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SYNTHESIS OF 6-CARBOXY-2,2-DIMETHYLCHROMANS AND CHROMENES

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Abstract—The condensation of hydroxybenzoic acids and their methyl esters with isoprene in the presence of orthophosphoric acid gives corresponding 2,2-dimethylchromans, which can be dehydrogenated with DDQ or NBS to give the corresponding 6-carboxy-2,2-dimethylchromenes. The synthesis of β-tubaic acid, a natural compound, has also been achieved.

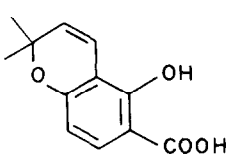
6-Carboxy-2,2-dimethylchromans and chromenes occur very infrequently among natural products; the only example known so far is β-tubaic acid (**1**), recently isolated by Yoshihiko *et al.*[1] from the roots of *Derris elliptica* and has been shown to exhibit *antimicrobial activity*. They are also obtained as degradation products in the course of structure elucidation of a number of naturally occurring prenylated compounds,[2,3-9] and can be used as starting materials for the synthesis of pyranoxanthones.

Earlier 6-carboxy-2,2-dimethylchromans and chromenes have been prepared by (i) condensation of appropriate phenol with 2-hydroxy-2-methylbut-3-yne[10] (ii) oxidation of formyl substituted 2,2-dimethylchromans[11] (iii) Clemmensen reduction of 2,2-dimethylchroman-4-ones[12] and (iv) oxidative cyclization of the appropriate C-prenyl derivatives.[2] Method (i) is of historic importance only as the yields obtained are seldom more than 2–3%. Methods (ii)–(iv) suffer from the disadvantage that the appropriate starting materials are difficult to prepare. Thus a convenient method for their synthesis is needed.

A new method of nuclear isoprenylation leading to exclusive formation of 2,2-dimethylchromans in good yields has recently been developed in our laboratory.[13,14] The method consists in condensation of appropriate phenol with 2-methyl-1,3-butadiene (isoprene) in presence of orthophosphoric acid at 30–35°. Acid catalysed condensation of hydroxybenzoic acids and their methyl esters with isoprene, under the above mentioned conditions, was undertaken with a view to develop a convenient method for the synthesis of 6-carboxy-2,2-dimethylchromans and chromenes.

Thus, condensation of 4-hydroxybenzoic acid with isoprene in presence of orthophosphoric acid gave only one product (yield 80%), which on elemental analysis showed the introduction of one isoprene unit. Its NMR spectrum indicated the presence of a 2,2-dimethylchroman ring. The gem-dimethyl group appeared as singlet at δ 1.39, the methylene groups appeared as two distinct triplets ($J = 7$ Hz) at δ 1.86 and 2.83 besides other signals. The condensation product was therefore assigned the structure 2,2-dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylic acid (**2**). Similarly methyl 4-hydroxybenzoate on condensation with isoprene gave only one product (yield 75%), which was assigned the structure methyl 2,2 - dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylate (**3**), identical with methyl ester of 2. **3** on dehydrogenation with DDQ gave the corresponding 2,2-dimethylchromene, methyl 2,2 - dimethyl - 2H - 1 - benzopyran - 6 - carboxylate (**4**). The dehydrogenation of **3** with NBS in presence of benzoyl peroxide also gave the same product (4).

Similarly condensation of 2,3,4-trihydroxybenzoic acid and its methyl ester with isoprene gave 7,8 - dihydroxy - 2,2 - dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylic acid (**5**) and methyl 7,8 - dihydroxy - 2,2 - dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylate (**6**), respectively in 70–80% yield. The assigned structures (**5** and **6**) were in agreement with their elemental analysis and NMR spectrum. They were further characterised as their diacetates. Either of the compound 5 or 6 on methylation gave methyl 7,8 - dimethoxy - 2,2 - dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylate (**7**), which on dehydrogenation with DDQ or NBS gave the corresponding chromene, methyl 7,8 - dimethoxy - 2,2 - dimethyl - 2H - 1 - benzopyran - 6 - carboxylate (**8**).



