982. *Reaction of Some Chromens and Naphthopyrans with Bromine and Chlorine. Part III* [1,2]

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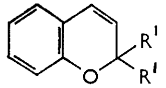
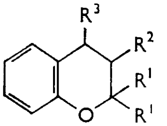
3,4-Dibromo-2,2-diphenylchroman, 3,4-dichloro-2,2-diphenylchroman, and 3,4-dichloro-2,2-dimethylchroman have been prepared, and some of the properties of their derivatives investigated, including the ring opening with hydrogen chloride of the epoxide derived from the bromohydrin.

2,2-DIMETHYL-[3] and 2,2-DIPHENYL-CHROMEN (Ia) and (Ib)[4] in chloroform reacted with chlorine to give the respective 3,4-dichloro-derivatives (IIa) and (IIb). Treatment of the dichloro-compounds in boiling acetone with a molecular proportion of an aqueous potassium hydroxide solution gave 3-chloro-2,2-dimethylchroman-4-ol (IIc) and 3-chloro-2,2-diphenylchroman-4-ol (IId) yielding on oxidation with chromium trioxide in acetic acid the 3-chlorochromanones (IIIa) and (IIIb), which, on boiling with zinc dust and acetic acid, afforded 2,2-dimethyl- and 2,2-diphenyl-chroman-4-one (IVa) and (IVb), respectively. Treatment of 3,4-dichloro-2,2-diphenylchroman in acetone with an aqueous solution of silver nitrate gave 3-chloro-2,2-diphenylchroman-4-yl nitrate (IIe). 3,4-Dibromo-2,2-diphenylchroman when caused to react under similar conditions gave a gum containing some of the nitrate derivative, which decomposed during attempts to crystallise, whereas 3,4-dibromo- and 3,4-dichloro-2,2-dimethylchroman gave the respective 3-halogenochroman-4-ol.

a; R^1 = Me
b; R^1 = Ph

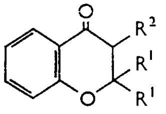


(I)

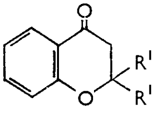


(II)

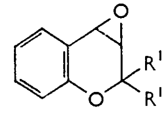
a; R^1 = Me, R^2 = R^3 = Cl
b; R^1 = Ph, R^2 = R^3 = Cl
c; R^1 = Me, R^2 = Cl, R^3 = OH
d; R^1 = Ph, R^2 = Cl, R^3 = OH
e; R^1 = Ph, R^2 = Cl, R^3 = NO_3
f; R^1 = Ph, R^2 = R^3 = Br
g; R^1 = Ph, R^2 = Br, R^3 = OH
h; R^1 = Me, R^2 = OH, R^3 = Cl
i; R^1 = Ph, R^2 = OH, R^3 = Cl
j; R^1 = Me, R^2 = OH, R^3 = OMe
k; R^1 = Ph, R^2 = OH, R^3 = OMe
l; R^1 = Me, R^2 = OH, R^3 = OEt
m; R^1 = Ph, R^2 = OH, R^3 = OEt
n; R^1 = Ph, R^2 = OH, R^3 = H
o; R^1 = Ph, R^2 = H, R^3 = OH



(III)
a; R^1 = Me, R^2 = Cl
b; R^1 = Ph, R^2 = Cl
c; R^1 = Ph, R^2 = Br



(IV)
a; R^1 = Me
b; R^1 = Ph



(V)
a; R^1 = Me
b; R^1 = Ph

2,2-Diphenylchromen (Ib)[4] in chloroform reacted with bromine to give 3,4-dibromo-2,2-diphenylchroman (IIf). 3-Bromo-2,2-diphenylchroman-4-ol (IIg), unlike the corresponding 2,2-dimethyl compound,[2] was not obtained on shaking the dibromochroman in acetone with one molecular proportion of potassium hydroxide in water. The chromanol (IIg) was only obtained on boiling as in the preparation of the chlorohydrins (IIc) and (IId).

