

Benzodipyrans. Part V.¹ Synthesis of a Linear Dihydrobenzodipyran-dione Isolated from Dill and of Other Similar Benzodipyrandiones

By Ashok S. Mujumdar and Ramesh N. Usgaonkar,* Institute of Science, 15, Madame Cama Road, Bombay-400032, India

7,8-Dihydro-8,8-dimethylbenzo[1,2-*b*:5,4-*b'*]dipyran-2,6-dione (IX) has been synthesised from 3,4-dihydro-7-hydroxycoumarin in three steps. Application of the same reaction sequence to 3,4-dihydro-5,7-dihydroxycoumarin yielded the angular isomer (XII) of the naturally occurring clausenin. Bromination of 7-hydroxy-2,2-dimethylchroman-4-one gave its 8-bromo-derivative with *N*-bromosuccinimide and its 6-bromo-derivative with bromine-chloroform. The former failed to undergo Pechmann condensation with malic acid but the latter condensed readily

6,7-DIHYDRO-8,8-DIMETHYLBENZO[1,2-*b*:5,4-*b'*]DIPYRAN-2,6-DIONE (IX), isolated² from Dill (*Anethum graveolens*), has been synthesised from 3,4-dihydro-7-hydroxycoumarin (I) in three steps (Scheme 1) in good yield. The dihydrocoumarin (I) condensed with $\beta\beta$ -dimethylacrylic acid in the presence of phosphoric trichloride and zinc chloride, with simultaneous cleavage of the lactone ring, to give the chromanone (VII). The latter cyclised readily on heating, and the product (VIII) was dehydrogenated by heating with palladium in diphenyl ether. The constitution of the intermediate benzodipyran (VIII) follows from that of the end product (IX) and from its n.m.r. spectrum, which showed aromatic proton singlets at δ 6.7 and 7.83, indicating the condensation to have taken place at position 6 of the dihydrocoumarin (I).

We had previously hoped to synthesise the benzodipyran (IX) from 7-hydroxy-2,2-dimethylchroman-4-one (XIIIb) *via* the 8-bromo-derivative (XVIb) by a scheme similar to that given for the 6-bromo-derivative (XIVb) (Scheme 2). The 8-bromo-derivative was obtained by peroxide-catalysed bromination with *N*-bromosuccinimide (NBS); its constitution was evident from its

n.m.r. spectrum, which showed doublets (J 8 Hz) at δ 6.66 and 7.75. However, it did not condense with malic acid.

Bromination of the chromanone (XIIIb) with bromine in chloroform or in glacial acetic acid gave the 6-bromo-derivative, showing aromatic proton n.m.r. singlets at δ 6.58 and 7.91. The same substance was obtained when 4-bromoresorcinol was condensed with $\beta\beta$ -dimethylacrylic acid. The 6-bromo-derivative readily condensed with malic acid to give the angular benzodipyran (XVb), debromination of which with copper-benzoic acid afforded the known³ angular benzodipyran (XVIII). A similar sequence of reactions starting with 7-hydroxy-2-methylchromanone (XIIIa) led to the synthesis of (XIVa) and (XVa). However, peroxide-catalysed bromination with NBS gave the dibromo-derivative (XVIc), whose n.m.r. spectrum showed only one aromatic proton signal.

3,4-Dihydro-5,7-dihydroxycoumarin (II) was obtained in pure crystalline state and in good yield by condensing acrylonitrile with phloroglycinol in presence of zinc