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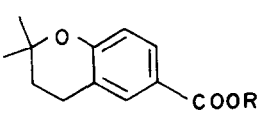
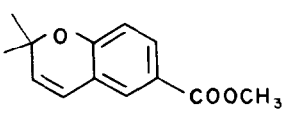
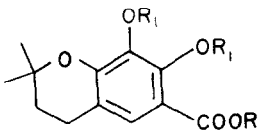


2,3



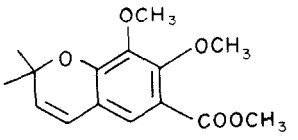
4

2: R = H
3: R = CH_3



5–7

	R	R_1
5:	H	H
6:	CH_3	H
7:	CH_3	CH_3



8

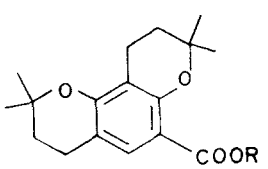
2,4-Dihydroxybenzoic acid on similar condensation with isoprene gave a mixture of three products in the ratio of 1:2:7 (overall yield, 75%), which were separated by column chromatography. The first compound on elemental analysis showed the introduction of two isoprene units. It gave negative ferric reaction and was assigned the dichroman structure 2,2,8,8 - tetramethyl - 3,4,9,10 - tetrahydro - 2H,8H - benzo[1,2-b:3,4-b']dipyran - 6 - carboxylic acid (**9**) which was in agreement with its NMR spectrum. NMR of second compound, which gave positive ferric reaction, showed the signals characteristic of 2,2-dimethylchroman ring. The two aromatic protons appeared as doublets ($J = 9$ Hz) at δ 6.32 and 7.62. It was therefore assigned the structure as 5 - hydroxy - 2,2 - dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylic acid (**10**). The third compound was found to be an isomer of **10** on elemental analysis and gave positive ferric reaction. It was assigned the structure 7 - hydroxy - 2,2 - dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylic acid (**11**) on the basis of its NMR spectrum which showed the two aromatic protons as singlets at δ 6.20 and 7.60 besides other signals.

A regiospecific synthesis of linear chroman (**11**) has also been achieved by blocking the more reactive 3-position of 2,4-dihydroxybenzoic acid with iodine a group, easily introduced and removed. Thus, iodination[15] of 2,4-dihydroxybenzoic acid with iodine and periodic acid gave 2,4-dihydroxy-3-iodobenzoic acid (**12**). The assigned structure (**12**) was in agreement with its NMR spectrum which showed the presence of two ortho coupled aromatic protons as doublets ($J = 9$ Hz) at δ 6.50 and 7.66. Condensation of **12** with isoprene in presence of orthophosphoric acid gave only one product (yield 70%). It was assigned the structure 7 - hydroxy - 8 - iodo - 2,2 - dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylic acid (**13**) on the basis of its NMR spectrum. **13** on deiodination with Zn–HCl gave 11 identical (m.p., mmp and IR) with the compound prepared above.

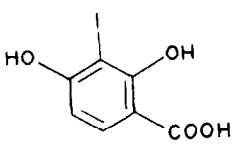
Methyl 2,4-dihydroxybenzoate, when subjected to similar reaction, gave a mixture of three products, methyl 5 - hydroxy - 2,2 - dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylate (**14**), methyl 7 - hydroxy - 2,2 - dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylate (**15**) and methyl 2,2,8,8 - tetramethyl - 3,4,9,10 - tetrahydro - 2H,8H - benzo[1,2-b:3,4-b']dipyran - 6 - carboxylate (**16**), which were separated by column chromatography and structures assigned on the basis of elemental analysis and NMR.

Either **11** or **15** on methylation gave methyl 7 - methoxy - 2,2 - dimethyl - 3,4 - dihydro - 2H - 1 - benzopyran - 6 - carboxylate (**17**), which on dehydrogenation with DDQ or NBS gave the corresponding chromene, methyl 7 - methoxy - 2,2 - dimethyl - 2H - 1 - benzopyran - 6 - carboxylate (**18**). Similarly methyl 5 - methoxy - 2,2 - dimethyl - 2H - 1 - benzopyran - 6 - carboxylate (**19**) was synthesised by dehydrogenation with DDQ or NBS of the corresponding chroman (**20**), which was obtained by methylation of **10** or **14**.

