a); $R^1 = H$, $R^2 = OH$, $R^3 = OEt$
(b); $R^1 = H$, $R^2 = OAc$, $R^3 = OEt$
(c); $R^1 = R^2 = H$, $R^3 = OAc$
(d); $R^1 = H$, $R^2 = OH$, $R^3 = OMe$
(e); $R^1 = H$, $R^2 = R^3 = OH$
(f); $R^1 = H$, $R^2 = Br$, $R^3 = OH$
(g); $R^1 = H$, $R^2 = Br$, $R^3 = OMe$
(h); $R^1 = R^2 = Br$; $R^3 = OMe$
(i); $R^1 = H$, $R^2 = OH$, $R^3 = Br$
(j); $R^1 = H$, $R^2 = OMe$, $R^3 = Br$
(k); $R^1 = R^3 = Br$, $R^2 = OMe$

Treatment of the epoxide (V) with lithium aluminium hydride in ether gave 2,2-dimethylchroman-3-ol,[1] and with very dilute sulphuric acid the 3,4-diol (VIIe). Boiling the bromohydrin (II) in acetone with aqueous potassium hydroxide solution also yielded the diol; 3-bromo-4-methoxy-2,2-dimethylchroman (VIIj) failed to react under similar conditions. 3-Bromo-2,2-dimethylchroman-4-yl acetate (as II) when boiled with sodium ethoxide gave the ethoxy-alcohol (VIIa). The bromohydrin (II), when boiled with sodium methoxide, afforded 3-methoxy-2,2-dimethylchroman-4-ol (VIId) and with acetic acid, 3-bromo-2,2-dimethylchromen.[1]

Similar results were obtained with the bromohydrin (IX) [1] from 6,6-dimethylnaphtho(2′,1′:2,3)pyran (VIII), which on treatment with chromium trioxide and then with zinc dust in acetic acid, gave 2,2-dimethyl-5,6-benzochroman-4-one (X). Reduction of the bromohydrin (IX) in ethanol with sodium amalgam gave 4,5-dihydro-6,6-dimethylnaphtho(2′,1′:2,3)pyran-5-ol (XII) *via* the epoxide (XI).

The compounds listed as (VII, f—h), (XIII, a and b) in Part I are therefore (VII, i—k) (XIII, c and d), respectively.

The correct orientations of 4-bromo-2,2-dimethylchromen [1] and 4-bromo-6,6-dimethylnaphtho(2′,1′:2,3)pyran [1] are 3-bromo-2,2-dimethylchromen and 5-bromo-6,6-dimethylnaphtho(2′,1′:2,3)pyran, respectively. 3,4-Dibromo-2,2-dimethylchroman in acetone gave 3-bromo-2,2-dimethylchroman-4-ol on treatment with an equimolar amount of aqueous potassium hydroxide at room temperature. 4,5-Dibromo-4,5-dihydro-6,6-dimethylnaphtho(2′,1′:2,3)pyran failed to react under similar conditions and also on boiling.



(a) R¹ = Br, R² = OH
(b) R¹ = Br, R² = OMe
(c) R¹ = OH, R² = Br
(d) R¹ = OMe, R² = Br

EXPERIMENTAL

M. p.s were taken on the Kofler block. The acetates were prepared in the cold by use of acetic anhydride and pyridine.

3-Bromo-2,2-dimethylchroman-4-ol (II).—3,4-Dibromo-2,2-dimethylchroman (9·8 g.) in acetone (100 c.c.) was shaken with potassium hydroxide (1·73 g.) in water (20 c.c.) for a few minutes and then poured into water. The precipitate gave, on crystallisation from light petroleum (b. p. 60—80°), 3-bromo-2,2-dimethylchroman-4-ol, m. p. 106° (5·59 g., 71·3%).[1]

3-Bromo-2,2-dimethylchroman-4-one (III).—3-Bromo-2,2-dimethylchroman-4-ol (2·8 g.) and chromium trioxide solution (9·5 g. of trioxide, 53 c.c. of acetic acid, and 6·5 c.c. of water) (8 c.c.) were set aside for 2 hr. at 50—60°, and then poured into water; the precipitate, when recrystallised from light petroleum (b. p. 40—60°), gave *3-bromo-2,2-dimethylchroman-4-one*, m. p. 62—63° (2·01 g., 71·8%) (Found: C, 52·0; H, 4·5; Br, 31·15. $C_{11}H_{11}BrO_2$ requires C, 51·8; H, 4·3; Br, 31·3%).