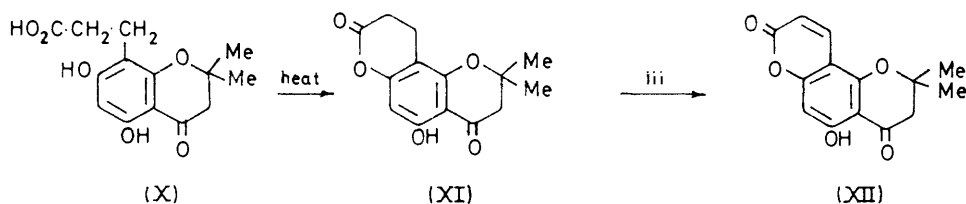
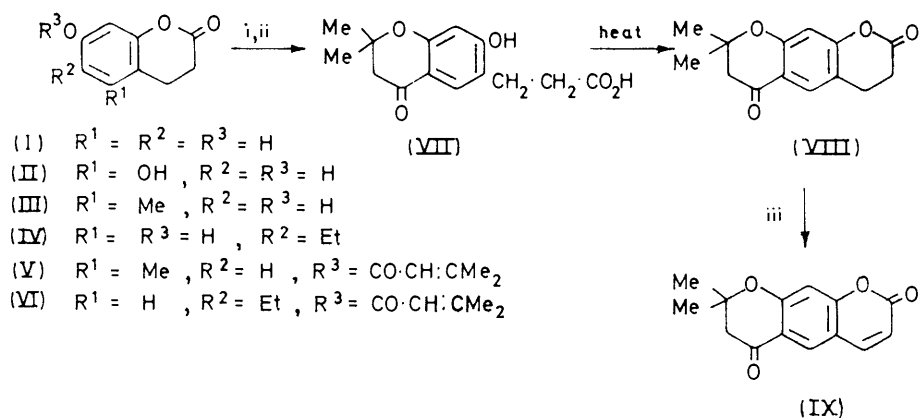
¹ Part IV, S. S. Patwardhan and R. N. Usgaonkar, *Indian J. Chem.*, in the press.

² R. T. Aplin and C. B. Page, *J. Chem. Soc. (C)*, 1967, 2593.

³ A. S. Mujumdar and R. N. Usgaonkar, *Indian J. Chem.*, 1971, 9, 294.

chloride and dry hydrogen chloride. This condensation is described in the literature⁴ as giving the dihydrocoumarin as a sticky mass, and no elemental analysis is reported. The dihydrocoumarin (II) condensed with

charcoal then gave (XII), the angular isomer of clausenin, identical with material previously synthesised by two different methods.^{3,5} Condensations of $\beta\beta$ -dimethylacrylic acid with 3,4-dihydro-7-hydroxy-5-methylcou-

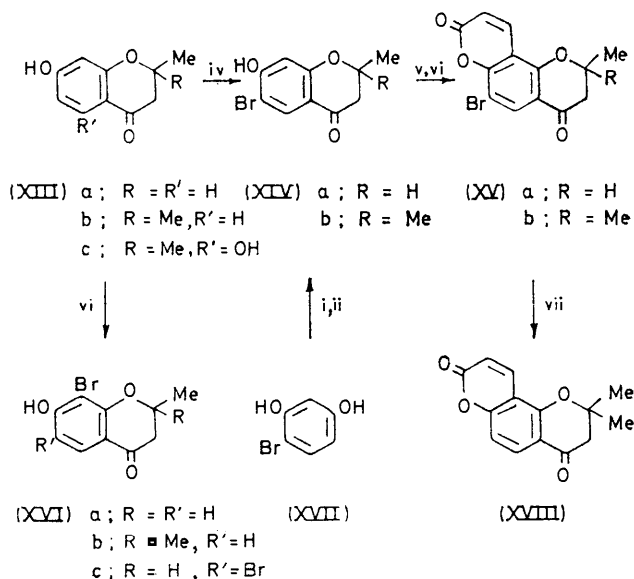


SCHEME 1

Reagents: i, $Me_2C=CH \cdot CO_2H$; ii, $POCl_3-ZnCl_2$; iii, $Pd-C, Ph_3O$

$\beta\beta$ -dimethylacrylic acid to give the chromanone (X) in good yield, which cyclised on heating to give the benzodipyrandione (XI). Dehydrogenation with palladium-

marin (III) and with 6-ethyl-3,4-dihydro-7-hydroxycoumarin (IV) under similar conditions surprisingly gave the esters (V) and (VI), as shown by their elemental analyses and their failure to form 2,4-dinitrophenylhydrazone derivatives.



SCHEME 2

Reagents: i—iii as Scheme 1; iv, Br_2 in $CHCl_3$ or $AcOH$; v, malic acid; vi, H_2SO_4 ; vii, $Cu-PhCO_2H$; viii, $NBS-CCl_4$

EXPERIMENTAL

Microanalyses were carried out by Mrs. J. A. Patankar. N.m.r. spectra were measured with Varian A60 and HA-100 spectrometers. U.v. spectra were measured with a Zeiss VSU2 P spectrophotometer. All extracts were dried over anhydrous sodium sulphate and the purity of compounds was tested by t.l.c.