β-Tubaic acid (**1**), a natural compound, was synthesised by dehydrogenation of **14** with DDQ, followed by saponification with methanolic sodium hydroxide[10] of the resulting β-tubaic acid methyl ester (**21**). 21 has also been synthesised by the partial propynylation of methyl 2,4-dihydroxybenzoate with 3-chloro-3-methylbut-1-yne in dry acetone, in presence of anhydrous K_2CO_3 and KI, followed by thermal rearrangement of the formed methyl

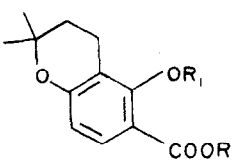


9,16



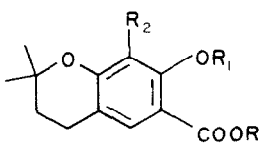
12

9: **R = H**
16: R = CH_3



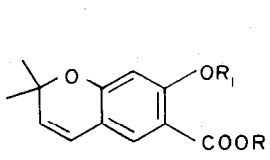
10,14,20

	R	R_1
10:	H	H
14:	CH_3	H
20:	CH_3	CH_3

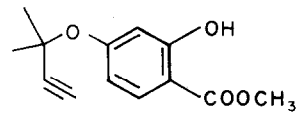


11,13,15,17

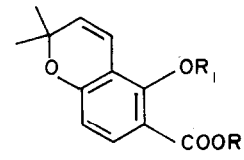
	R	R_1	R_2
11:	H	H	H
13:	H	H	I
15:	CH_3	H	H
17:	CH_3	CH_3	H



18,23,24



22



19,21

	R	R_1
18:	CH_3	CH_3
23:	H	H
24:	CH_3	H

	R	R_1
19:	CH_3	CH_3
21:	CH_3	H

2 - hydroxy - 4 - (1,1 - dimethylprop - 2 - ynyloxy) - benzoate (**22**) in N,N-dimethylaniline. Similarly linear isomer of β-tubaic acid, 7 - hydroxy - 2,2 - dimethyl - 2H - 1 - benzopyran - 6 - carboxylic acid (**23**) was synthesised by saponification of 24, which was obtained by dehydrogenation of **15** with DDQ.

EXPERIMENTAL

M.ps are uncorrected. NMR spectra were recorded on a Perkin–Elmer R-32 spectrometer with TMS as an internal standard.

Reaction of 4-*hydroxybenzoic acid with isoprene*

A soln of isoprene (0.5 ml) in xylene (2.0 ml) was added to a mixture of 4-hydroxybenzoic acid (0.5 g), orthophosphoric acid (85%; 1.0 ml) and xylene (1.0 ml) with constant stirring at 30–35° during 2 h. Stirring was continued for further 6 h and then ether (50.0 ml) added. It was washed with water, dried (Na_2SO_4) and distilled. The residue thus obtained was purified by column chromatography and the column eluted with benzene to give 2 as colourless needles (0.52 g), m.p. 176–177° (Found: C, 69.6; H, 7.0. $C_{12}H_{14}O_3$ requires C, 69.9; H, 6.8%). NMR($CDCl_3 + CF_3COOH$) δ: 1.39 [s, 6H, $C(CH_3)_2$]; 1.86, 2.83 (each *t*, $J = 7$ Hz, each 2H, H3 and H4 respectively); 6.73 d, $J = 9$ Hz, 1H, H8) and 7.70 (m, 2H, H5 and H7).

Reaction of methyl 4-*hydroxybenzoate with isoprene*

A soln of isoprene (0.5 ml) in petroleum ether (2.0 ml) was added to a mixture of methyl 4-hydroxybenzoate (0.5 g), orthophosphoric acid (85%; 1.0 ml) and petrol (2.0 ml) with constant stirring at 30–35° during 2 h. Stirring was continued for further 2 h and then working up the reaction gave residual oil, which was purified by column chromatography and the column eluted with petroleum ether to give **3** as colourless prisms (0.5 gm), m.p. 83–84° (Found: C, 70.7; H, 7.4. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.3%). NMR ($CDCl_3$) δ: 1.44 [*s*, 6H, $CCH_3)_2$]; 1.93, 2.92 (each *t*, $J = 7$ Hz, each 2H, H3 and H4 respectively); 3.96 (s, 3H, $COOCH_3$ at C_6); 6.72 (d, $J = 9$ Hz, 1H, H8) and 7.72 (m, 2H, H5 and H7).

Methyl 2,2 - *dimethyl* - 2H - 1 - *benzopyran* - 6 - *carboxylate* (**4**)

Method (*i*). **3** (0.2 g) in carbon tetrachloride (50.0 ml) was refluxed for 4 h with NBS (0.16 g) and benzoyl peroxide (0.01 g). The soln was filtered and filtrate distilled. The residual oil thus obtained was purified by column chromatography and the column eluted with petrol to give 4 as colourless oil (0.15 g) (Found: C, 71.4; H, 6.6. $C_{13}H_{14}O_3$ requires C, 71.6; H, 6.4%). NMR ($CDCl_3$) δ: 1.43[s, 6H, $C(CH_3)_2$]; 3.82 (s, 3H, $COOCH_3$ at C_6); 5.55, 6.25 (each d, $J = 10$ Hz, each 1H, H3 and H4 respectively); 6.72 (d, $J = 9$ Hz, 1H, H8) and 7.70 (m, 2H, H5 and H7).

