CYCLIZATION OF *o*-(3-HYDROXY-3-METHYLBUTYNYL)-PHENOLS WITH BORON TRIBROMIDE TO 4-BROMO-2,2-DIMETHYLCHROMENES AND THEIR ELECTROREDUCTION TO 2,2-DIMETHYLCHROMENES

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Abstract —— Cyclization of *o*-(3-hydroxy-3-methylbutynyl)phenols (**2**) with boron tribromide gave easily 4-bromo-2,2-dimethylchromenes (**3**). Electrolytic reduction of **3** at a Hg-pool electrode afforded the corresponding 2,2-dimethylchromenes (**6**) in high yields.

The literature has shown a variety of methods to prepare halogenated 2*H*-1-benzopyrans.[1-7] For example, 4-chloro- and 4-bromochromenes were prepared from aryl 3-halopropargyl ethers under thermal conditions.[5] As the continuation of our recent research on electrosynthesis of 2,2-dimethylchromenes,[8] we now wish to report on cyclization of *o*-(3-hydroxy-3-methylbutynyl)phenols to 4-bromo-2,2-dimethylchromenes with boron tribromide and electrosynthesis of 2,2-dimethylchromenes from the resulting 4-bromochromenes. This type of cyclization of *o*-alkynylphenols and electroreductive conversion of the resulting 4-bromo-2,2-dimethylchromenes is hitherto unknown and provides a new synthetic route for 2,2-dimethylchromenes. The reinvestigation of the reaction of *o*-(3-hydroxy-3-methylbutynyl)phenols with boron tribromide revealed that the structure of the products was 4-bromo-2,2-dimethylchromenes but not 2-(1-bromo-1-methylethyl)benzofurans deduced in the previous paper,[8] as the result of ^{13}C-^{1}H two-dimensional NMR and an X-Ray crystallographic analysis. Therefore, we wish here to correct the errors present in the original study.[8]

RESULTS AND DISCUSSION

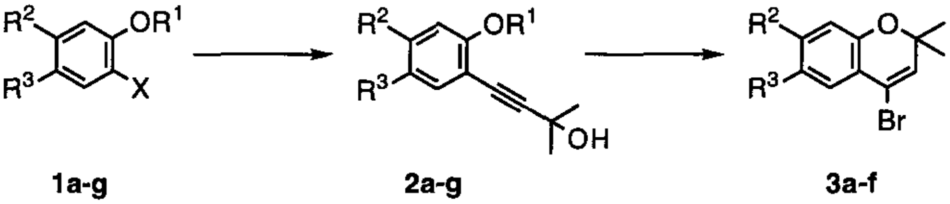
Alkynylation of *o*-halophenols (1) and cyclizayion of the resulting compounds (2)

2-Benzyloxy-4-methoxyiodobenzene (**1f**) and 4-methoxy-2-methoxymethoxyiodobenzene (**1g**) were prepared by benzylation and methoxymethylation of 2-hydroxy-4-methoxyiodobenzene, which was synthesized by iodine-silver trifluoroacetate method. Other iodophenols were synthesized according to the literature procedure.[8,9] The coupling reaction of the halophenols (**1**) with 2-methyl-3-butyn-2-ol in the presence of Pd(0) under suitable conditions gave the corresponding *o*-(3-hydroxy-3-methylbutynyl)phenols (**2**) in high yields.[10,11] The cyclization of **2** with boron tribromid in dichloromethane gave 4-bromo-2,2-

dimethylchromenes (**3**) in moderate yields (Scheme 1 and Table 1).

o-(3-Hydroxy-3-methylbutynyl)phenols (**2d** and **2g**) were more easily converted into 4-bromo-2,2-dimethylchromenes (**3c** and **3f**) than conversion of **2c** and **2f** into **3c** and **3f**, because of easier demethoxymethylation of **2d** and **2g** than debenzylation of **2c** and **2f** (Table 1). In the cyclization of **2e** with boron tribromide, 2',4'-dihydroxy-5'-(3-hydroxy-3-methylbutynyl)acetophenone (**4**) (18% yield) and 2',4'-dihydroxy-5'-(3-methyl-3-buten-1-yl)acetophenone (**5**) (14% yield) were obtained as by-products besides **3d** as a major product (Scheme 2). The acetophenone (**4**) was cyclized to 4-bromochromene (**3d**) with boron tribromide in 80% yield. Compound (**3d**) was converted into the methyl ether (**3e**) by dimethyl sulfate-potassium carbonate method. On the basis of these results, a plausible reaction mechanism is proposed for the cyclization of **2** to **3** as illustrated in Scheme 3.

