Synthesis of chromans from the reaction of *o*-quinone methide precursor with substituted styrenes

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In this work, the inverse-electron demanded Diels–Alder cycloaddition reaction of 1-dimethylaminomethyl-2-naphthol and 2-dimethylaminomethyl-4,5-dimethylphenol with (un)substituted styrenes were investigated. 3,4-Dihydro 2-(un)substitutedphenyl-2*H*-benzo[*f*]chromenes and 2-(un)substitutedphenyl-6,7-dimethylchromans were isolated from the reaction of 1-dimethylaminomethyl-2-naphthol and 2-dimethylaminomethyl-4,5-dimethylphenol with (un)substituted styrenes. The yields of the Mannich bases and the reactions of them with (un)substituted styrene appeared to be increased from *ortho*- to *para*- substitution.

Keywords: chroman, quinone methide, styrene, Diels–Alder, cycloaddition

o-Quinone-methides as a heterodiene component in Diels–Alder cyclo addition reaction with olefins, enol-ethers and enamines have received great attention in organic chemistry and biochemistry.[1-5] We had reported general synthesis of polycycloheteroaromatic compounds by generating *o*-quinone-methide from quinone-methide precursors, naphthalene, phenanthrene, pyridones and pyrimidine Mannich bases with aromatic amines.[6,7] *o*-Quinone-methides are reactive intermediates.[8a,b] We intended to expand the synthesis to new chroman derivatives,[9,10] which are used as antiinflammatory agent,[11] in arthritis,[12] in anxiety[4] and used as antioxidants for fats and oils and some of them show weak estrogenic activity.[13] We decided to investigate the inverse electron demanded Diels–Alder cycloaddition reaction of the 2-naphtol 1 and 3,4-dimethylphenol Mannich bases **4** as the quinone-methides precursors **5** and **6** with (un) (R=H, *o*-, *m*-, *p*-CH_3 and Cl) substituted styrenes for the synthesis of 3,4-dihydro-2-((un) substituted phenyl)-2*H*-benzo[*f*]chromenes **7** (R=H, *o*-, *m*-, *p*-CH_3 and Cl) and 2-((un) substituted phenyl)-6,7-)dimethylchromans **10** (R=H, *o*-, *m*-, *p*-CH_3 and Cl). We aimed to investigate the effect of electron donating substituents in the benzenoid ring of the styrene to the yields in the synthesis of substituted 3,4-dihydro-2*H*-benzo[*f*]chromenes **7** (R=H, *o*-, *m*-, *p*-CH_3 and Cl) and substituted-6,7-dimethylchromans **10** (R=H, *o*-, *m*-, *p*-CH_3 and Cl). Therefore 2-naphthol Mannich base **1** and the 3,4-dimethylphenol Mannich base **4** were reacted with styrenes in refluxing diphenylether under nitrogen for 20 hours.

The 3,4-dihydro-2-phenyl-2H-benzo[*f*]chromen **7** (R=H) and 2-phenyl-6,7-dimethylchroman **10** (R=H) were obtained in 52 and 53% yields (Table 1). When the Mannich bases **1** and **4** were reacted with *o*-methylstyrene under the same conditions; 3,4-dihydro-2-(*o*-methylphenyl)-2*H*-benzo[*f*]chromen, **7** (R=*o*-CH_3) and 2-(*o*-methylphenyl)-6,7-dimethylchroman **10** (R=*o*-CH_3) were obtained in 12 and 21% yields respectively. It was observed that the yields of the products were lower than that of styrenes products (Table 1). This could be attributed to the steric effect of the methyl group in the *ortho*- position on the styrene.

The same reaction were repeated with *m*-methylstyrene and 3,4-dihydro-2-(*m*-methylphenyl)-2*H*-benzo[*f*]chromene **7** (R=*m*-CH_3), 2-(*m*-methylphenyl)-6,7-dimethylchroman **10** (R=*m*-CH_3) were obtained in 18 and 25% yields respectively (Table 1). When the reactions were carried out under the same condition with *p*-methylstyrene, it was found that the product 3,4-dihydro-2-(*p*-methylphenyl)-2*H*-benzo[*f*]chromen **7** (R=*p*-CH_3) and 2-(*p*-methylphenyl)-6,7-dimethylchroman **10** (R=*p*-CH_3) were formed in 53 and 38% yields (Table 1).