Method (*ii*). **3** (0.2 g) in dry benzene (30.0 ml) was refluxed for 100 h with DDQ (0.2 g). The soln was filtered, the filtrate distilled and residue thus obtained was purified by column chromatography and the column eluted with petroleum ether to give **4** as a colourless oil (0.05 g), identical with the chromene prepared by the NBS method

Reaction of 2,3,4-*trihydroxybenzoic acid with isoprene*

A soln of isoprene (0.5 ml) in xylene 2.0 ml) was added to a mixture of 2,3,4-trihydroxybenzoic acid (0.5 g), orthophosphoric acid (85%; 1.0 ml) and xylene (1.0 ml) with constant stirring at 30–35° during 2 h. Stirring was continued for further 6 h and then the mixture neutralized with 2% aq $NaHCO_3$. The aq layer separated, acidified with dil HCl and extracted with ether. Ether extract was washed with water, dried (Na_2SO_4) and distilled. The residue thus obtained was crystallised from ethyl acetate–benzene to give **5** as pale yellow prisms (0.51 g), m.p. 155–156° (Found: C, 60.2; H, 6.0. $C_{12}H_{14}O_5$ requires C, 60.5; H, 5.9%). NMR ($CDCl_3$) δ: 1.35 [s, 6H, $C(CH_3)_2$]; 1.77, 2.66 (each t, $J = 7$ Hz, each 2H, H3 and H4 respectively) and 7.42 (s, 1H, H5). Its diacetate (Ac_2O–pyridine) was crystallised from aq EtOH as colourless needles, m.p. 143–145° Found: C, 59.4; H, 5.6. $C_{16}H_{18}O_7$ requires C, 59.6; H, 5.6%). NMR ($CDCl_3$) δ: 1.35 [s, 6H, $C(CH_3)_2$]; 1.85 (t, $J = 7$ Hz, 2H, H3); 2.30 (s, 6H, $OCOCH_3$ at C_7 and C_8); 2.82 (t, $J = 7$ Hz, 2H, H4) and 7.69 (s, 1H, H5).

Reaction of methyl 2,3,4-*trihydroxybenzoate with isoprene*

A soln of isoprene (0.5 ml) in petrol (2.0 ml) was added to a mixture of methyl 2,3,4-trihydroxybenzoate (0.5 g), orthophosphoric acid (85%; 1.0 ml) and petrol (2.0 ml) with constant stirring at 30–35° during 2 h. Stirring was continued for a further 2 h and then working up the reaction gave residual oil, which was purified by column chromatography and the column eluted with benzene to give **6** as colourless needles (0.49 g), m.p. 94° (Found: C, 61.8; H, 6.3. $C_{13}H_{16}O_5$ requires C, 61.9; H, 6.3%). NMR ($CDCl_3$) δ 1.37 [s, 6H, $C(CH_3)_2$]; 1.83, 2.73 (each t, $J = 7$ Hz, each 2H, H3 and H4 respectively); 3.88 (s, 3H, $COOCH_3$ at C_6); 5.40 (s, 1H, exchanged with D_2O, OH at C_8); 7.30 (s, 1H, H5) and 10.8 s, 1H, exchanged with D_2O, OH at C_7). Its diacetate (Ac_2O–pyridine) was crystallised from petrol as colourless plates, m.p. 96–97° (Found: C, 60.5; H, 6.1. $C_{17}H_{20}O_7$ requires C, 60.7; H, 6.0%). NMR (CCl_4) δ: 1.26 [s, 6H; $C(CH_3)_2$]; 1.75 t, $J = 7$ Hz, 2H, H3); 2.21 (s, 6H, $OCOCH_3$ at C_7 and C_8); 2.70 (t, $J = 7$ Hz, 2H, H4); 3.70 (s, 3H, $COOCH_3$ at C_6) and 7.50 (s, 1H, H5).