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[1] Part I, R. Livingstone, D. Miller, and S. Morris, *J.*, 1960, 3094.
[2] Part II, R. Livingstone, *J.*, 1962, 76.
[3] R. L. Shriner and A. G. Sharp, *J. Org. Chem.*, 1939, **4**, 475.
[4] A. Löwenbein, *Ber.*, 1924, **57**, 1517.

Oxidation of the bromohydrin with chromium trioxide in acetic acid gave 3-bromo-2,2-diphenylchroman-4-one (IIIc), which on boiling with zinc dust and glacial acetic acid afforded 2,2-diphenylchroman-4-one (IVb).[5]

3-Bromo-2,2-diphenylchroman-4-ol (IIg) on prolonged stirring in dry ether with powdered potassium hydroxide yielded 3,4-epoxy-2,2-diphenylchroman (Vb), also obtained when the bromohydrin (IIg) was boiled with an aqueous acetone solution of potassium hydroxide. The epoxides (Va)[2] and (Vb) reacted with hydrogen chloride in dry ether to give 4-chloro-2,2-dimethyl- and 4-chloro-2,2-diphenyl-chroman-3-ol (IIh) and (IIi). The chlorochromanols (IIh) and (IIi) on boiling with methanol gave 4-methoxy-2,2-dimethyl- and 4-methoxy-2,2-diphenyl-chroman-3-ol (IIj) and (IIk), identical with the compounds obtained on boiling 3,4-epoxy-2,2-dimethyl- and -2,2-diphenyl-chroman with methanol, and methanol containing a trace of acid or alkali, respectively. Under the same conditions with ethanol the 4-ethoxy-derivatives (IIl) and (IIm) were obtained from the 4-chlorochromanols and the epoxides. Boiling with either methanol or ethanol alone had no effect on 3,4-epoxy-2,2-diphenylchroman. The methoxy- and ethoxy-compounds obtained from 3,4-epoxy-2,2-dimethylchroman had been given previously the wrong orientation namely 3-methoxy- and 3-ethoxy-2,2-dimethylchroman-4-ol.[2] Attempts to oxidise the methoxychromanols (IIj) and (IIk) to the 3-chromanones either with chromic oxide in acetic acid or by an Oppenauer reaction using aluminium isopropoxide and an acetone–benzene or a cyclohexanone–xylene mixture were unsuccessful.

Shaking 3,4-epoxy-2,2-diphenylchroman and platinum oxide in ethyl acetate with hydrogen afforded 2,2-diphenylchroman-3-ol (IIm) and not 2,2-diphenylchroman-4-ol(IIo).

EXPERIMENTAL

3,4-*Dichloro*-2,2-*dimethylchroman*.—Chlorine [from potassium permanganate (4·6 g.) and concentrated hydrochloric acid] was passed into a solution of 2,2-dimethylchroman (10·0 g.) in chloroform (125 ml.). Removal of the solvent afforded a colourless gum; recrystallisation from light petroleum (b. p. below 40°) gave 3,4-*dichloro*-2,2-*dimethylchroman* (8·35 g., 62%) as plates, m. p. 59—60° (Found: C, 57·35; H, 5·2; Cl, 30·7. $C_{11}H_{12}Cl_2O$ requires C, 57·1; H, 5·2; Cl, 30·7%).

3-*Chloro*-2,2-*dimethylchroman*-4-*ol*.—3,4-Dichloro-2,2-dimethylchroman (4·7 g.), in acetone (35 ml.) and water (20 ml.), was boiled with potassium hydroxide (1·2 g.) for 2·5 hr.; pouring on to water followed by filtration afforded a solid. Recrystallisation from light petroleum (b. p. 40—60°) gave 3-*chloro*-2,2-*dimethylchroman*-4-*ol* (2·55 g., 61%) as needles, m. p. 77—78° (Found: C, 62·0; H, 6·0; Cl, 15·8. $C_{11}H_{13}ClO_2$ requires C, 62·1; H, 6·1; Cl, 16·7%).