3,4-Dihydro-5,7-dihydroxycoumarin (II).—Phloroglucinol (10 g) and acrylonitrile (10 ml) were dissolved in dry ether (150 ml) and fused zinc chloride (15 g) was added. A slow stream of dry hydrogen chloride was passed through the solution, maintained at 0° . The mixture was left at room temperature overnight and then treated with crushed ice. The ethereal layer was separated and the aqueous solution was saturated with sodium chloride and extracted with ethyl acetate. The organic solutions were combined and evaporated to leave a semi-solid that slowly crystallised. It was washed with cold ether (10 ml) and recrystallised from ethyl acetate-petroleum (b.p. $60-80^\circ$) to give pale

⁴ W. D. Langley and R. Adams, *J. Amer. Chem. Soc.*, 1922, **44**, 2320.

⁵ A. K. Ganguly, B. S. Joshi, V. N. Kamat, and A. K. Manmade, *Tetrahedron*, 1967, **23**, 4777.

yellow *needles* (4.5 g), m.p. 198—199° (Found: C, 60.0; H, 4.7. $C_9H_8O_4$ requires C, 59.9; H, 4.4%), λ_{\max} (MeOH) 210 (log ϵ 4.23), 275 (4.78), and 320 nm (2.15).

7-Hydroxy-2,2-dimethyl-4-oxochroman-6-propionic Acid (VII).—A mixture of 3,4-dihydro-7-hydroxycoumarin (I) ⁴ (4 g), $\beta\beta$ -dimethylacrylic acid (4 g), fused zinc chloride (5 g), and phosphoric trichloride (20 ml) was kept overnight at room temperature and then poured on crushed ice. The solid product crystallised from water-acetone as *needles* (3.8 g), m.p. 210—211° (Found: C, 63.4; H, 5.9. $C_{14}H_{16}O_5$ requires C, 63.6; H, 6.0%), λ_{\max} (MeOH) 240 (log ϵ 4.63), 280 (4.62), and 325 nm (4.36), ν_{\max} (KBr) 3180 (bonded OH), 3000—2950 (OH of CO_2H), 1700 (C=O of CO_2H), 1650 (aryl C=O), 1605 and 1510 (benzene), 1395 and 1380 (CM_e_2), and 1240 and 1020 cm^{-1} (aryl C—O—C).

5,7-Dihydroxy-2,2-dimethyl-4-oxochroman-8-propionic Acid (X).—A similar condensation of 3,4-dihydro-5,7-dihydroxycoumarin (II) (4 g) with $\beta\beta$ -dimethylacrylic acid (5 g) in the presence of fused zinc chloride (8 g) and phosphoric trichloride (15 ml) gave the *acid* (X) as yellow *needles* (3.5 g), m.p. 214—215° (from benzene-acetone) (Found: C, 60.4; H, 6.1. $C_{14}H_{16}O_6$ requires C, 59.9; H, 5.7%), λ_{\max} (MeOH) 295 nm (log ϵ 3.25), ν_{\max} (KBr) 3200—3000 (bonded OH), 3000—2600 (OH of CO_2H), 1700 (C=O of CO_2H), 1645 (bonded C=O), 1610 and 1500 (benzene), and 1385 and 1380 cm^{-1} (CM_e_2).

7-($\beta\beta$ -Dimethylacryloyloxy)-3,4-dihydro-5-methylcoumarin (V).—The dihydrocoumarin (III) ⁴ (1.5 g), phosphoric trichloride (10 ml), and fused zinc chloride (2 g) were mixed and the reaction was carried out as described for compound (VII). The mixture was poured on crushed ice and the product extracted into benzene. Evaporation left a sticky solid that crystallised from petroleum (b.p. 60—80°) as clusters of *needles* (0.75 g), m.p. 92—93° (Found: C, 69.0; H, 6.3. $C_{15}H_{16}O_4$ requires C, 69.25; H, 6.15%), λ_{\max} (MeOH) 280 nm (log ϵ 4.13).