Methyl 7,8 - *dimethoxy* - 2,2 - *dimethyl* - 3,4 - *dihydro* - 2H - 1 - *benzopyran* - 6 - *carboxylate* (**7**)

5 (1.0 g) in dry acetone (50.0 ml) was refluxed with Me_2SO_4 (1.5 ml) in presence of anhyd K_2CO_3 (4.0 g) for 4 h. Inorganic salts were filtered and washed with more acetone. The combined filtrate distilled and the residue extracted with ether. Ethereal layer washed successively with 5% Na_2CO_3 aq, water, dried (Na_2SO_4) and distilled to give 7 as pale yellow oil (0.95 g) (Found: C, 64.2; H, 7.1. $C_{15}H_{20}O_5$ requires C, 64.3; H, 7.1%). NMR ($CDCl_3$) δ: 1.26 [s, 6H, $C(CH_3)_2$]; 1.68, 2.63 (each t, $J = 9$ Hz, each 2H, H3 and H4 respectively); 3.74, 3.78 and 3.81 (each s, each 3H, OCH_3 at C_7, C_8 and $COOCH_3$ at C_6) and 7.20 (s, 1H, H5). 7 was found to be identical with dimethyl ether (Me_2SO_4–K_2CO_3–Acetone) of 6.

Methyl 7,8 - *dimethoxy* - 2,2 - *dimethyl* - 2H - 1 - *benzopyran* - 6 - *carboxylate* (**8**)

Method (*i*). **7** (0.1 g) in CCl_4 (25.0 ml) was refluxed for 4 h with

NBS (0.065 g) and benzoyl peroxide (0.005 g). Working-up as usual of the reaction mixture yielded residual oil, which was purified by prep TLC (benzene:ethyl acetate:acetic acid = 80:1:1) to give **8** as pale yellow oil (0.07 g) (Found: C, 64.6; H, 6.8. $C_{15}H_{18}O_5$ requires C, 64.7; H, 6.5%). NMR ($CDCl_3$) δ: 1.45 [s, 6H, $C(CH_3)_2$]; 3.86, 3.90 (each s, 6H and 3H respectively, OCH_3 at C_7, C_8 and $COOCH_3$ at C_6); 5.55, 6.25 (each d, J = 10 Hz, each 1H, H3 and H4 respectively) and 7.20 (s, 1H, H5).

Method (ii). **7** (0.1 g) in dry benzene (15.0 ml) was refluxed for 80 h with DDQ (0.09 g). The soln was filtered, the filtrate distilled and residue, thus obtained taken in ether. The ethereal layer was washed successively with 5% $NaHCO_3$ aq, water, dried (Na_2SO_4) and distilled to give 8 as pale yellow oil (0.08 g). It was identical with the chromene prepared by NBS method.

Reaction of 2,4-*dihydroxybenzoic acid with isoprene*

A soln of isoprene (1.2 ml) in xylene (3.0 ml) was added to a mixture of 2,4-dihydroxybenzoic acid (1.0 g), orthophosphoric acid (85%; 2.0 ml) and xylene (3.0 ml) with constant stirring at 30–35° during 2 h. Stirring was continued for further 5 h and then working up the reaction gave a residue which was found to be mixture of three products (TLC). Hence it was subjected to column chromatography and the column eluted successively with (i) petrol (ii) benzene:petrol (1:9) and (iii) benzene:petrol ether (3:7) giving the following three fractions. Fraction A crystallised from petrol ether, yielding **9** (0.1 g), m.p. 148–149° (Found: C, 70.0; H, 7.6. $C_{17}H_{22}O_4$ requires C, 70.3; H, 7.6%). NMR ($CDCl_3$) δ: 1.30, 1.39 [each s, each 6H, $2\times C(CH_3)_2$]; 1.77 (m, 4H, H3 and H9); 2.63 (m, 4H, H4 and H10) and 7.70 (s, 1H, H5). Fraction B crystallised from benzene–petrol, yielding 10 (0.2 g), m.p. 170–171° (lit[10] 170–171). NMR ($CDCl_3$) δ: 1.30 [s, 6H, $C(CH_3)_2$]; 1.72, 2.62 (each t, J = 7 Hz, each 2H, H3 and H4 respectively); 6.32 and 7.62 (each d, J = 9 Hz, each 1H, H8 and H7 respectively). Fraction C crystallised from ethyl acetate–benzene yielding 11 (0.7 g), m.p. 192–193° (lit[12] 191–192°). NMR (CD_3COCD_3) δ: 1.32 [s, 6H, $C(CH_3)_2$]; 1.80, 2.72 (each t, J = 7 Hz, each 2H, H3 and H4 respectively); 6.20 and 7.60 (each s, each 1H, H8 and H5 respectively).