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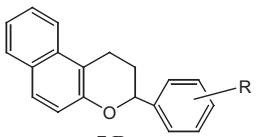
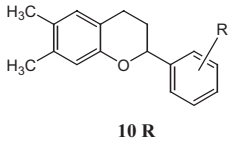
Table 1 The yields of chromenes (**7R**) and chromans(**10R**)



7 R



10 R

Chromene		Chromene	
R	Yield/%	R	Yield/%
H	52	H	53
o-CH_3	12	*o*-CH_3	21
m-CH_3	18	*m*-CH_3	25
p-CH_3	53	*p*-CH_3	38
o-Cl	8	*o*-Cl	16
m-Cl	20	*m*-Cl	20
p-Cl	33	*p*-Cl	28

These increases in the yields could be attributed to the methyl groups hyperconjugative effects in the para-position of the styrene.

To see the affect of the substituent, we tried the reaction of 2-naphthol Mannich base **1** and phenol Mannich base **4** with *ortho*-, *meta*- and *para*-chlorostyrenes. When the reactions were repeated under the same conditions, the yields of 3,4-dihydro-2-*(o*-, *m*- and *p*-chlorophenyl)-2*H*-benzo[*f*]chromen and 2-(*o*-, *m*- and *p*-chloro)phenyl-6,7-dimethylchroman were in 8% 7(R=*o*-Cl), 20% R=*m*-Cl); 33% (**7**, R=*p*-Cl); 16% **10** (R=o-Cl); 20% **10** (R=*m*-Cl) and 28% **10** (R=*p*-Cl) respectively (Table 1) when chlorine was substituted instead of methyl group on the phenyl ring on styrene.

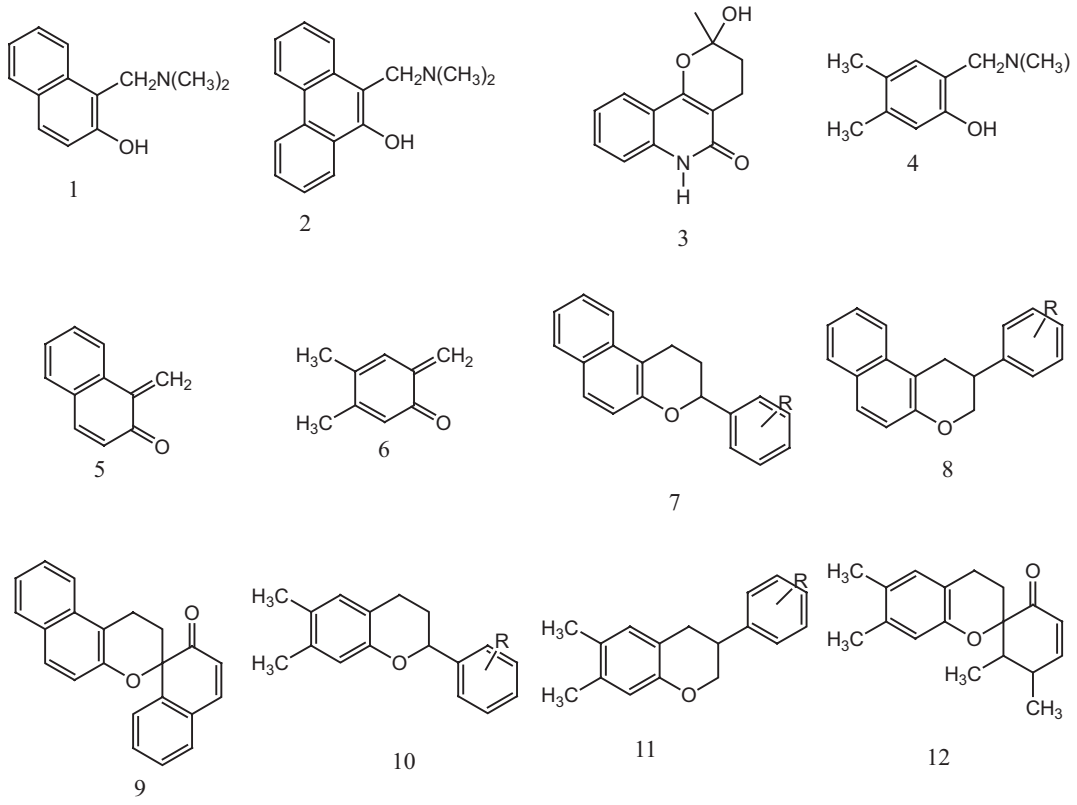
These decreases in the yields could be attributed to the inductively deactivating property of the chlorine. There were a smooth increase in the formation of chromens **7**R and chromans **10**R on going from *o*-, to *m*- and to *p* substituted styrenes.