3-*Chloro*-2,2-*dimethylchroman*-4-*one*.—3-Chloro-2,2-dimethylchroman-4-ol (0·69 g.) in acetic acid (5 ml.) and chromic oxide solution [from chromic oxide (9·5 g.) in water (6·5 ml.) and acetic acid (53 ml.)] (2 ml.) was set aside for 2 hr. at 70°. Pouring into water gave an oil which was isolated with ether and chromatographed on alumina from benzene affording a gum. Recrystallisation from light petroleum (b. p. <40°) gave 3-*chloro*-2,2-*dimethylchroman*-4-*one* (0·50 g., 73%) as needles, m. p. 57—58° (Found: C, 63·0; H, 5·3; Cl, 16·9. $C_{11}H_{11}ClO_2$ requires C, 62·7; H, 5·2; Cl, 16·5%).

2,2-*Dimethylchroman*-4-*one*.—3-Chloro-2,2-dimethylchroman-4-one (0·33 g.) was boiled with powdered zinc (1·0 g.) and acetic acid (10 ml.) for 1 hr. Filtration followed by pouring into water afforded a solid. Recrystallisation from light petroleum (b. p. 40—60°) gave 2,2-dimethylchroman-4-one (0·15 g., 55%) as colourless needles, m. p. and mixed m. p. 88—89°.

4-*Chloro*-2,2-*dimethylchroman*-3-*ol*.—A stirred solution of 3,4-epoxy-2,2-dimethylchroman (3·0 g.) in dry ether (100 c.c.) was saturated with dry hydrogen chloride. After stirring for a further 2 hr. removal of the solvent at room temperature afforded a gummy solid. Recrystallisation from light petroleum (b. p. 40—60°) gave 4-*chloro*-2,2-*dimethylchroman*-3-*ol* (1·23 g., 34%) as needles, m. p. 83—84, mixed m. p. 60—65° with 3-chloro-2,2-dimethylchroman-4-ol (Found: C, 62·0; H, 6·1; Cl, 15·7%).

4-*Methoxy*-2,2-*dimethylchroman*-3-*ol*.—4-Chloro-2,2-dimethylchroman-3-ol (0·2 g) was boiled with methanol (25 c.c.) for 2 hr. Removal of the solvent followed by recrystallisation from

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[5] J. Cottam, R. Livingstone, M. Walshaw, K. D. Bartle and D. W. Jones, preceding Paper.

light petroleum (b. p. 60—80°) yielded 4-methoxy-2,2-dimethylchroman-3-ol (0·16 g., 78%) as needles, m. p. and mixed m. p. 111—112°.

4-*Ethoxy*-2,2-*dimethylchroman*-3-*ol*.—4-Chloro-2,2-dimethylchroman-3-ol (0·01 g.) was boiled with ethanol (10 c.c.) for 2 hr. Removal of the solvent followed by recrystallisation from light petroleum (b. p. 80—100°) afforded 4-ethoxy-2,2-dimethylchroman-3-ol (0·007 g., 67%), m. p. and mixed m. p. 85—86°.

3,4-*Dibromo*-2,2-*diphenylchroman*.—Bromine (1·45 c.c.) in chloroform (20 c.c.) was added to 2,2-diphenylchromen (7·9 g.) in chloroform (10 c.c.) during 10 min., the temperature being kept below 20°. Removal of the solvent afforded a gum which on recrystallisation from light petroleum (b. p. 100—120°) yielded 3,4-*dibromo*-2,2-*diphenylchroman* (11·0 g., 89%), m. p. 137—138°) (Found: C, 56·5; H, 3·7. $C_{21}H_{16}Br_2O$ requires C, 56·8; H, 3·6%).

3,4-*Dichloro*-2,2-*diphenylchroman*.—Chlorine (from potassium permanganate and concentrated hydrochloric acid) in 10% excess was bubbled through a solution of 2,2-diphenylchromen (10 g.) in chloroform (150 ml.). Removal of the solvent and addition of light petroleum (b. p. below 40°) afforded a gummy solid. Recrystallisation from light petroleum (b. p. 60—80°) gave 3,4-*dichloro*-2,2-*diphenylchroman* (7·2 g., 57·5%), m. p. 99—100° (Found: C, 70·7; H, 4·6; Cl, 20·2. $C_{21}H_{16}Cl_2O$ requires C, 71·0; H, 4·5; Cl, 20·0%).