The structure of **3d** was absolutely verified by a representative X-Ray crystallographic analysis of **3d** to be 6-acetyl-4-bromo-7-hydroxy-2,2-dimethylchromene. Measurement of the ^{13}C NMR spectrum of **3d**

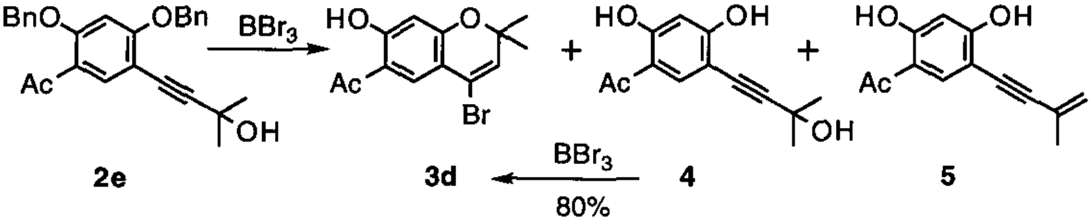


1a-g, 2a-g

a : R^1=Me, R^2=R^3=H, X=I
b : R^1=Bn, R^2=H, R^3=Me, X=Br
c : R^1=Bn, R^2=H, R^3=Ac, X=I
d : R^1=MOM, R^2=H, R^3=Ac, X=I
e : R^1=R^2=Bn, R^3=Ac, X=I
f : R^1=Bn, R^2=OMe, R^3=H, X=I
g : R^1=MOM, R^2=OMe, R^3=H, X=I

3a : R^2=R^3=H
3b : R^2=H, R^3=Me
3c : R^2=H, R^3=Ac
3d : R^2=OH, R^3=Ac
3e : R^2=OMe, R^3=Ac
3f : R^2=OMe, R^3=H

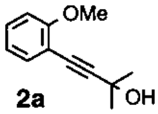
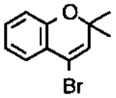
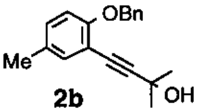
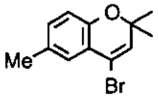
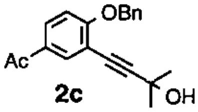
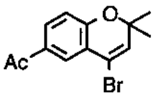
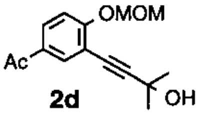
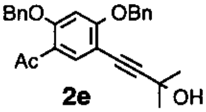
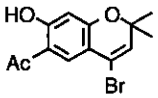
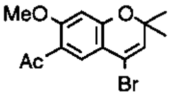
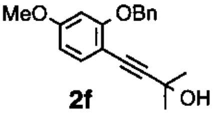
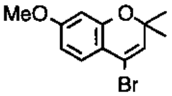
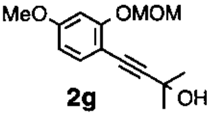
Scheme 1