However, in none of the products were the yields greater than that of styrenes itself **7** (R=H) and **10** (R=H). In all the reactions, products **8**R and **11**R were obtained, and the dimers **9** and **12** were isolated as side products (Scheme 1).[8b]

Experimental

General details

Melting points were determined on Electrothermal melting points apparatus. IR spectra were recorded on 1710 Perkin-Elmer Fourier Transform machine. UV spectra were recorded on PU 8720 Philips spectra. ^{1}H and ^{13}C NMR spectra were determined at 500 and 75 MHz respectively using a Bruker AMX 500 spectrometer for solutions in deuteriochloroform. Mass spectra were recorded on VD-Autospec Fisana Instrument, Merk Kieselgel F_{254} type^{60} and Kieselgel 40–60 μm type were used for TLC and column chromatography.



R=H, R = *o-,m- and p-* CH_3; R = *o-,m- and p-* Cl

Scheme 1

Preparing chromenes

Mannich base **1** (0.804 g, 4 mmol) and hydroquinone (20 mg) in diphenylether (20 ml) were treated with styrene (1 ml, 4 mmol) under nitrogen. This mixture was heated under nitrogen at 200°C for 20 h. The solvent was removed *in vacuo* to afford a brown oil which was chromatographed with SiO_2 (ethylacetate: petroleum ether 1 : 1) afforded 3,4-dihydro-2-phenyl-2*H*-benzo[*f*]chromene **7** (R=H) (0.416 g) (52%) which was recrystallised from ethanol as light yellow prisms. M.p. 85–86°C (lit. 86°C,[14] (Found: C, 87.5; H, 6.2 $C_{19}H_{16}O$ requires: C, 87.7; H, 6.2%)); M^+: 260; IR (KBr): 1621 (aromatic), 1262 (C–O–C) cm^{-1}; UV (MeOH): 229.7, 267.3, 277.6, 289.0, 320.2 and 334.3 nm; δ_H 2.29 (1H, m, 3-H), 2.45 (1H, m, 3-H), 3.21 (2H, m, 4-H), 5.18 (1H, dd, *J* = 2.3 and 7.9 Hz, 2-H), 7.26–7.90 (11H, m, Ar–H).

3,4-Dihydro-2-(o-methylphenyl)-2H-benzo[f]chromene **7** *(R=o-*CH_3*)*: Mannich base (1) (3.216 g, 16 mmol) and hydroquinone (20 mg) in diphenylether (20 ml) were treated with *o*-methylstyrene (2.1 ml, 16 mmol) under similar conditions. A brown oil was obtained and crystallised from ethanol to give 3,4-dihydro-2-(*o*-methylphenyl)-2*H*-benzo[*f*]chromene **7** (R=*o*-CH_3) (0.386 g) (12%). This was recrystallised from ethanol as pale white needles. M.p. 103–104°C (Found: C, 87.1; H, 6.6 $C_{20}H_{18}O$ requires C, 87.6; H, 6.6%); M^+: 274; IR (KBr): 1621 (aromatic), 1261 (C–O–C) cm^{-1}; UV (MeOH): 233.5, 267.2, 277.7, 289.2 and 334.4 nm; ^{1}H NMR ($CDCl_3$) δ: 2.21 (1H, m, *J* = 3.6 Hz, 3-H), 2.40 (1H, m, *J* = 2.1 Hz, 3-H), 2.45 (3H, s, -CH_3), 2.45 (2-H, m, *J* = 3.1 Hz, 4-H), 5.32 (1H, dd, *J* = 2 and 8.7 Hz, 2-H), 7.20–7.88 (10H, m, *J* = 5.6 Hz, Ar–H).

