618. *Reaction of Some Chromens and Naphthopyrans with Bromine. Part I.*

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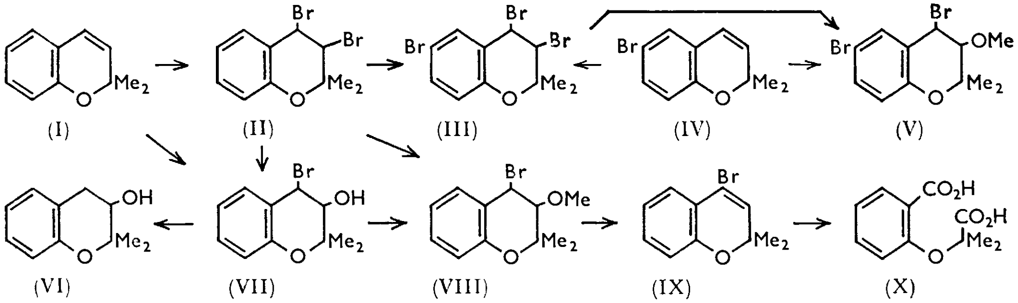
The action of bromine on 2,2-dimethylchromens and 6,6-dimethylnaphthopyrans resulted in addition or substitution products, depending on the conditions. Treatment of the addition products with dilute methanolic hydrogen chloride resulted in replacement of the bromine atom attached to the carbon atom adjacent to the *gem*-dimethyl group by a methoxyl group.

TREATING 2,2-dimethylchromen [1] (I) in chloroform or carbon disulphide with bromine gives, first, 3,4-dibromo- (II) and then 3,4,6-tribromo-2,2-dimethylchroman (III). The 3-bromine atom in each of these products is reactive, for treatment with methanolic hydrogen chloride affords 4-bromo- (VIII) and 4,6-dibromo-3-methoxy-2,2-dimethylchroman (V) respectively, the former of which is also obtained by methylating the bromohydrin (VII) that is formed on reaction of the chromen (I) with hypobromous acid. 4-Bromo-3-methoxy-2,2-dimethylchroman with boiling acetic acid yields 4-bromo-2-dimethylchromen (IX). Moreover, the dibromo-derivative (II) with an equimolar amount of boiling aqueous potassium hydroxide gave the bromohydrin (VII).



The tribromo-compound (III) was also obtained by addition of bromine to 6-bromo-2,2-dimethylchromen (IV) (obtained [2] by reaction of methylmagnesium iodide with 6-bromocoumarin).

Somewhat similar results were obtained with 6,6-dimethylnaphtho(2′,1′:2,3)pyran [3]

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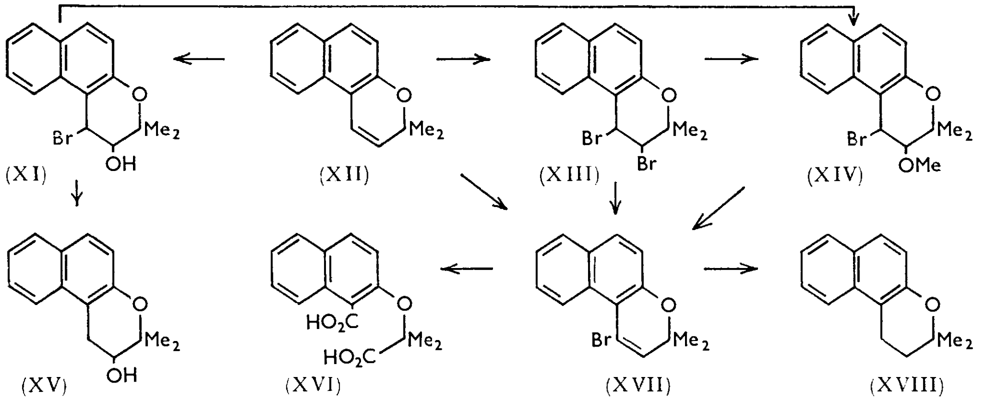
[1] Shriner and Sharp, *J. Org. Chem.*, 1939, **4**, 575.
[2] Pandya and Pandya, *Proc. Indian Acad. Sci.*, 1943, **18**, *A*, 164.
[3] Livingstone, Miller, and Watson, *J.*, 1958, 2422.