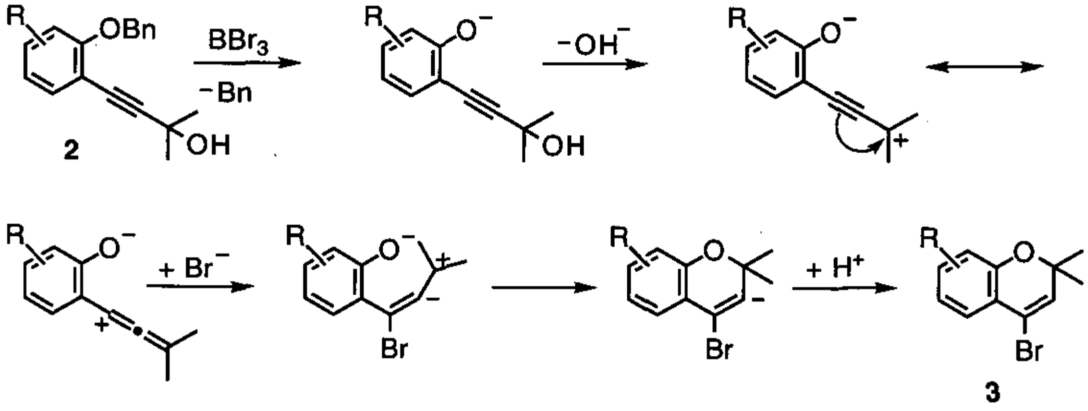
Scheme 2

coupled with that of the heteronuclear ^{13}C-^{1}H chemical shift correlated spectrum (HETEROCOSY) led us to assign all the carbon signals (Table 2). On the basis of these results, the structures of **3a-f** were confirmed to be the corresponding 4-bromo-2,2-dimethylchromenes. The results indicated that the structure of 2-(1-bromo-1-methylethyl)benzofurans present in the previous paper[8] was incorrect.

Table 1. Synthesis of 4-bromo-2,2-dimethylchromenes (**3**)

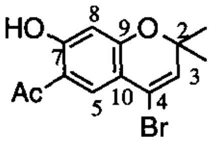
Substrate	BBr$_3$ (equiv.)	React. cond.		Product (Yield %)		
 **2a**	4.0	0°C	5 min	**3a**	54	
 **2b**	2.6	25°C	5 min	**3b**	40	
 **2c**	2.5	-70°C	15 min	**3c**	30	
 **2d**	1.0	-70°C	10 min	**3c**	52	
 **2e**	4.0	0°C	5 min	**3d**	54	
				3e$^{1)}$	95	
 **2f**	2.0	-70°C	10 min	**3f**	48	
 **2g**	1.0	-70°C	15 min	**3f**	58	

1) **3e** was obtained by methylation of **3d** .



Scheme 3

Table 2 ^1H and ^{13}C NMR (400 MHz) spectral data for compound (3d) in $CDCl_3$

Compound	δ (ppm)							
 **3d**	C-2	80.1	C-3	130.1	C-4	112.9	C-5	129.8
			H(s)	5.97			H(s)	7.74
	C-6	114.1	C-7	165.9				
			OH(s)	12.77				
	C-8	104.6	C-9	159.7	C-10	115.6	$(CH_3)_2$	28.2
	H(s)	6.33					6H(s)	1.47
	CH_3	26.3	CO	202.6				
	3H(s)	2.60						

Electroreduction of 4-bromo-2,2-dimethylchromenes (3)

Polarography. The dc polarogram of **3e** at a dropping mercury electrode in acetonitrile (MeCN) containing 0.1 mol dm^{-3} tetrabutylammounium perchlorate (Bu_4NClO_4) in the absence of proton donors exhibited two waves with the half-wave potentials ($E_{1/2}$) of -2.42 and -2.64 V. When benzoic acid (2 equiv.) was added to the medium as a proton donor, these waves merged to a single wave as shown by curve **b** in Figure 1 because $E_{1/2}$ of the first reduction wave was not changed, but that of the second reduction wave was shifted to more positive potential by the addition of benzoic acid. The differential pulse polarogram in the presence of benzoic acid showed, however, equivocal two peaks as shown by curve **c** in Figure 1. Therefore, $E_{1/2}$s of the first and second waves in the presence of benzoic acid can not be exactly estimated.

The second reduction wave of **3e** in the absence of proton donors will be ascribed to the reduction of **6e**, since its $E_{1/2}$ (-2.63 V) agreed closely with $E_{1/2}$ (-2.64 V) for the second wave of **3e** and was shifted to more positive potential by the addition of benzoic acid as did **3e**. This is strengthened by the evidence that **6e** was produced in a high yield in the controlled potential macroelectrolysis of at the plateau potential of the first reduction wave (see Table 3).

The dc polarograms of **3a**, **3b** and **3c** also showed two waves as well as **3e** and their $E_{1/2}$s were -2.63, -2.65, and -2.31 V for the first reduction wave, and -3.03, -3.04, and -2.52 V for the second one, respectively. The compound **3f** showed only a wave with $E_{1/2}$ of -2.85 V and was the most difficult to be reduced among 4-bromo-2,2-dimethylchromenes studied.