2,2-Dimethylchroman-4-one (IV).—3-Bromo-2,2-dimethylchroman-4-one (2·01 g.), zinc dust (4 g.), and acetic acid (15 c.c.) were boiled for 2½ hr. Isolation with ether and recrystallisation from light petroleum (b. p. 40—60°) gave 2,2-dimethylchroman-4-one,[2] m. p. and mixed m. p. 88—89° (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 222—223°).

2,2-Dimethyl-5,6-benzochroman-4-one (X).—5-Bromo-5,6-dihydro-6,6-dimethylnaphtho-(2′,1′:2,3)pyran-4-ol (0·11 g.), acetic acid (5 c.c.), and chromium trioxide solution (see above) (0·3 c.c.) were set aside for 2 hr. at 50—60°. After isolation with ether and removal of solvent, the product (0·09 g.) was boiled with glacial acetic acid (5 c.c.) and zinc dust (1 g.) for 3 hr. Filtration and isolation with ether, followed by removal of solvent, gave a gum (0·5 g.) which with Brady's reagent afforded 2,2-dimethyl-5,6-benzochroman-4-one 2,4-dinitrophenylhydrazone,[3] m. p. and mixed m. p. 258—259° (0·01 g.).

3,4-Epoxy-2,2-dimethylchroman.—(*a*) 3-Bromo-2,2-dimethylchroman-4-ol (10·45 g.) and powdered potassium hydroxide (10 g.) in ether (250 c.c.) were stirred intermittently for 14 hr. during 5 days. Filtration and removal of solvent gave the *epoxide* (6·0 g., 97%), m. p. 29—30° (Found: C, 74·9; H, 7·0. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·8%).

(*b*) 3-Bromo-2,2-dimethylchroman-4-ol (0·79 g.) was set aside for 1 hr. with a solution of sodium ethoxide [from sodium (0·1 g.) and ethanol (3 c.c.)]. Addition of ether precipitated sodium bromide. After filtration and removal of solvent the product was taken up in light petroleum (b. p. 40°). Removal of the solvent then gave 3,4-epoxy-2,2-dimethylchroman, m. p. and mixed m. p. 27—29°. Boiling with ethanol gave *3-ethoxy-2,2-dimethylchroman-4-ol* (0·13 g., 29%) as needles, m. p. 85—86° (Found: C, 70·3; H, 8·1. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%).

3-Ethoxy- (VIIa) *and 3-Methoxy-2,2-dimethylchroman-4-ol* (VIId).—(*a*) 3,4-Epoxy-2,2-dimethylchroman (1·22 g.) was boiled with ethanol (18 c.c.) for 4 hr. The product was isolated

---

[2] Baker, Floyd, McOmie, Pope, Weaving, and Wild, *J.*, 1956, 2015.
[3] Livingstone, Miller, and Watson, *J.*, 1958, 2422.

with ether and dried ($CaCl_2$). Removal of the solvent and crystallisation of the residue from light petroleum (b. p. 40—60°) afforded 3-ethoxy-2,2-dimethylchroman-4-ol (0·94 g., 61%), m. p. and mixed m. p. 85—86° [*acetate*, m. p. 85—86°, from light petroleum (b. p. 40—60°) (Found: C, 67·9; H, 7·6. $C_{15}H_{20}O_4$ requires C, 68·1; H, 7·6%)].

3-*Methoxy*-2,2-*dimethylchroman*-4-*ol*, m. p. 112°, was similarly obtained [from light petroleum (b. p. 60—80°)] (65%) [*acetate*, needles, m. p. 70°, from light petroleum (b. p. 40°), at −15° (Found: C, 67·4; H, 7·5. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%)].

(*b*) 3,4-Epoxy-2,2-dimethylchroman (1·64 g.) was boiled with ethanol (20 c.c.) and concentrated sulphuric acid (2 drops) for 3¼ hr. Pouring the mixture into water gave a solid (0·27 g.) which on recrystallisation from ethyl acetate–ethanol afforded needles, m. p. 194—195° (Found: C, 74·6; H, 6·95. $C_{22}H_{24}O_4$ requires C, 75·0; H, 6·8%).