3,4-Dihydro-2-(m-methylphenyl)-2H-benzo[f]chromene **7**, *(R=m-*CH_3*)*: Mannich base (**1**) (3.216 g, 16 mmol) and hydroquinone (20 mg) in diphenylether (20 ml) were treated with *m*-methylstyrene (2.1 ml, 16 mmol) under similar conditions. The residue yielded a brown oil which was crystallised from light petroleum and afforded 3,4-dihydro-2-(*m*-methylphenyl)-2*H*-benzo[*f*]chromene **7** (R=*m*-CH_3) (0.579 g) (18%). This was recrystallised from light petroleum as pale light yellow needles. M.p. 81–82°C; (Found: C, 87.4; H, 6.6; $C_{20}H_{18}O$ requires C, 87.6; H, 6.6%); M^+: 274, IR (KBr): 1620 (aromatic), 1263 (C–O–C) cm^{-1}; UV (MeOH): 210.1, 228.0, 267.2, 277.6, 320.3 and 334.4 nm; ^{1}H NMR ($CDCl_3$), δ: 2.26 (1H, m, *J* = 3.2 Hz, 3-H), 2.39 (1H, m, *J* = 2.3 Hz, 3-H), 2.46 (3H, s, -CH_3), 3.18 (2H, m, *J* = 4.6 Hz, 4-H), 5.11(1H, dd, *J* = 2.3 and 8.2 Hz, 2-H), 7.21–8.89 (10H, m, *J* = 5.6 Hz, Ar–H).

3,4-Dihydro-2-(p-methylphenyl)-2H-benzo[f]chromene **7** *(R=p-*CH_3*)*: Mannich base (**1**) (3.216 g, 16 mmol) and hydroquinone (20 mg) in diphenylether (20 ml) were treated with *p*-methylstyrene (2.1 ml, 16 mmol) under similar conditions. A brown oily residue was obtained and crystallised from ethyl acetate as pale light yellow prisms to afford 3,4-dihydro-2-(*p*-methylphenyl)-2*H*-benzo[*f*]chromene **7**, (R=*p*-CH_3) (17,9 g) (53%) m.p. 113–114°C; (Found: C, 87.4; H, 6.6; $C_{20}H_{18}O$ requires C, 87.6; H, 6.6%); M^+: 274, IR (KBr): 1621 (aromatic), 1263 (C–O–C) cm^{-1}; UV (MeOH): 229.9, 267.5, 278.1, 289.4, 320.4 and 334.7 nm; ^{1}H NMR ($CDCl_3$), δ: 2.43 (1H, m, *J* = 4.2 Hz, 3-H), 2.54 (1H, m, *J* = 4.2 Hz, 3-H), 2.67 (3H, s, –CH_3), 3.32 (2H, t, *J* = 4.5 Hz, 4-H), 5.29 (1H, d, *J* = 1.3 Hz, 2-H), 7.48–8.06 (10H, m, *J* = 7.6 Hz, Ar–H).

3,4-Dihydro-2-(o-chlorophenyl)-2H-benzo[f]chromene **7** *(R=o-Cl)*: Mannich base (**1**) (3.216 g, 16 mmol) and hydroquinone (20 mg) in diphenylether (20 ml) were treated with o-chlorostyrene (2.1 ml, 16 mmol) under similar conditions. A brown oily residue was obtained and crystallised from methanol to afford 3,4-dihydro-2-(*o*-chlorophenyl)-2*H*-benzo[*f*]chromene **7** (R=*o*-Cl) (0.258 g) (8%). This was recrystallised from methanol-chloroform as light yellow prisms. M.p. 108–109°C (Found: C, 77.3; H, 5.1; $C_{19}H_{15}OCl$ requires C, 77.4; H, 5.1%); M^+: 294; IR (KBr): 1622 (aromatic), 1260 (C–O–C) cm^{-1}; UV (MeOH): 232.8, 267.2, 277.3, 288.8, 319.2 and 333.2 nm; ^{1}H NMR ($CDCl_3$) δ: 2.09 (1H, m, *J* = 2.5 Hz, 3-H), 2.58 (1H, m, *J* = 2.3 Hz, 3-H), 3.23 (2H, m, *J* = 3.9 Hz, 4-H), 5.55 (1H, dd, *J* = 2.3 and 8.0 Hz, 2-H), 7.21–7.89 (10H, m, *J* = 5.6 Hz, Ar–H).