7-($\beta\beta$ -Dimethylacryloyloxy)-6-ethyl-3,4-dihydrocoumarin (VI).—A similar condensation of the dihydrocoumarin (IV) ⁶ gave an *oil*, b.p. 144—146° at 2.2 mmHg (Found: C, 70.25; H, 6.4. $C_{16}H_{18}O_4$ requires C, 70.05; H, 6.55%).

3,4,7,8-Tetrahydro-8,8-dimethylbenzo[1,2-b:5,4-b']dipyran-2,6-dione (VIII).—The chromanone (VII) (5 g) was heated at 240—250° for 2 h, cooled, and extracted with ethyl acetate. The extract was treated with charcoal and washed with aqueous sodium hydrogen carbonate. Removal of ethyl acetate left a solid that crystallised from petroleum (b.p. 60—80°) as *needles* (2 g), m.p. 136—137° (Found: C, 68.7; H, 5.3. $C_{14}H_{14}O_4$ requires C, 68.3; H, 5.6%), λ_{\max} (MeOH) 240 (log ϵ 4.57), 255 (4.18), 275 (4.55), and 320 nm (4.35), δ [60 MHz; $CDCl_3$] 1.49 (6H, s, CM_e_2), 2.7 (2H, s, $CO\cdot CH_2$), 2.82 (2H, t, J 4 Hz, $O\cdot CO\cdot CH_2\cdot CH_2$), 3.92 (2H, t, J 4 Hz, $O\cdot CO\cdot CH_2\cdot CH_2$), 6.7 (1H, s, H-10), and 7.83 (1H, s, H-5); the 2,4-dinitrophenylhydrazone crystallised from ethanol as *needles*, m.p. 226—227° (Found: N, 13.4. $C_{20}H_{16}N_4O_7$ requires N, 13.1%).

2,3,9,10-Tetrahydro-5-hydroxy-2,2-dimethylbenzo[1,2-b:3,4-b']dipyran-4,8-dione (XI).—The chromanone (X) (3 g) was heated at 220—230° for 2 h, then cooled. The product was washed with aqueous sodium hydrogen carbonate by trituration and then with water. It crystallised from ethyl acetate-petroleum (b.p. 60—80°) as *cubes* (1.2 g), m.p. 164—165° (Found: C, 64.4; H, 4.4. $C_{14}H_{12}O_5$ requires

C, 64.6; H, 4.6%), λ_{\max} (MeOH) 210 (log ϵ 4.30) and 330 nm (3.73), ν_{\max} (KBr) 3400—3520 (free OH), 3010br (intramolecular bonded OH), 1790 (lactonic C=O), 1640 (bonded C=O), and 1600 and 1500 cm^{-1} (benzene), δ (60 MHz; $CDCl_3$) 1.48 (6H, s, CM_e_2), 2.75 (2H, s, 7- H_2), ca. 2.85 (4H, m, $O\cdot CO\cdot CH_2\cdot CH_2$), 6.12 (1H, s, H-10), and 12.2 (1H, s, OH).

7,8-Dihydro-8,8-dimethylbenzo[1,2-b:5,4-b']dipyran-2,6-dione (IX).—The benzodipyran (VIII) (1 g) was refluxed in diphenyl ether (10 ml) with palladium-charcoal (0.3 g; 10%) for 6 h. The solution was filtered hot and distilled under reduced pressure. The residue crystallised from methanol as pale yellow *needles* (0.5 g), m.p. 175—176° (lit.² m.p. of natural product 177.5—178°) (Found: C, 68.9; H, 5.0. $C_{14}H_{12}O_4$ requires C, 68.8; H, 4.9%), λ_{\max} (MeOH) 255 (log ϵ 4.64), 300 (4.22), 3.7 (4.20), 330 (4.19), and 345 nm (4.23), ν_{\max} (Nujol) 1730 (lactonic C=O), 1680 (aryl ketone), 1625 (conj. C=C), 1600 and 1540 (benzene), and 820 cm^{-1} (CH=CH), δ (60 MHz; $CDCl_3$) 1.51 (6H, s, CM_e_2), 2.8 (2H, s, CH_2), 6.32 (1H, d, J 10 Hz, $O\cdot CO\cdot CH=CH$), 7.75 (1H, d, J 10 Hz, $O\cdot CO\cdot CH=CH$), 6.82 (1H, s, H-10), and 8.08 (1H, s, H-5). The 2,4-dinitrophenylhydrazone crystallised from ethanol as *needles*, m.p. 288—289° (Found: N, 13.6. $C_{20}H_{14}N_4O_7$ requires N, 13.2%).