3-*Bromo*-2,2-*diphenylchroman*-4-*ol*.—(*a*) 2,2-Diphenylchromen (0·73 g.) in ether (10 ml.) was shaken intermittently with a solution of hypobromous acid (25 c.c.) for 2 hr. After separation, the ether layer was washed with sodium hydrogen carbonate solution followed by water, and then dried (Na_2SO_4). Removal of the solvent gave a gum which, on recrystallisation from light petroleum (b. p. 80—100°), afforded 3-bromo-2,2-diphenylchroman (0·08 g., 8·2%), m. p. 140—141°.

(*b*) 3,4-Dibromo-2,2-diphenylchroman (11·0 g.) in acetone (80 c.c.) was boiled with potassium hydroxide (1·4 g.) in water (13 c.c.) for 2 hr. Pouring into water afforded a gum which was isolated with ether and recrystallised from light petroleum (b. p. 80—100°) to give 3-*bromo*-2,2-*diphenylchroman*-4-*ol* (3·7 g., 39%), m. p. and mixed m. p. 139—141° (Found: C, 65·7; H, 4·5; Br, 18·8. $C_{21}H_{17}BrO_2$ requires C, 66·1; H, 4·5; Br, 21·0%).

3-*Chloro*-2,2-*diphenylchroman*-4-*ol*.—3,4-Dichloro-2,2-diphenylchroman (0·5 g.) was boiled with potassium hydroxide (0·11 g.) in acetone (15 c.c.) and water (8 c.c.) for 10 hr. Pouring into water and isolation with ether gave a gum (0·4 g.) which was chromatographed on alumina (type H) from benzene to give an uncharacterised gum (0·18 g.). Further elution with methanol afforded a white solid. Recrystallisation from light petroleum (b. p. 80—100°)–cyclohexane yielded 3-*chloro*-2,2-*diphenylchroman*-4-*ol* (0·13 g., 27·5%), m. p. 115—118°, mixed m. p. with 4-chloro-2,2-diphenylchroman-3-ol 80—85° (Found: C, 72·9; H, 5·0; Cl, 9·7. $C_{21}H_{17}ClO_2$ requires C, 73·3; H, 5·1; Cl, 9·2%); acetate, m. p. 163—164° (from methanol).

3-*Bromo*-4-*methoxy*-2,2-*diphenylchroman*.—(*a*) 3-Bromo-2,2-diphenylchroman-4-ol (0·27 g.) was refluxed with methanol (10 c.c.) saturated with dry hydrogen chloride for 3 hr. Concentration and cooling gave 3-bromo-4-methoxy-2,2-diphenylchroman (0·24 g., 82%), m. p. 131—132°.

(*b*) 3,4-Dibromo-2,2-diphenylchroman (0·47 g.) was boiled with methanol (15 c.c.) and methanol saturated with dry hydrogen chloride (2 c.c.) for 3 hr. Concentration and cooling yielded 3-*bromo*-4-*methoxy*-2,2-*diphenylchroman* (0·35 g., 84%), m. p. and mixed m. p. 131—132° (Found: C, 66·8; H, 5·0; Br, 20·25; OMe, 9·2. $C_{22}H_{19}BrO_2$ requires C, 66·45; H, 4·9; Br, 20·2; OMe, 7·9%).

3-*Chloro*-2,2-*diphenylchroman*-4-*yl Nitrate*.—3,4-Dichloro-2,2-diphenylchroman (1·1 g.) in acetone (30 c.c.) and silver nitrate (1·0 g.) in water (10 c.c.) were set aside for 10 min. After removal of the silver bromide by filtration, pouring into water and isolation with ether afforded a gum which crystallised on addition of methanol. Recrystallisation from light petroleum (b. p. 100—120°) gave 3-*chloro*-2,2-*diphenylchroman*-4-*yl nitrate* (0·6 g., 50%) as colourless crystals, m. p. 127—128° (Found: C, 66·1; H, 4·2; N, 3·7; Cl, 9·3. $C_{21}H_{16}ClNO_4$ requires C, 66·1; H, 4·2; N, 3·6; Cl, 9·5%).