2,4-*Dihydroxy*-3-*iodobenzoic acid* (**12**)

2,4-Dihydroxybenzoic acid (5.0 g) was dissolved in minimum amount of ethanol, iodine (3.5 g) and periodic acid (1.0 g, in water) added and mixture stirred for 2 h at 60–70°. It was diluted with water, the residue thus obtained was purified by column chromatography and the column eluted with benzene to give **12** as light brown prisms (2.6 g), m.p. 198–199° (Found: C, 30.2; H, 1.8. $C_7H_5O_4I$ requires C, 30.0; H, 1.8%). NMR (CD_3COCD_3) δ: 6.50 and 7.66 (each d, J = 9 Hz, each 1H, H5 and H6 respectively).

Reaction of **12** *with isoprene*

A soln of isoprene (1.1 ml) in xylene (3.0 ml) was added to a mixture of 12 (1.0 g), orthophosphoric acid (85%; 2.0 ml) and xylene (3.0 ml) with constant stirring at 30–35° during 2 h. Stirring was continued for further 5 h and then working up the reaction yielded a residue which was crystallised from ethyl acetate–benzene to give **13** as colourless plates (1.0 g) m.p. 185–186° (Found: C, 41.2; H, 3.9. $C_{12}H_{13}O_4I$ requires C, 41.4; H, 3.7%). NMR (CD_3COCD_3) δ: 1.40 [s, 6H, $C(CH_3)_2$]; 1.85, 2.78 (each t, J = 7 Hz, each 2H, H3 and H4 respectively) and 7.65 (s, 1H, H5).

Deiodination of **13**

A soln of **13** (1.0 g) in ethanol (30.0 ml) was refluxed with zinc dust (0.5 g) and conc. HCl (3.0 ml) for 4 h. The soln was filtered, distilled and the separated product crystallised from ethyl acetate–benzene to give **11** as colourless plates (0.45 g) identical (m.p., mmp and IR) with the compound prepared above.

Reaction of methyl 2,4-*dihydroxybenzoate with isoprene*

A soln of isoprene (1.1 ml) in petrol (4.0 ml) was added to a mixture of methyl 2,4-dihydroxybenzoate (1.0 g), orthophosphoric acid (85%; 2.0 ml) and petrol (4.0 ml) with constant stirring at 30–35° during 2 h. Stirring was continued for further 2 h. Work-up as above yielded a mixture of three compounds (TLC), separated by column chromatography and the column eluted with petrol ether to give successively the following three fractions. Fraction D crystallised from petrol ether yielding **14** (0.1 g), m.p. 57–58° (lit[2] oil). NMR($CDCl_3$) δ: 1.27 [s, 6H, $C(CH_3)_2$]; 1.73, 2.60 (each t, J = 7 Hz, each 2H, H3 and H4 respectively); 3.78 (s, 3H, $COOCH_3$ at C_6); 6.28, 7.51 (each d, J = 9 Hz, each 1H, H8 and H7 respectively) and 11.4 (s, 1H, exchanged with D_2O, OH at C_5). Fraction E crystallised from petrol ether yielding **15** (0.05 g), m.p. 60–61° (Found: C, 65.9; H, 6.9. $C_{13}H_{16}O_4$ requires C, 66.1; H, 6.8%). NMR (CCl_4) δ: 1.28 [s, 6H, $C(CH_3)_2$]; 1.71, 2.60 (each t, J = 7 Hz, each 2H, H3 and H4 respectively); 3.78 (s, 3H, $COOCH_3$ at C_6); 6.12, 7.31 (each s, each 1H, H8 and H5 respectively) and 10.54 (s, 1H, exchanged with D_2O, OH at C_7). Fraction F crystallised from petrol yielding 16 (0.8 g), m.p. 92–93° (Found: C, 70.8; H, 8.0. $C_{18}H_{24}O_4$ requires C, 71.0; H, 7.9%). NMR (CCl_4) δ: 1.34 [s, 12H, $2\times C(CH_3)_2$]; 1.74 (t, J = 7 Hz, 4H, H3 and H9); 2.57, 2.66 (each t, J = 9 Hz, each 2H, H4 and H10); 3.74 (s, 3H, $COOCH_3$ at C_6) and 7.32 (s, 1H, H5).