(XII). With bromine in carbon disulphide it gave the addition product (XIII), but in chloroform the substitution product (XVII) was formed. The dibromo-product (XIII) with methanolic hydrogen chloride gave the 4-bromo-5-methoxy-derivative (XIV), which was also obtained by methylation of the bromohydrin (XI), prepared together with the monobromo-derivative (XVII) by the action of hypobromous acid on the parent naphthopyran (XII) in ether. Pyrolysis of 4,5-dibromo- or 4-bromo-4,5-dihydro-5-methoxy-6,6-dimethylnaphtho(2′,1′:2,3)pyran gave 4-bromo-6,6-dimethylnaphtho(2′,1′:2,3)pyran (XII).

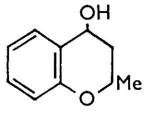
The monobromo-derivatives (IX) and (XVII) with potassium permanganate in acetone gave acids (X) and (XVI), identical with those afforded by oxidation of 2,2-dimethylchromen (I) and 6,6-dimethylnaphtho(2′,1′:2,3)pyran (XII), respectively, indicating absence of substitution in the aromatic nucleus. Hydrogenation of these monobromo-derivatives over platinum gave the bromine-free 2,2-dimethylchroman and the dihydronaphthopyran (XVIII) respectively, ruling out the possibility of molecular rearrangement during their formation from the dibromo-compounds (II) and (XIII).

The compounds described were inter-related and their structures proved partly by the above reactions and in addition as follows. The bromohydrins (VII) and (XI) were reduced by sodium amalgam in ethanol to the corresponding hydroxy-derivatives (VI) and (XV), different from the hydroxy-compounds (XIX) and which were obtained by reduction of the respective chromanones [2,4] with lithium aluminium hydride.

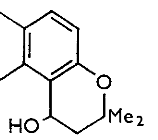


Attempts to isolate 4,6-dibromo-2,2-dimethylchroman-3-ol, the dibromo-analogue of (VI), after treatment of the tribromo-derivative (III) with aqueous potassium hydroxide were unsuccessful. As a result it was not possible to obtain 6-bromo-2,2-dimethylchroman-3-ol and thus ascertain the position of the methoxy-group in 4,6-dibromo-3-methoxy-2,2-dimethylchroman (V); this is, however, assumed by analogy with the methoxy-compounds (VIII) and (XIV).

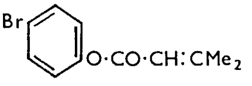
6-Bromo-2,2-dimethylchroman-4-one (XXII) was obtained by extension of the method



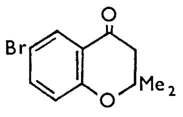
(XIX)



(XX)



(XXI)



(XXII)

of Cavill *et al.*[5] for preparation of substituted chromanones, namely, by esterification of *p*-bromophenol with 3-methylbut-2-enoyl chloride, Fries rearrangement of the product (XXI), and ring closure in the absence of a solvent.

The reactivity of the bromine atom attached to the carbon atom adjacent to the

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[4] Baker, Floyd, McOmie, Pope, Weaving, and Wild, *J.*, 1956, 2015.

[5] Cavill, Dean, McGookin, Marshall, and Robertson, *J.*, 1954, 4173.

gem-dimethyl group is surprising when compared with the relative inactivity of the other bromine atoms contained in the above-mentioned di- and tri-bromo-derivatives.

EXPERIMENTAL

Bromination of Chromen and Pyrans.—Bromine (0·1 mole) in chloroform (50 c.c.) was added at $-15°$ to the chromen or pyran (0·1 mole) dissolved in chloroform (70 c.c.). The solvent was removed immediately at $<50°$ and the product recrystallised from light petroleum (b. p. 40—60°). The following were thus obtained.

3,4-*Dibromo*-2,2-*dimethylchroman* (II) (from 2,2-dimethylchromen), m. p. 81—82° (82%) (Found: C, 41·8; H, 4·1; Br, 50·7. $C_{11}H_{12}OBr_2$ requires C, 41·3; H, 3·8; Br, 50·0%).

4-*Bromo*-6,6-*dimethylnaphtho*(2′,1′:2,3)*pyran* (XVII) (bromination mixture in chloroform set aside for 3 days), m. p. 81—82° (31%) (Found: C, 62·6; H, 4·4; Br, 26·2. $C_{15}H_{13}OBr$ requires C, 62·3; H, 4·5; Br, 27·6%).

4,5-*Dibromo*-4,5-*dihydro*-6,6-*dimethylnaphtho*(2′,1′:2,3)*pyran* (XIII) (bromination mixture in carbon disulphide set aside overnight at $-15°$), m. p. 97—98° (43%) (Found: C, 48·6; H, 3·9; Br, 43·9. $C_{15}H_{14}OBr_2$ requires C, 48·65; H, 3·8; Br, 44·05%).