3,4-dihydro-2-(m -chlorophenyl)-2H-benzo[f]chromene **7** *(R=m-Cl)*: Mannich base (**1**) (3.216 g, 16 mmol) and hydroquinone (20 mg) in diphenylether (20 ml) were treated with *m*-chlorostyrene (2.1 ml, 16 mmol) under similar conditions to afford a brown oil which was crystallised from light petroleum, to give white needles of a crystalline compound identified as 3,4-dihydro-2-(*m*-chlorophenyl)-2*H*-benzo[*f*]chromene **7** *(R=m-Cl)* (0.644 g) (20%). M.p. 86°C (Found: C, 77.4; H, 5.1); $C_{19}H_{15}OCl$ requires, C, 77.4; H, 5.1%); M^+: 294; IR (KBr): 1620 (aromatic), 1263 (C–O–C) cm^{-1}; UV (MeOH): 202.7, 233.0, 267.2, 276.9, 320.0 and 333.6 nm; ^{1}H NMR ($CDCl_3$), δ: 2.21 (1H, m, *J* = 2.4 Hz, 3-H), 2.40 (1H, m, *J* = 2.4 Hz, 3-H), 3.17 (2H, m, *J* = 3.6 Hz, 4-H), 5.09 (1H, dd, *J* = 2.3 and 8.0 Hz, 2-H), 7.31–7.92 (10H, m, J: 5.6 Hz, Ar–H).

3,4-Dihydro-2-(p-chlorophenyl)-2H-benzo[f]chromene **7** *(R=p-Cl)*: Mannich base (**1**) (3.216 g, 16 mmol) and hydroquinone (20 mg) in diphenylether (20 ml) were treated with *p*-chlorostyrene (2.0 ml, 16 mmol) under similar conditions. The brown oil was crystallised from ethyl acetate and afforded 3,4-dihydro-2-(*p*-chlorophenyl)-2*H*-benzo[*f*]chromene **7** *(R=p-Cl)* 1.046 g) (33%). This was recrystallised from ethyl acetate as pale light brown prisms. M.p. 143–144°C (Found: C, 74.7; H, 4.9; $C_{19}H_{15}OCl$ 0.5, H_2O requires C, 75.1; H, 5.3%); $M^{+\cdot}$ 294; IR (KBr): 1621 (aromatic), 1262 (C–O–C) cm^{-1}; UV (MeOH): 233.3, 267.3, 277.6, 289.3, 320.6 and 333.9 nm; ^1H NMR ($CDCl_3$) δ: 2.20 (1H, m, *J* = 2.3 Hz, 3-H), 2.40 (1H, m, *J* = 2.3 Hz, 3-H), 3.18 (2H, m, *J* = 3.5 Hz, 4-H), 5.10 (1H, dd, *J* = 2.3 and 7.9 Hz, 2-H), 7.22–7.88 (10H, m, *J* = 1.0 Hz, Ar–H).

2-Dimethylaminomethyl-4,5-dimethylphenol **4**: The Mannich base (**4**) was prepared according to the method of Caldwell and Thompson.[13] 3,4-Dimethylphenol (12.2 g, 0.1 mol) and dimethyl amine (35%, 5 ml, 0.1 mol) in ethyl alcohol (75 ml) were stirred at 25–35°C for 5 min. Formaldehyde (37%, 2.8 ml, 0.1 mol) was added dropwise to this mixture in 1 h and the mixture was left overnight to afford a white solid. Crystallisation from ethylalcohol gave colourless crystals as 2-dimethylaminomethyl-4,5-dimetylphenol 5 m.p. 79–80°C; yield: 6 g, 33%. Found: C, 73.1; H, 9.4; $C_{11}H_{17}NO$ requires: C, 73.7; H, 9.5; IR (KBr), ν_{max}: 3366 (phenol), 1640 (aromatic); UV (MeOH), λ_{max} (log ε): 218.2 (0.568), 235.1 (2.205), 285.7 (1.939), 325.0 (0.023) nm; ^1H NMR ($CDCl_3$), δ: 2.84 (3H, s, 5-H, $–CH_3$), 3.25 (3H, s, 4-H, $–CH_3$), 4.35 (6H, s, $–N(CH_3)_2$), 3.70 (2H, s, 7-H), 6.75 (1H, s, Ar–3–H), 6.84 (1H, s, Ar–6–H), 9.95 (1H, broad singlet, OH). ^{13}C NMR ($CDCl_3$), ppm: 19.146 (5-C–CH_3), 20.047 (4-C–CH_3), 44.906 (8-C), 62.944 (7-C), 117.639 (6-C), 119.436 (2-C), 127.006 (4-C), 129.778 (3-C), 137.625 (5-C), 156.146 (1-C).