(*c*) 3-Bromo-2,2-dimethylchroman-4-yl acetate (0·74 g.), m. p. 63—63·5° [from light petroleum (b. p. 40°)], and a solution of sodium ethoxide [from sodium (0·08 g.) and ethanol (2 c.c.)] were boiled for 1 hr. and then poured into water. Crystallisation of the solid from light petroleum (b. p. 40—60°) gave 3-ethoxy-2,2-dimethylchroman-4-ol (0·39 g., 79%), m. p. and mixed m. p. 85—86°.

(*d*) 3-Bromo-2,2-dimethylchroman-4-ol (0·039 g.) and a solution of sodium methoxide [from sodium (0·035 g.) and methanol (3 c.c.)] were boiled for 2½ hr. to give 3-methoxy-2,2-dimethylchroman-4-ol (54·5%), m. p. and mixed m. p. 112°.

2,2-*Dimethylchroman*-3-*ol* (VIIb).—3,4-Epoxy-2,2-dimethylchroman (1·41 g.) in ether (40 c.c.) was added dropwise to lithium aluminium hydride (0·55 g.) in ether (30 c.c.), and the mixture refluxed for 2 hr. After the addition of dilute sulphuric acid the product was isolated with ether and dried (Na_2SO_4). Removal of the solvent gave 2,2-dimethylchroman-3-ol as a gum (1·08 g.) [*acetate* (1·02 g., 57·3%), m. p. 58—59°, from light petroleum (b. p. 40°), at −15°].[1]

Reduction of 3,4-*Epoxy*-2,2-*dimethylchroman and* 3-*Bromo*-2,2-*dimethylchroman*-4-*ol*.—Sodium amalgam (24 g.) and the compound (0·01 mole) in ethanol (20 c.c.) were set aside for 2 days. Isolation with ether gave a liquid which was converted into the acetate. Fractional crystallisation from light petroleum (b. p. 40°) gave 3-ethoxy-2,2-dimethylchroman-4-yl acetate, m. p. and mixed m. p. 85—86° (7—11%), and 2,2-dimethylchroman-3-yl acetate, m. p. and mixed m. p. 58—59° (4—11%).

Using methanol instead of ethanol for reduction of the oxide, isolation with ether followed by drying ($CaCl_2$) and removal of solvent gave a crystalline solid and gum. The solid left after dissolving the gum in light petroleum (b. p. 40°) gave, on recrystallisation from light petroleum (b. p. 60—80°), 3-methoxy-2,2-dimethylchroman-4-ol as needles, m. p. and mixed m. p. 112—112·5° (20%). The gum was converted into 2,2-dimethylchroman-3-yl acetate, m. p. and mixed m. p. 58—59° (16%).

2,2-*Dimethylchroman*-3,4-*diol* (VIIe).—(*a*) 3,4-Epoxy-2,2-dimethylchroman (1·33 g.) in ether (40 c.c.) and dilute sulphuric acid (1%; 50 c.c.) was set aside for 6 days. Isolation with ether followed by crystallisation from light petroleum (b. p. 80—100°) gave 2,2-*dimethylchroman*-3,4-*diol* (0·2 g., 13·7%), m. p. 57—58° (Found: C, 67·1; H, 7·2. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%).

(*b*) 3-Bromo-2,2-dimethylchroman-4-ol (0·7 g.) in acetone (10 c.c.) was boiled with potassium hydroxide (0·4 g.) in water (10 c.c.) for 3 hr. Isolation and crystallisation as above gave the diol (0·17 g., 32·3%), m. p. and mixed m. p. 57—58°.

3-*Bromo*-2,2-*dimethylchromen*.[1]—3-Bromo-2,2-dimethylchroman-4-ol (9·24 g.) was boiled in glacial acetic acid (50 c.c.) for 3 hr. Isolation with ether followed by distillation gave 3-bromo-2,2-dimethylchromen (5·45 g., 63·4%), b. p. 126—128°/10 mm.

The author thanks Professor P. Yates, University of Toronto, for his interest in this work. A grant from Imperial Chemical Industries Limited is gratefully acknowledged.

COLLEGE OF TECHNOLOGY, HUDDERSFIELD.

[*Received, February 8th*, 1961.]