Methyl 7 - *methoxy* - 2,2 - *dimethyl* - 3,4 - *dihydro* - 2H - 1 - *benzopyran* - 6 - *carboxylate* (**17**)

11 (0.5 g) in dry acetone (20.0 ml) was refluxed with Me_2SO_4 (0.46 ml) in presence of anhyd K_2CO_3 (2.0 g) for 4 h. Working up of reaction mixture as usual yielded **17**, which crystallised from petrol as pale yellow prisms (0.45 g), m.p. 113–114° (lit[11] 112–113°). NMR (CCl_4) δ: 1.29 [s, 6H, $C(CH_3)_2$]; 1.72, 2.65 (each t, J = 7 Hz, each 2H, H3 and H4 respectively); 3.74, 3.76 (each s, each 3H, OCH_3 at C_7 and $COOCH_3$ at C_6); 6.21 and 7.45 (each s, each 1H, H8 and H5 respectively). **17** was found to be identical with methyl ether (Me_2SO_4–K_2CO_3–acetone) of **15**.

Methyl 7 - *methoxy* - 2,2 - *dimethyl* - 2H - 1 - *benzopyran* - 6 - *carboxylate* (**18**)

Method (i). **17** (0.1 g) in CCl_4 (15.0 ml) was refluxed for 3 h with NBS (0.072 g) and benzoyl peroxide (0.005 g). Working-up as usual yielded a residual oil, which was purified by preparative TLC (benzene:petrol, 3:1) to give **18** as pale yellow oil (0.07 g) (Found: C, 67.8; H, 6.5. $C_{14}H_{16}O_4$ requires C, 67.7; H, 6.4%). NMR ($CDCl_3$) δ: 1.39 [s, 6H, $C(CH_3)_2$]; 3.78, 3.80 (each s, each 3H, OCH_3 at C_7 and $COOCH_3$ at C_6); 5.42, 6.20 (each d, J = 10 Hz, each 1H, H3 and H4 respectively); 6.31 and 7.43 (each S, each 1H, H8 and H5 respectively).

Method (ii). **17** (0.1 g) in dry benzene (15.0 ml) was refluxed for 150 h with DDQ (0.1 g). Working up of reaction mixture as usual yielded **18** as pale yellow oil (0.08 g) identical with the chromene prepared by NBS method.

Methyl 5 - *methoxy* - 2,2 - *dimethyl* - 3,4 - *dihydro* - 2H - 1 - *benzopyran* - 6 - *carboxylate* (**20**)

10 (0.25 g) in dry acetone (10.0 ml) was refluxed with Me_2SO_4 (0.23 ml) in presence of anhyd K_2CO_3 (1.0 g) for 4 h. Working up of reaction mixture as usual yielded **20** as pale yellow oil (0.24 g) (lit[2] oil). NMR ($CDCl_3$) δ: 1.30 [s, 6H, $C(CH_3)_2$]; 1.72, 2.70 (each t, J = 7 Hz, each 2H, H3 and H4 respectively); 3.77 (s, 6H, OCH_3 at C_5 and $COOCH_3$ at C_6); 6.44 and 7.54 (each d, J = 9 Hz, each 1H, H8 and H7 respectively). **20** was found to be identical with methyl ether (Me_2SO_4–K_2CO_3-acetone) of **14**.

Methyl 5 - *methoxy* - 2,2 - *dimethyl* - 2H - 1 - *benzopyran* - 6 - *carboxylate* (**19**)

Method (i). **20** (0.1 g) in carbon tetrachloride (20.0 ml) was refluxed for 2 h with NBS (0.08 g) and benzoyl peroxide (0.001 g). Working-up of the reaction mixture as usual yielded residual oil, which was purified by preparative TLC (benzene:petrol ether; 1:1) to give **19** as colourless oil (0.066 g) (lit[2] oil). NMR ($CDCl_3$) δ: 1.42 [s, 6H, $C(CH_3)_2$]; 3.80, 3.81 (each s, each 3H, OCH_3 at C_5 and $COOCH_3$ at C_6); 5.55 (d, J = 10 Hz, 1H, H3); 6.48 (d, J = 9 Hz, 1H, H8); 6.55 (d, J = 10 Hz, 1H, H4) and 7.56 (d, J = 9 Hz, 1H, H7).

Method (ii). **20** (0.05 g) in dry benzene (10.0 ml) was refluxed for 140 h with DDQ (0.05 g). Working up of reaction mixture as usual yielded **19** as colourless oil (0.04 g), identical with the chromene prepared by NBS method.