2,3-Dihydro-5-hydroxy-2,2-dimethylbenzo[1,2-b:3,4-b']dipyran-4,8-dione (XII).—Dehydrogenation of the benzodipyran (XI) (1 g) with Pd-C (0.4 g; 10%) was carried out as above. The product crystallised from ethyl acetate-petroleum (b.p. 60—80°) as fluffy *needles*, m.p. 219—220°, identical (mixed m.p.; u.v. and i.r. spectra) with authentic material.³

6-Bromo-7-hydroxy-2,2-dimethylchroman-4-one (XIVb).—(a) The chromanone (XIIIb) ⁷ (1 g) was suspended in chloroform (20 ml) and a solution of bromine in chloroform (8.4 ml; 10%) was added with shaking. The mixture was set aside for 2 h at room temperature with occasional shaking, then washed with aqueous sodium hydrogen sulphite and water and evaporated to leave a sticky residue that was washed with cold benzene. The resulting solid crystallised from aqueous ethanol as pale yellow plates (0.45 g), m.p. 204—205° (Found: C, 49.1; H, 4.0. $C_{11}H_{11}BrO_3$ requires C, 48.7; H, 4.05%), λ_{\max} (MeOH) 275 (log ϵ 4.03) and 330 nm (3.98), ν_{\max} (KBr) 3100—3000 (OH), 1645 (aryl C=O), 1615 and 1580 (benzene), and 1385 and 1345 cm^{-1} (CM_e_2), δ [60 MHz; $(CD_3)_2CO$] 1.45 (6H, s, CM_e_2), 2.7 (2H, s, CH_2), 6.58 (1H, s, H-8), 7.91 (1H, s, H-3), and 9.8 (1H, s, OH). A similar reaction in glacial acetic acid gave the same substance.

(b) 4-Bromoresorcinol (XVII) ⁸ (1 g) was condensed with $\beta\beta$ -dimethylacrylic acid (1 g) in the presence of phosphoric trichloride (10 ml) and zinc chloride (1.5 g). The product was worked up as for compound (VII) and was crystallised as in (a); m.p. and mixed m.p. 204—205°; yield 0.7 g.

6-Bromo-7-hydroxy-2-methylchroman-4-one (XIVa).—To the chromanone (XIIIa) ⁹ (0.89 g) dissolved in glacial acetic acid (10 ml), bromine in acetic acid (8 ml; 10%) was added with shaking. The mixture was set aside 2 h, then diluted with water and extracted with chloroform. Removal of the chloroform left a solid that crystallised from benzene-petroleum (b.p. 60—80°) as *needles* (0.45 g), m.p. 158—159° (Found: C, 47.1; H, 3.6. $C_{10}H_9BrO_3$ requires C, 46.7; H, 3.5%), λ_{\max} (MeOH) 210 (log ϵ 4.31), 275 (4.03), and 330

⁸ R. B. Sandin and R. A. McKee, *Org. Synth.*, Coll. Vol. II, 1946, p. 100.

⁹ M. Miyano and M. Matsui, *Bull. Chem. Soc. Japan*, 1958, **31** 397.

⁶ D. K. Chatterjee and K. Sen, *J. Indian Chem. Soc.*, 1969, **46**, 275.

⁷ P. R. Iyer and G. D. Shah, *Indian J. Chem.*, 1968, **4**, 227.

nm (4.06), δ [60 MHz; $(\text{CD}_3)_2\text{CO}$] 1.46 (3H, d, J 6 Hz, CH_3), 2.6 (2H, d, J 8 Hz, CH_2), 4.6 (1H, sextet, J 7 Hz, H-2), 6.58 (1H, s, H-8), and 7.92 (2H, s, H-5). A similar reaction in chloroform gave the same substance.