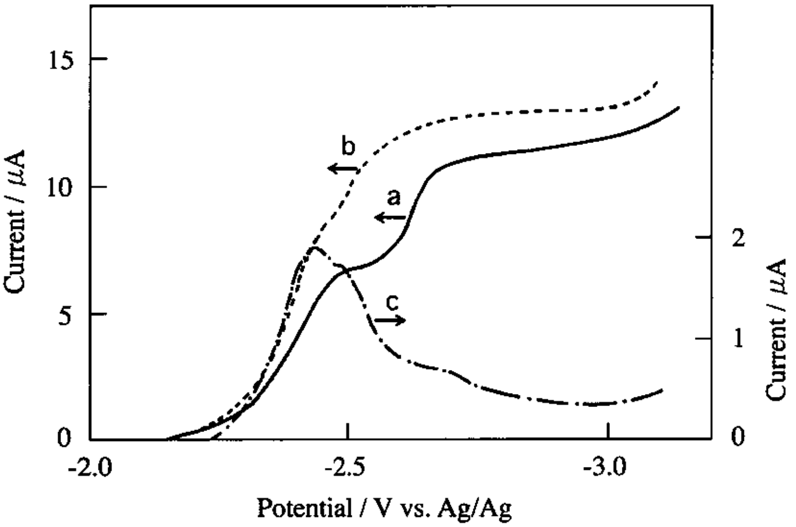
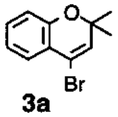
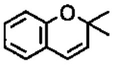
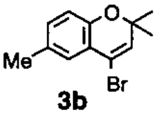
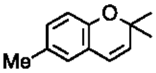
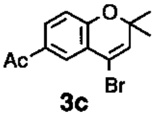
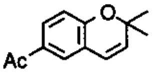
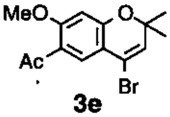
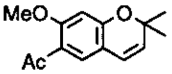
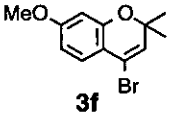
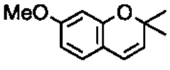


Figure 1 Dc polarograms (**a** and **b**) and differential pulse polarogram (**c**) of 1.0 x 10^{-3} mol dm^{-3} **3e** in MeCN containing 0.1 mol dm^{-3} Bu_4NClO_4 at 27 °C. Curve **a** : In the absence of proton donors. Curves **b** and **c** : In the presence of 2 x 10^{-3} mol dm^{-3} benzoic acid.

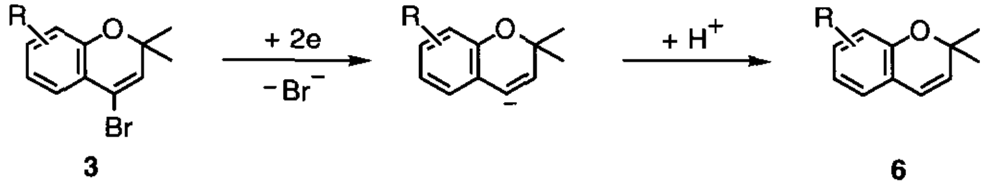
Macroelectrolysis. A series of controlled potential macroelectrolyses of **3a-c** and **3e-f** were carried out at a Hg-pool cathode at the potential of the first reduction wave in MeCN containing 0.1 mol dm^{-3} tetraethylammonium *p*-toluenesulfonate (Et_4NOTs) in the absence and presence of benzoic acid as a proton donor at room temperature. The results of these macroelectrolyses are listed in Table 3. The coulometric *n*-values (electrons per molecule) were obtained from the amount of substrate added and the quantity of electricity passed until the electrolysis finished. The 4-bromo-2,2-dimethylchromenes (**3a-c** and **3e-f**) were electrochemically reduced to give the debrominated products (**6a-c** and **6e-f**). The yields of **6** were affected to an extent by the substituent groups of **3**. For example, the electroreduction of **3b** and **3f** bearing an electron-releasing group such as Me and OMe led to **6b** and **6f** in high yields as much as **3a** respectively. Although **3c** and **3e** bearing an electron-withdrawing group (MeCO) were reduced more