Methyl 5 - hydroxy - 2,2 - dimethyl - 2H - 1 - benzopyran - 6 - carboxylate (**21**)

Method (i). **14** (0.05 g) in dry benzene (10.0 ml) was refluxed for 25 h with DDQ (0.05 g). The soln was filtered, the filtrate distilled and the residue thus obtained was purified by column chromatography. The column on elution with petrol gave **21** as colourless prisms (0.04 g), m.p. 75–76° (lit[2,8,10] oil). NMR ($CDCl_3$) δ: 1.40 [s, 6H, $C(CH_3)_2$]; 3.80 (s, 3H, $COOCH_3$ at C_6); 5.49 (d, J = 10 Hz, 1H, H3); 6.25 (d, J = 9 Hz, 1H, H8); 6.67 (d, J = 10 Hz, 1H, H4); 7.52 (d, J = 9 Hz, 1H, H7) and 11.2 (s, 1H, exchanged with D_2O, OH at C_5).

Method (ii).

(*i*) *Methyl 2 - hydroxy - 4 - (1,1 - dimethyl - prop - 2 - ynyloxy) - benzoate* (**22**). Methyl 2,4 - dihydroxybenzoate (1.0 g), 3 - chloro - 3 - methylbut - 1 - yne (3.0 ml), anhyd K_2CO_3 (3.0 g) and anhyd KI (1.0 g) in dry acetone (30.0 ml) were refluxed for 50 h. Working up of reaction mixture as usual yielded **22** (0.74 g) as pale yellow oil (Found: C, 66.5; H, 6.2. $C_{13}H_{14}O_4$ requires C, 66.7; H, 6.0%). NMR ($CDCl_3$) δ: 1.65 [s, 6H, $C(CH_3)_2$]; 2.63 (s, 1H, C≡CH); 3.84 (s, 3H, $COOCH_3$ at C_1); 6.56 (dd, J = 9 Hz, 2.5 Hz, 1H, H5); 6.78 (d, J = 2.5 Hz, 1H, H3); 7.62 (d, J = 9 Hz, 1H, H6) and 10.8 (s, 1H, exchanged with D_2O, OH at C_2).

(ii) *Methyl 5 - hydroxy - 2,2 - dimethyl - 2H - 1 - benzopyran - 6 - carboxylate* (**21**). **22** (0.7 g) was refluxed with N,N-dimethylaniline (1.0 ml) for 2 h. The mixture was cooled and ether (50.0 ml) added. Ethereal layer washed successively with HCl (5%, 35.0 ml), water, dried Na_2SO_4) and distilled. The residual oil thus obtained was purified by column chromatography and the column eluted with petrol to give **21** as colourless prisms (0.60 g). It was identical (m.p. mmp and IR) with the chromene prepared by dehydrogenation of **14** with DDQ.

Methyl 7 - hydroxy - 2,2 - dimethyl - 2H - 1 - benzopyran - 6 - carboxylate (**24**)

15 (0.1 g) in dry benzene (20.0 ml) was refluxed for 30 h with DDQ (0.1 g). Working up of reaction mixture as usual yielded a residue which was purified by column chromatography. The column on elution with benzene:petrol (1:9) gave 24 as colourless plates (0.08 g), m.p. 74–75° (lit.[12] 76°). NMR ($CDCl_3$) δ: 1.30 [s, 6H, $C(CH_3)_2$]; 3.74 (s, 3H, $COOCH_3$ at C_6); 5.46, 6.18 (each d, J = 10 Hz, each 1H, H3 and H4 respectively); 6.30, 7.35 (each s, each 1H, H8 and H5 respectively) and 10.9 (s, 1H, exchanged with D_2O, OH at C_7).

7 - Hydroxy - 2,2 - dimethyl - 2H - 1 - benzopyran - 6 - carboxylic acid (**23**)

24 (0.06 g) was refluxed with methanol (10.0 ml) and NaOH (20%, 3.0 ml) for 2 h. Methanol was distilled under vacuum, residue treated with crushed ice and acidified with dil HCl. The separated solid was then crystallised from ethyl acetate–benzene to give 23 as colourless plates, (0.05 g), m.p. 183° decomposed (lit[12] 183° decomposed). NMR ($CDCl_3 + CF_3COOH$) δ: 1.46 [s, 6H, $CCH_3)_2$]; 5.58, 6.25 (each d, J = 10 Hz, each 1H, H3 and H4 respectively); 6.39 and 7.50 (each s, each 1H, H8 and H5 respectively).

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