For the preparation of 3,4,6-*tribromo*-2,2-*dimethylchroman* (III) from 3,4-dibromo-2,2-dimethylchroman or 2,2-dimethylchromen, the mixture containing 1 or 2 mol. respectively of bromine was set aside overnight, then washed with sodium hydrogen sulphite solution and water, and dried (Na_2SO_4). Removal of solvent and recrystallisation gave material (14—17%) of m. p. 60° (Found: C, 33·2; H, 2·8; Br, 60·7. $C_{11}H_{11}OBr_3$ requires C, 33·1; H, 2·8; Br, 60·15%).

Action of Bromine Water on 6,6-*Dimethylnaphtho*(2′,1′:2,3)*pyran.*—6,6-Dimethylnaphtho-(2′,1′:2,3)pyran (2·3 g.) was treated in ether (40 c.c.) with saturated bromine water (60 c.c.) and water (60 c.c.). After ½ hr., the ether layer was separated, washed with dilute sodium hydroxide solution and water, and dried (Na_2SO_4). Removal of the solvent gave a yellow gum (3·3 g.) which on crystallisation from light petroleum (b. p. 80—100°) yielded 4-*bromo*-4,5-*dihydro*-6,6-*dimethylnaphtho*(2′,1′:2,3)*pyran*-5-*ol* as needles, m. p. 140° (1·0 g., 30%) (Found: C, 58·2; H, 5·1; Br, 26·3. $C_{15}H_{15}O_2Br$ requires C, 58·7; H, 4·9; Br, 26·1%).

A second crop of crystals was obtained (m. p. 76—78°; 0·6 g., 20%); when recrystallised from methanol, it was 4-bromo-6,6-dimethylnaphtho(2′,1′,2,3)pyran, m. p. and mixed m. p. 80—81°.

Formation of Methoxy-compounds.—The dibromo- or the bromo-hydroxy-derivative (0·1 mole) was boiled with methanol (230 c.c.) and methanolic hydrogen chloride (saturated in the cold) (70 c.c.) for 3 hr. The product was isolated with ether, and recrystallised, to give the following compounds:

4-*Bromo*-3-*methoxy*-2,2-*dimethylchroman* (VIII) (from 3,4-dibromo- or 4-bromo-3-hydroxy-2,2-dimethylchroman), m. p. 74° (44%) [from light petroleum (b. p. 40—60°)] (Found: C, 53·2; H, 5·6; Br, 30·1; OMe, 10·4. $C_{12}H_{15}O_2Br$ requires C, 53·1; H, 5·5; Br, 29·5; OMe, 11·4%).

4,6-*Dibromo*-3-*methoxy*-2,2-*dimethylchroman* (V) (from 3,4,6-tribromo-2,2-dimethylchroman), m. p. 54° (88%) [from light petroleum (b. p. 40—60°)] (Found: C, 41·7; H, 3·8; Br, 45·6. $C_{12}H_{14}O_2Br_2$ requires C, 41·2; H, 4·0; Br, 45·6%).

4-*Bromo*-4,5-*dihydro*-5-*methoxy*-6,6-*dimethylnaphtho*(2′,1′:2,3)*pyran* (XIV) [from 4,5-dibromo-4,5-dihydro- or 4-bromo-4,5-dihydro-6,6-dimethylnaphtho(2′,1′:2,3)pyran-5-ol; solution boiled for ¼ hr.; solid separated on cooling], needles, m. p. 112—113° (67%) (from methanol) (Found: C, 59·5; H, 5·4; Br, 25·2; OMe, 10·2. $C_{16}H_{17}O_2Br$ requires C, 59·8; H, 5·3; Br, 24·9; OMe, 9·65%).

Preparation of Bromo-hydroxy-derivatives.—The chroman or naphthopyran(0·01 mole) was treated in ether (60 c.c.) with aqueous hypobromous acid (120 c.c.) [prepared by the action of mercuric oxide on saturated bromine water (60 c.c.) and water (60 c.c.)]. After ½ hr., the ether layer was separated, washed with dilute sodium hydroxide solution and water, and dried (Na_2SO_4). Removal of the solvent followed by crystallisation gave the following derivatives:

4-*Bromo*-2,2-*dimethylchroman*-3-*ol* (VII) (from 2,2-dimethylchroman), m. p. 106° (17%) [from light petroleum (b. p. 40—60°)] (Found: C, 52·0; H, 5·4; Br, 32·4. $C_{11}H_{13}O_2Br$ requires C, 51·4; H, 5·1; Br, 31·1%).