2-Phenyl-6,7-dimethylchroman **10** *(R=H)*: Mannich base (**4**) (2.15 g, 12 mmol) and styrene (1.3 ml, 12 mmol) were treated in diphenylether (20 ml) in the presence of hydroquinone (20 mg). The resulting mixture was heated under dry nitrogen atmosphere at 200°C for 20 hours. The solvent was removed *in vacuo* and the residue was crystallised from ethylacetate to give colourless crystals as 2-phenyl-6,7-dimethylchroman **7**, (R=H) m.p. 111–112°C; yield: 1.98 g, 58%. Found: C, 85.0; H, 7.5; $C_{17}H_{18}O$ requires C, 85.6; H, 7.5; IR (KBr), ν_{max}: 1574 (aromatic), 1268 (C–O–C) cm^{-1}; UV (MeOH), λ_{max}(log ε): 191.9 (1.697), 193.8 (0.308), 197.1 (0.625), 199.2 (0.933), 204.0 (1.167), 208.0 (1.536), 210.1 (1.467), 284.8 (0.141) nm; ^1H NMR ($CDCl_3$) δ: 2.16–2.41 (2H, m, 3-H), 2.49 (6H, s, 6 and 7 Me's), 3.13–2.83 (2H, m, 4-H), 5.15 (1H, dd, *J* = 2.5 and 2.5 Hz, 2-H), 7.60–6.91 (6H, m, Ar–H). ^{13}C NMR ($CDCl_3$), ppm: 18.877 (7-C–CH_3), 19.628 (6-C–CH_3), 24.715 (4-C), 30.545 (3-C), 77.608 (2-C), 117.844 (8-C), 118.979 (4a-C), 126.434 (4'-C), 128.329 (3'-C), 28.560 (2'-C), 129.831 (6-C), 130.400 (5-C), 136.182 (7-C), 142.096 (1'-C), 153.073 (8a-C).

2-(o-Methylphenyl)-6,7-dimethylchroman **10** *(R=o-CH_3)*: Mannich base (**4**) (1.5 g, 8 mmol) and 2-methylstyrene (1.1 ml, 8 mmol) were treated in diphenylether (20 ml) in the presence of hydroquinone (20 mg) under similar conditions. The residue was chromatographed (SiO_2, pet.ether. 60–80°C) to give a yellow oil 2-(*o*-methylphenyl)-6,7-dimethylchroman **7**,(R=*o*-CH_3) Yield: 0.46 g, 21.7%. Found: C, 82.7; H, 7.5; $C_{18}H_{20}O$ requires: C, 85.6; H, 7.9%. IR (KBr), ν_{max}: 1625 (aromatic), 1264 (C–O–C) cm^{-1}; UV (MeOH), λ_{max}(log ε): 191.4 (0.292), 195.2 (0.287), 209.3 (1.569), 282.4 (0.105) nm; ^1H NMR ($CDCl_3$) δ: 2.43–2.11 (2H, m, 3-H), 2.44 (6H, s, 6 and 7 Me's), 2.64 (3H, s, 2'Me), 3.22–3.01(2H, m, 4-H), 5.45 (1H, dd, *J* = 1.8 and 8.7 Hz, 2-H), 7.78–7.43 (6H, m, Ar–H). ^{13}C NMR ($CDCl_3$), ppm: 18.813 (7-C–CH_3), 19.044 (6-C–CH_3), 19.556 (2'-CH_3), 25.213 (4-C), 28.914 (3-C), 74.884 (2-C), 117.798 (8-C), 188.858 (4a-C), 125.696 (5'-C), 126.322 (4'-C), 127.618 (6'-C), 128-305 (3'-C), 130.353 (6-C), 130.349 (5-C), 134.718 (7-C), 135.639 (2'-C), 139.836 (1'-C), 153.363 (8a-C).