3-*Bromo*-2,2-*diphenylchroman*-4-*one*.—3-Bromo-2,2-diphenylchroman-4-ol (2·12 g.) and chromic oxide solution (5 c.c.) [from chromic oxide (9·5 g.), water (6·5 c.c.) and acetic acid (53 c.c.)] were set aside for 2·5 hr. at 60—70°. Pouring into water gave a white solid, m. p. 194—195°. Recrystallisation from light petroleum (b. p. 100—120°) yielded 3-*bromo*-2,2-*diphenylchroman*-4-*one* (1·85 g., 87%), m. p. 195° (Found: C, 66·5; H, 4·0; Br, 21·1. $C_{21}H_{15}BrO_2$ requires C, 66·45; H, 3·8; Br, 19·8%).

3-*Chloro*-2,2-*diphenylchroman*-4-*one*.—3-Chloro-2,2-diphenylchroman-4-ol (0·8 g.) and chromic oxide solution (3 c.c.) were set aside for 1 hr. at 70°. Pouring into water and isolation with ether afforded a pale yellow solid. Elution down a short column of alumina (type H) with benzene followed by recrystallisation from light petroleum (b. p. 100—120°) gave 3-*chloro*-2,2-*diphenylchroman*-4-*one* (0·4 g., 50%) as colourless crystals, m. p. 159—160° (Found: C, 75·8; H, 4·5; Cl, 10·45. $C_{21}H_{15}ClO_2$ requires C, 75·3; H, 4·5; Cl, 10·6%).

2,2-*Diphenylchroman*-4-*one*.—(*a*) Zinc dust (1·0 g.) was added over 1 hr. to 3-bromo-2,2-diphenylchroman-4-one (0·35 g.) in acetic acid (5 c.c.) at 80—90°. Following filtration the addition of a few drops of water afforded a white solid. Recrystallisation from light petroleum (b. p. 60—80°) gave 2,2-diphenylchroman-4-one (0·11 g., 40%), m. p. 136—137°.

(*b*) 3-Chloro-2,2-diphenylchroman-4-one (0·3 g.) in acetic acid (10 c.c.) was boiled with zinc dust (1·0 g.) for 1 hr. Filtration, followed by pouring into water and isolation with ether, afforded a gum (0·22 g.). Elution down a short column of activated alumina (type H) with benzene, followed by recrystallisation from light petroleum (b. p. 60—80°), gave 2,2-diphenylchroman-4-one (0·15 g., 56%), m. p. and mixed m. p. 136—138°.

3,4-*Epoxy*-2,2-*diphenylchroman*.—(*a*) 3-Bromo-2,2-diphenylchroman-4-ol (8·5 g.) and powdered potassium hydroxide (9 g.) in dry ether were set aside with intermittent stirring for 3 days. Filtration, followed by removal of solvent, yielded a gum. Recrystallisation from methanol gave 3,4-epoxy-2,2-diphenylchroman, m. p. 111°.

(*b*) Potassium hydroxide (0·24 g.) in water (3 c.c.) was added to 3-bromo-2,2-diphenylchroman-4-ol (0·40 g.) in acetone (10 c.c.). Boiling for 3 hr., followed by pouring into water, filtration, and recrystalisation from methanol yielded 3,4-*epoxy*-2,2-*diphenylchroman* (0·35 g., 90·5%), m. p. and mixed m. p. 109—111° (Found: C, 83·9; H, 5·5. $C_{21}H_{16}O_2$ requires C, 84·0; H, 5·3%).

4-*Chloro*-2,2-*diphenylchroman*-3-*ol*.—3,4-Epoxy-2,2-diphenylchroman (0·28 g.) in dry ether (15 c.c.) was saturated with dry hydrogen chloride and set aside for 0·5 hr. Removal of the solvent and recrystallisation from light petroleum (b. p. 60—80°) gave 4-*chloro*-2,2-*diphenylchroman*-3-*ol* (0·18 g., 53%), m. p. 143—144° (Found C, 75·3; H, 5·3; Cl, 10·4. $C_{21}H_{17}ClO_2$ requires C, 74·9; H, 5·05; Cl, 10·55%).