4-Bromo-4,5-dihydro-6,6-dimethylnaphtho(2′,1′:2,3)pyran-5-ol (XI) [from 6,6-dimethylnaphtho(2′,1′:2,3)pyran], needles, m. p. 139—140° (78%) [from light petroleum (b. p. 80—100°)].

4-*Bromo*-2,2-*dimethylchroman*-3-*ol* (VII).—3,4-Dibromo-2,2-dimethylchroman (0·1 mole) was boiled with potassium hydroxide (0·1 mole) and water (360 c.c.) for 1⅓ hr. A solid separated on cooling, which on recrystallisation from light petroleum (b. p. 60—80°) gave 4-bromo-2,2-dimethylchroman-3-ol, m. p. 106° (44%).

4-*Bromo*-6,6-*dimethylnaphtho*(2′,1′:2,3)*pyran*.—(*a*) 4,5-Dibromo-4,5-dihydro-6,6-dimethylnaphtho(2′1′:2,3)pyran (0·24 g.) was heated for 3 min. at 110° until evolution of hydrogen bromide ceased and then at 150° for 5 min. Crystallisation from ethanol gave 4-bromo-6,6-dimethylnaphtho(2′,1′:2,3)pyran as needles, m. p. and mixed m. p. 81—82° (0·1 g., 53%).

(*b*) 4-Bromo-4,5-dihydro-5-methoxy-6,6-dimethylnaphtho(2′,1′:2,3)pyran (1 g.) was heated at 190° for 5 min. On cooling, a brown gum was obtained which on crystallisation from ethanol gave the preceding product, m. p. and mixed m. p. 81—82° (0·58 g., 64%).

4-*Bromo*-2,2-*dimethylchromen*.—4-Bromo-3-methoxy-2,2-dimethylchroman (0·96 g.) was boiled in glacial acetic acid (10 c.c.) for 3½ hr. Isolation with ether followed by distillation gave 4-*bromo*-2,2-*dimethylchromen*, b. p. 86°/6 mm. (Found: C, 55·8; H, 4·8; Br, 35·5. $C_{11}H_{11}OBr$ requires C, 55·2; H, 4·6; Br, 33·5%).

Oxidation of Chromens, Naphthopyrans, and Bromo-derivatives.—The compound (0·01 mole), powdered potassium permanganate (0·05 mole), and acetone (50 c.c.) were refluxed for 6 hr., then cooled, and the mixture was filtered. The residue was suspended in water (100 c.c.), acidified with dilute sulphuric acid, and treated with sulphur dioxide until the manganese dioxide had dissolved. Isolation with ether followed by crystallisation from benzene gave o-(1-*carboxy*-1-*methylethoxy*)*benzoic acid* (X) (from 2,2-dimethylchromen or 4-bromo-2,2-dimethylchromen), needles, m. p. 116—117° (62%) (Found: C, 58·6; H, 5·3. $C_{11}H_{12}O_5$ requires C, 58·9; H, 5·4%), and 2-(1-*carboxy*-1-*methylethoxy*)-1-*naphthoic acid* (XVI) [from 6,6-dimethyl- or 4-bromo-6,6-dimethyl-naphtho(2′,1′:2,3)pyran], plates, m. p. 118° (65%) (Found: C, 66·0; H, 5·4. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·1%).

6-*Bromo*-2,2-*dimethylchromen*.—6-Bromocoumarin (1·32 g.) in dry benzene (20 c.c.) was added during ½ hr. to a stirred solution from methyl iodide (2 c.c.), magnesium (0·8 g.), and ether (15 c.c.). The solution was refluxed for 1½ hr. and set aside overnight. Decomposition with 22% ammonium chloride solution and extraction with ether gave an ethereal solution, which was washed with water and dried (Na_2SO_4). Removal of the solvent left a gum which was boiled with glacial acetic acid (15 c.c.) for 4 hr. Cooling the solution and pouring it into water, isolation of the product with ether, and distillation gave 6-*bromo*-2,2-*dimethylchromen* (0·24 g.), b. p. 116°/5 mm. (Found: C, 55·8; H, 4·8; Br, 35·5. $C_{11}H_{11}OBr$ requires C, 55·2; H, 4·6; Br, 33·5%). With bromine (as above) this gave 3,4,6-tribromo-2,2-dimethylchroman, m. p. and mixed m. p. 60° (0·30 g., 77%).

p-*Bromophenyl* 3-*Methylbut*-2-*enoate* (XXI).—*p*-Bromophenol (10 g.), 3-methylbut-2-enoyl chloride (6·9 g.), and magnesium (1·5 g.) were refluxed in benzene (50 c.c.) for 2 hr., yielding the *ester*, b. p. 123—127°/1 mm., m. p. 25—26° (10·07 g., 77%) (Found: C, 52·0; H, 4·4; Br, 31·1. $C_{11}H_{11}O_2Br$ requires C, 51·8; H, 4·3; Br, 31·4%).