2-(m-Methylphenyl)-6,7-dimethylchroman **10** *(R=m-CH_3)*: Mannich base (**4**) (2.16 g, 12 mmol) and 3-methylstyrene (1.6 ml, 16 mmol) were treated in diphenylether (20 ml) in the presence of hydroquinone (20 mg) under similar conditions.The residue was chromatographed (SiO_2,hexane/chloroform) to afford 2-*m*-methylphenyl)-6,7-dimethylchroman **7**, (R=*m*-CH_3). Crystallisation from ethylacetate gave pale yellow crystals m.p. 50–51°C: yield: 0.78 g, 25%. Found: C, 83.6; H, 8.0; $C_{18}H_{20}O$ requires: C, 85.6; H, 7.9%. IR (KBr), ν_{max}: 1627 (aromatic), 1264 (C–O–C) cm^{-1}; UV (MeOH), λ_{max}(log ε): 195.0 (0.492), 211.5 (2.001), 281.6 (0.292) nm; ^1H NMR ($CDCl_3$) δ: 2.35–2.21 (2H, m, 3-H), 2.39 (6H, s, 6 and 7 Me's), 2.80 (3H, s, 3'Me), 3.18–2.90 (2H, m, 4-H), 5.16 (1H, dd, *J* = 2.3 and 7.6 Hz, 2-H), 7.51–7.06 (6H, m, Ar–H). ^{13}C NMR ($CDCl_3$), ppm: 19.422 (7-C–CH_3), 20.164 (6-C-CH_3), 22.033 (3'-CH_3), 25.408 (4-C), 30.918 (3-C), 78.713 (2-C), 118.747 (8-C), 199.420 (4a-C), 124.090 (6'-C), 127.315 (5'-C), 128.723 (6-C), 128-797 (4'-C), 129.120 (2'-C), 130.905 (5-C), 136.192 (7-C), 128.666 (3'-C), 142.566 (1'-C), 153.657 (8a-C).

2-(p-Methylphenyl)-6,7-dimethylchroman **10** *(R=p-CH_3)*: Mannich base (**4**) (1.5 g, 8 mmol) and *p*-methylstyrene (1.1 ml, 8 mmol) were treated in diphenylether (20 ml) in the presence of hydroquinone (20 mg) under similar conditions. The precipitate was purified by column chromatography (SiO_2, hexane/chloroform). Crystallisation from ethylacetate afforded colourless crystals as 2-(*p*-methylphenyl)-6,7-dimethylchroman **7** (R=*p*-CH_3) m.p. 116–117°C: yield: 1.17 g, 38%. Found: C, 85.7; H, 7.9; $C_{18}H_{20}O$ requires: C, 85.6; H, 7.9. IR (KBr), ν_{max}: 1625 (aromatic), 1262 (C–O–C) cm^{-1}; UV (MeOH), λ_{max}(log ε): 231.4 (0.892), 286.4 (0.359) nm; ^1H NMR ($CDCl_3$) δ: 2.18 (2H, m, 3-H), 2.22 (6H, s, 6 and 7 Me's), 2.46 (3H, s, 4'Me), 3.05–2.78 (2H, m, 4-H), 5.07 (1H, dd, *J* = 6.2 Hz, 2-H), 7.40–6.82 (6H, m, Ar–H). ^{13}C NMR ($CDCl_3$), ppm: 18.827 (7-C–CH_3), 19.578 (6-C–CH_3), 21.220 (4'-CH_3), 24.745 (4-C), 30.193 (3-C), 77.499 (2-C), 117.382 (8-C), 118.832 (4a-C), 126.015 (2'-C), 128.239 (6-C), 129.186 (3'-C), 130.324 (5-C), 135.660 (7-C), 137.456 (4'-C), 139.032 (1'-C), 153.081 (8a-C).

2-(o-Chlorophenyl)-6,7-dimethylchroman **10** *(R=o-Cl)*: Mannich base (**4**) (1.45 g, 8 mmol) and *o*-chlorostyrene (1 ml, 8 mmol) were treated in diphenylether (20 ml) in the presence of hydroquinone (20 mg) under similar conditions. The residue was chromatographed (SiO_2, hexane/chloroform) to give a brown oil as 2-(*o*-chlorophenyl)-6,7-dimethylchroman **7**, (R=*o*-Cl): yield: 0.36 g, 16%. Found: C, 74.1; H, 5.5; $C_{17}H_{17}OCl$ requires: C, 74.8; H, 6.2. IR (KBr), ν_{max}: 1626 (aromatic); 1264 (C–O–C) cm^{-1}; UV (MeOH), λ_{max}(log ε): 191.2 (0.396), 195.3 (0.430), 211.3 (1.949), 283.5 (0.235), 289.1 (0.235), 324.5 (0.007) nm; ^1H NMR ($CDCl_3$) δ: 1.83–1.75 (2H, m, 3-H), 2.11 (6H, s, 6 and 7 Me's), 2.91–2.56 (2H, m, 4-H), 5.30 (1H, dd, *J* = 1.8 and 8.1 Hz, 2-H), 7.50–6.64 (6H, m, Ar–H). ^{13}C NMR ($CDCl_3$), ppm: 19.277 (7-C–CH_3), 20.028 (6-C–CH_3), 25.136 (4-C), 29.292 (3-C), 75.014 (2-C), 118.237 (8-C), 119.362 (4a-C), 127.613 (6'-C), 127.699 (5'-C), 128.880 (3'-C), 129.133 (4'-C), 129.866 (6-C), 130.819 (5-C), 132.013 (2'-C), 136.182 (7-C), 140.110 (1'-C), 153.377 (8a-C).