4-*Methoxy*-2,2-*diphenylchroman*-3-*ol*.—(*a*) 3,4-Epoxy-2,2-diphenylchroman (0·35 g.) was refluxed with potassium hydroxide (0·2 g.) in methanol (10 c.c.) for 0·5 hr. Pouring into dilute hydrochloric acid followed by filtration, drying, and recrystallisation from light petroleum (b. p. 60—80°) yielded 4-*methoxy*-2,2-*diphenylchroman*-3-*ol* (0·14 g., 36%), m. p. 149—150°.

(*b*) 3,4-Epoxy-2,2-diphenylchroman (1·37 g.) was refluxed with methanol (50 c.c.) containing sulphuric acid (1 drop) for 1 hr. Pouring into water followed by filtration, drying, and recrystallisation from light petroleum (b. p. 60—80°) gave 4-methoxy-2,2-diphenylchroman-3-ol (1·31 g., 86%), m. p. and mixed m. p. 149—150°.

(*c*) 4-Chloro-2,2-diphenylchroman-3-ol (0·019 g.) was boiled with methanol (7 c.c.) for 3 hr. Removal of solvent followed by recrystallisation from light petroleum (b. p. 60—80°) gave 4-*methoxy*-2,2-*diphenylchroman*-3-*ol* (0·15 g., 80%), m. p. and mixed m. p. 148—150° (Found: C, 79·2; H, 6·0; OMe, 8·5. $C_{22}H_{20}O_3$ requires C, 79·5; H, 6·1; OMe, 9·3%).

4-*Ethoxy*-2,2-*diphenylchroman*-3-*ol*.—(*a*) 3,4-Epoxy-2,2-diphenylchroman (0·41 g.) was refluxed with potassium hydroxide (0·2 g.) in ethanol (10 c.c.) for 0·5 hr. Pouring into water followed by filtration, drying, and recrystallisation from light petroleum (b. p. 60—80°) gave 4-ethoxy-2,2-diphenylchroman-3-ol (0·17 g., 36%), m. p. 146—147°.

(*b*) 3,4-Epoxy-2,2-diphenylchroman (0·28 g.) was boiled with ethanol (10 c.c.) containing sulphuric acid (1 drop). Pouring into water followed by filtration, drying, and recrystallisation from light petroleum (b. p. 60—80°) afforded 4-ethoxy-2,2-diphenylchroman-3-ol, (0·21 g., 65%), m. p. and mixed m. p. 146—147°.

(*c*) 4-Chloro-2,2-diphenylchroman-3-ol (0·021 g.) was boiled with ethanol (8 c.c.) for 3 hr. Removal of the solvent and recrystallisation from light petroleum (b. p. 40—60°) gave 4-*ethoxy*-2,2-*diphenylchroman*-3-*ol* (0·007 g., 29%), m. p. and mixed m. p. 146—147° (Found: C, 79·8; H, 6.6. $C_{23}H_{22}O_3$ requires C, 79·7; H, 6·4%).

2,2-*Diphenylchroman*-3-*ol*.—3,4-Epoxy-2,2-diphenylchroman (0·47 g.) in ethyl acetate (20 c.c.) and platinum oxide (0·06 g.) were shaken with hydrogen. Filtration followed by removal of solvent and recrystallisation from light petroleum (b. p. 60—80°) gave 2,2-*diphenylchroman*-3-*ol* (0·28 g., 59%), m. p. 115° (Found: C, 83·5; H, 5·8. $C_{21}H_{18}O_2$ requires C, 83·4; H, 6·0%).

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One of us (R. L.) wishes to correct a mis-statement of a communication from Professor P. Yates in the summary of Part II.[2] For "chromanones give different products on reduction with lithium aluminium hydride and" *read* "the 3-bromochroman-4-ol could give possibly 3-chromanol *via* the epoxide on reduction with."

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