6-*Bromo*-2,2-*dimethylchroman*-4-*one*.—The ester (XXI) (2·05 g.) and aluminium chloride (2·0 g.) were heated at 90° for 2 hr. and on decomposition with 2N-hydrochloric acid and extraction with ether gave a solid (0·94 g.). Recrystallisation from light petroleum (b. p. 60—80°) gave 6-*bromo*-2,2-*dimethylchroman*-4-*one* as needles, m. p. 105—106° (0·3 g.) (Found: C, 52·0; H, 4·4; Br, 31·3. $C_{11}H_{11}O_2Br$ requires C, 51·8; H, 4·3; Br, 31·4%).

Reduction of Chromanones.—The chromanone (0·2 g.) in ether (10 c.c.) was slowly added to an excess of lithium aluminium hydride in ether. The solution was refluxed for 2 hr. After decomposition, the product was isolated with ether, and crystallised from light petroleum (b. p. 40—60°).

This procedure afforded 2,2-dimethylchroman-4-ol (XIX) (from 2,2-dimethylchroman-4-one[4]), m. p. 42—43° [*acetate*, m. p. 74—75° (Found: C, 71·2; H, 7·4. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%)], and 4,5-*dihydro*-6,6-*dimethylnaphtho*(2′,1′:2,3)*pyran*-4-*ol* (XXI) (from 2,2-dimethyl-5,6-benzochroman-4-one), m. p. 120—121° (Found: C, 79·2; H, 7·1. $C_{15}H_{16}O_2$ requires C, 78·95; H, 7·0%).

2,2-*Dimethylchroman*-3-*ol and* 4,5-*Dihydro*-6,6-*dimethylnaphtho*(2′,1′:2,3)*pyran*-5-*ol*.—4-Bromo-2,2-dimethylchroman-3-ol or 4-bromo-4,5-dihydro-6,6-dimethylnaphtho(2′,1′:2,3)pyran-5-ol (0·5 g.) was dissolved in ethanol (10 c.c.) and treated in the cold with 3% sodium amalgam (8 g.) during 2 hr. The mixture was set aside for 3 hr. and the product isolated with ether. Removal of the solvent followed by crystallisation from light petroleum (b. p. 40—60°) gave

2,2-dimethylchroman-3-ol [*acetate*, m. p. 55—56° (Found: C, 71·0; H, 7·2. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%)], and 4,5-*dihydro*-6,6-*dimethylnaphtho*(2′,1′:2,3)*pyran*-5-*ol*, m. p. 116—117° (50%) (mixed m. p. with the 4-hydroxy-compound 89—95°) (Found: C, 79·0; H, 7·0. $C_{15}H_{16}O_2$ requires C, 78·95; H, 7·0%) [*acetate*, needles, m. p. 113—114° (Found: C, 75·65; H, 6·7. $C_{17}H_{18}O_3$ requires C, 75·55; H, 6·7%)].

2,2-*Dimethylchroman*.[1]—4-Bromo-2,2-dimethylchromen (1·53 g.), platinic oxide (0·08 g.), and methanol (20 c.c.) were shaken in hydrogen until absorption (2 mol.) was complete. Filtration, evaporation, and distillation gave 2,2-dimethylchroman, b. p. 84—85°/3·5 mm., n_D^{21} 1·5204 (Shriner and Sharp give b. p. 67·5—68°/2 mm., n_D^{20} 1·5264).

4,5-*Dihydro*-6,6-*dimethylnaphtho*(2′,1′:2,3)*pyran*.—(*a*) 6,6-Dimethylnaphtho(2′,1′:2,3)pyran (0·32 g.), platinic oxide (0·04 g.), and methanol (40 c.c.) were shaken in hydrogen until absorption (1 mol.) was complete. Filtration, evaporation, and recrystallisation from methanol gave the *dihydro-derivative* (0·18 g.) as plates, m. p. 78° (Found: C, 84·3; H, 7·55. $C_{15}H_{16}O$ requires C, 84·9; H, 7·5%).

(*b*) 4-Bromo-6,6-dimethylnaphtho(2′,1′:2,3)pyran (0·5 g.), platinic oxide (0·13 g.), and methanol (70 c.c.) were shaken in hydrogen until absorption (2 mol.) was complete. The product (0·18 g.) was as in experiment (*a*) (m. p. and mixed m. p. 78°).

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