Table 3 Controlled potential macroelectrolyses of **3a-d** at the first reduction potential of the Hg pool cathode in MeCN/0.1M Et_4NOTs

Bromobenzo-pyran	$E_{1/2}$/ V vs. Ag/0.1M $AgNO_3$	Proton donoer (PhCOOH) / equiv.	n-Value / F mol^{-1}	Product (Yield %)	
 **3a**	-2.6	none	2.1	87	 **6a**
		2.0	3.0	85	
 **3b**	-2.6	none	2.1	92	 **6b**
		2.0	2.6	86	
 **3c**	-2.3	none	1.5	60	 **6c**
		2.0	2.8	63	
 **3e**	-2.4	none	1.8	73	 **6e**
		2.0	2.8	61	
 **3f**	-2.8	none	2.1	91	 **6f**

easily than **3a**, **6c** and **6e** were produced in lower yields than **6a**. In spite of the fact that the reduction of **3** to **6** involves the addition of a proton, the addition of a proton donor such as benzoic acid had no significant influence on the yield of **6**. As shown in Table 3, polarography also showed that $E_{1/2}$ for the first reduction wave was not shifted by the addition of benzoic acid, suggesting that the potential-determining transition state does not contain a proton. The n-values for the electroreduction of **3a-c** and **3e-f** in the absence of the proton donor were about 2, while the n-values in the presence of benzoic acid were 3. The n-values of about 2 can be easily understood by the formation of **6**. However, no explanation for the increase in the n-values by the addition of benzoic acid can be offered at the present time. On the basis of our results, a plausible reaction mechanism is proposed for the electroreduction of **3** to **6** as illustrated in Scheme 4.

Bhuvaneswari *et al.* have shown the controlled potential electrolysis of 3-bromochromenes at -2.4 V at a Hg-pool cathode in MeCN containing acetic anhydride involves a ring-opening reaction yielding *o*-allenylphenyl acetate as major products with chromenes in minor amounts.[12] A similar electrolysis of **3e** was



Scheme 4

performed at -2.4 V at the Hg-pool cathode in MeCN containing acetic anhydride (5 equiv.). In our case, **6e** was produced in 86% yield, but a ring-opening product such as *o*-allenylphenyl acetate was not obtained.

Accordingly, the present method for synthesizing 2,2-dimethylchromenes (**6**) from *o*-(3-hydroxy-3-methylbutynyl)phenols (**2**) is an effective procedure.

EXPERIMENTAL

All the melting points are uncorrected. The ^{1}H NMR spectra were measured with a Hitachi R-24B spectrometer (60 MHz) and a JEOL EX400 MHz spectrometer (100.4 MHz for ^{13}C), using tetramethylsilane as an internal standard (δ, ppm). Column chromatography and thin layer chromatography (TLC) were carried out on Kieselgel 60(70-230 mesh) and with Kieselgel 60 F-254 (Merck).

2-Iodo-5-methoxyphenol. Silver trifluoroacetate (11.05 g, 50 mmol) was added to a solution of 3-methoxyphenol (6.21 g, 50 mmol) in chloroform (50 mL). To the suspension, was added a solution of iodine (12.7 g, 50 mmol) in chloroform (400 mL) dropwise with stirring over a period of 1.5 h at rt. After stirring an additional hour, the mixture was filtered and the separated silver iodide was washed with chloroform. The filtrate was washed with 5% aq $Na_2S_2O_3$, 5% aq sodium hydrogen carbonate, and water, and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the resulting compound was purified by silica gel column chromatography (dichloromethane as a solvent) to yield 2-iodo-5-methoxyphenol (7.75 g, 62%) as colorless plates, mp 70-71°C (from CCl_4). ^{1}H NMR(60 MHz; $CDCl_3$): δ 3.78(3H, s, OMe), 5.29(1H, s, OH), 6.31(1H, dd, J=2, 8 Hz, 4-H), 6.59(1H, d, J=2 Hz, 6-H), 7.48(1H, d, J=8 Hz, 3-H). Anal. Calcd for $C_7H_7O_2I$: C, 33.60; H, 2.82. Found: C, 33.46; H, 2.77.