6-Bromo-2,3-dihydro-2,2-dimethylbenzo[1,2-b:3,4-b']dipyran-4,8-dione (XVb).—The bromochromanone (XIVb) (0.5 g), malic acid (0.8 g), and concentrated sulphuric acid (10 ml) were heated together at 120–125° for 45 min with occasional shaking. The mixture was then poured on crushed ice and extracted with ethyl acetate. The extract was washed with aqueous sodium hydroxide (30 ml; 10%) and then water. Evaporation left a solid that crystallised from benzene–petroleum (b.p. 60–80°) as pale yellow fluffy needles (0.15 g), m.p. 185–186° (Found: C, 52.4; H, 3.6. $\text{C}_{14}\text{H}_{11}\text{BrO}_4$ requires C, 52.0; H, 3.4%), λ_{max} (MeOH) 260 (log ϵ 4.40) and 345 nm (3.65).

6-Bromo-2,3-dihydro-2-methylbenzo[1,2-b:3,4-b']dipyran-4,8-dione (XVa).—The bromochromanone (XIVa) (0.5 g) was similarly condensed with malic acid (1 g) in the presence of concentrated sulphuric acid (10 ml). The product crystallised from ethyl acetate–petroleum (b.p. 60–80°) as needles (0.08 g), m.p. 184–185° (Found: C, 50.6; H, 3.1. $\text{C}_{13}\text{H}_9\text{BrO}_4$ requires C, 50.5; H, 2.9%).

2,3-Dihydro-2,2-dimethylbenzo[1,2-b:3,4-b']dipyran-4,8-dione (XVIII).—An intimate mixture of the bromobenzo-dipyranone (XVb) (0.1 g) and benzoic acid (2.5 g) was melted by heating at 175–180°. Copper–bronze (1 g) was then added in pinches during 5 min and heating at the same temperature was continued for 0.5 h with stirring. After cooling, the solid mass was extracted with hot ethyl acetate. The extract was repeatedly shaken with aqueous sodium hydroxide (10%) and then with water, and the ethyl acetate was removed to leave a solid residue that crystallised from ethyl acetate–petroleum (b.p. 40–60°) as pale yellow needles (0.03 g), m.p. and mixed m.p.³ 211–212°.

8-Bromo-7-hydroxy-2,2-dimethylchroman-4-one (XVIb).—The chromanone (XIIIb)⁷ (0.39 g), NBS (0.36 g), benzoyl peroxide (0.07 g), and carbon tetrachloride (40 ml) were mixed together and refluxed for 6 h. After cooling, ethyl acetate (20 ml) was added to dissolve the separated solid. The solution was then shaken with dilute hydrochloric acid (50 ml; 1:1) and then with water. Removal of solvents left a semi-solid residue that crystallised from petroleum ether (b.p. 40–60°) to give needles (0.175 g), m.p. 162–163° (Found: C, 49.1; H, 4.3. $\text{C}_{11}\text{H}_{11}\text{BrO}_3$ requires C, 48.7; H, 4.05%), λ_{max} (MeOH) 240 (log ϵ 3.74), 273 (3.68), 293 (3.73), and 335 nm (4.20), ν_{max} (Nujol) 3200–3000 (bonded OH), 1680 (C=O), and 1600 and 1520 cm^{-1} (benzene), δ (100 MHz; CDCl_3) 1.5 (6H, s, CMe_2), 2.7 (s, CH_2), 6.46 (1H, s, OH), 6.66 (1H, d, J 8 Hz, H-6), and 7.75 (1H, d, J 8 Hz, H-5).

6,8-Dibromo-7-hydroxy-2-methylchroman-4-one (XVIc).—The chromanone (XIIIa)⁹ (0.3 g), NBS (0.3 g), carbon tetrachloride (50 ml), and benzoyl peroxide (0.07 g) were refluxed together. The product, worked up as described for (XVIb), crystallised from chloroform as needles (0.24 g), m.p. 214–215° (Found: C, 35.6; H, 2.6. $\text{C}_{10}\text{H}_8\text{Br}_2\text{O}_3$ requires C, 35.7; H, 2.4%), δ [60 MHz; $(\text{CD}_3)_2\text{CO}$] 1.55 (3H, d, J 7 Hz, CH_3), 2.7 (2H, d, J 8 Hz, CH_2), ca. 4.8 (1H, m, H-2), and 7.93 (1H, s, H-5).

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