2-(m-Chlorophenyl)-6,7-dimethylchroman **10** *(R=m-Cl)*: Mannich base (**4**) (3.21 g, 16 mmol) and *m*-chlorostyrene (2.1 ml, 16 mmol) were treated in diphenylether (20 ml) in the presence of hydroquinone (20 mg). The resulting mixture was heated under dry nitrogen atmosphere at 200°C for 20 hours. The solvent was removed *in vacuo* and the dark brown oily residue was purified by column chromatography (SiO_2,pet.ether 60–80°C) to give a yellow solid. Crystallisation from ethylacetate white needle-like crystals 2-*(m*-chlorophenyl)-6,7-dimetylchroman **7** (R=*m*-Cl) m.p. 50–51°C; yield: 0.64 g, 20%. Found: C, 74.5; H, 6.3; $C_{17}H_{17}OCl$ requires: C, 74.8; H, 6.2. IR (KBr), ν_{max}: 1626 (aromatic), 1260 (C–O–C) cm^{-1}; UV (MeOH), λ_{max}(log ε): 206.7 (1.331), 280.4 (0.093), 324.3 (-0.011) nm; ^1H NMR ($CDCl_3$) δ: 2.18-2.08 (2H, m, 3-H), 2.28 (6H, s, 6 and 7 Me's), 3.08–2.79 (2H, m, 4-H), 5.11 (1H, dd, *J* = 2.04 and 9.9 Hz, 2-H), 7.56–6.87 (6H, m, Ar–H). ^{13}C NMR ($CDCl_3$), ppm: 19.327 (7-C–CH_3), 20.077 (6-C–CH_3), 25.006 (4-C), 30.754 (3-C), 77.345 (2-C), 118.255 (8-C), 118.635 (4a-C), 124.682 (6'-C), 126.689 (5'-C), 128.324 (2'-C), 129.017 (6-C), 130.294 (4'-C), 130.848 (5-C), 134.882 (3'-C), 135.898 (7-C), 144.645 (1'-C), 153.600 (8a-C).

2-(p-Chlorophenyl)-6,7-dimethylchroman **10** *(R=p-Cl)*: Mannich base (4) (2.9 g, 16 mmol) and *p*-chlorostyrene (2 ml, 16 mmol) were treated in diphenylether (20 ml) in the presence of hydroquinone (20 mg) under similar conditions. The residue was chromatographed (SiO_2, hexane/chloroform) to afford a product 2-(*p*-chlorophenyl)-6,7-dimethylchroman **7** (R=*p*-Cl). Recrystallisation from ethylacetate gave colourless crystals m.p. 104–105°C; yield: 1.26 g, 28.5%. Found: C, 75.2; H, 6.3; $C_{17}H_{17}OCl$ requires: C, 74.8; H, 6.2. IR (KBr), ν_{max}: 1622 (aromatic); 1261 (C–O–C) cm^{-1}; UV (MeOH), λ_{max}(log ε): 218.4 (0.372), 231.2 (1.527), 283.3 (0.464), 290.3 (0.464) nm; ^1H NMR ($CDCl_3$) δ: 1.98–1.85 (2H, m, 3-H), 2.10 (6H, s, 6 and 7 Me's), 2.88–2.59 (2H, m, 4-H), 4.93 (1H, dd, *J* = 2.4 and 7.4 Hz, 2-H), 7.26–6.76 (6H, m, Ar–H). ^{13}C NMR ($CDCl_3$), ppm: 10.225 (7-C–CH_3), 19.880 (6-C–CH_3), 24.876 (4-C), 30.625 (3-C), 77.469 (2-C), 118.117 (8-C), 119.051 (4a-C), 127.796 (2'-C), 128.942 (6-C), 129.057 (3'-C), 130.732 (5-C), 133.807 (4'-C), 136.227 (7-C), 140.928 (1'-C), 153.082 (8a-C).

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