2-Benzyloxy-4-methoxyiodobenzene (1f). Benzyl chloride (7.26 mL, 24 mmol) was added to a solution of 2-iodo-5-methoxyphenol (5.0 g, 20 mmol) in *N,N*-dimethylformamide (DMF) (50 mL) in the presence of potassium carbonate (5.53 g, 40 mmol) at 50°C, and the mixture was stirred for 1 h at 50°C. After removal of potassium carbonate, the reactive mixture was extracted with ethyl acetate, and the extract was washed with dilute hydrochloric acid and water, and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the resulting compound was purified by silica gel column chromatography (hexane:ethyl acetate=5:1) to yield **1f** (6.6 g, 97%) as colorless oil. ^{1}H NMR(60 MHz; $CDCl_3$): δ 3.71(3H, s, OMe), 5.05(2H, s, OCH_2), 6.26(1H, dd, J=2, 8 Hz, 5-H), 6.43(1H, d, J=2 Hz, 3-H), 7.10-

7.60(5H, m, *Ph*CH_2), 7.57(1H, d, J=8 Hz, 6-H). Anal. Calcd for $C_{14}H_{13}O_2I$: C, 49.43; H, 3.85. Found: C, 49.49; H, 3.74.

4-Methoxy-2-methoxymethoxyiodobenzene (1g). A mixture of 2-iodo-5-methoxyphenol (1.0 g, 4 mmol), *N,N*-diisopropylethylamine (20.7 mL, 120 mmol) and methoxymethyl chloride (4.6 mL, 60 mmol) in dichloromethane (50 mL) was stirred for 40 min at rt. The reaction mixture was poured into a mixture of water and ice, and neutralized with 2% aq hydrochloric acid. The mixture was extracted with dichloromethane, and the extract was washed with water, and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the resulting compound was purified by column chromatography (chloroform) to yield **1g** (1.13 g, 95%) a pale yellow oil. ^1H NMR(60 MHz; $CDCl_3$): δ 3.49(3H, s, CH_2*OMe*), 3.73(3H, s, Ar-*OMe*), 5.18(2H, s, OCH_2), 6.32(1H, dd, J=2, 8 Hz, 5-H), 6.64(1H, d, J=2 Hz, 3-H), 7.55(1H, d, J=8 Hz, 6-H). Anal. Calcd for $C_9H_{11}O_3I$: C, 36.76; H, 3.77. Found: C, 36.94; H, 3.76.

General procedure for coupling reaction of *o*-halophenols (1) with 2-methyl-3-butyn-2-ol To a solution *o*-halophenol (**1**) (40 mmol) and 2-methyl-3-butyn-2-ol (10.1 g , 120 mmol) in a mixture of Et_3N (250 mL)-DMF (50 mL) was added $PdCl_2$ (3 mol%, 1.2 mmol), PPh_3 (6 mol%, 2.4 mmol), and CuI (3 mol%, 1.2 mmol). The mixture solution was stirred under nitrogen at 50−85°C for 0.5−20 h until completion of reaction by TLC. The reaction mixture was filtered through charcoal to remove the catalyst. The filtrate was concentrated under reduced pressure and then the residue was extracted with ethyl acetate, and the extract was washed with 2% aq HCl and water , and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the resulting compound was purified by silica gel column chromatography. Compounds (**2a**, **2c** and **2e**) were prepared according to the procedures as reported in the preceding paper.[10]

1-Benzyloxy-2-(3-hydroxy-3-methylbutynyl)-4-methylbenzene (2b). mp 46-47°C, 69% yield (from hexane), colorless prisms (chloroform as a solvent for chromatography). ^1H NMR(60 MHz; $CDCl_3$): δ 1.57 (6H, s, 2 x Me), 2.19(4H, s, Ar-*Me* and OH), 5.01(2H, s, OCH_2), 6.68(1H, d, J=8 Hz, 6-H), 6.93(1H, dd, J=2, 8 Hz, 5-H), 7.05-7.50(8H, m, 8 x Ar-*H*). Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19. Found: C, 81.32; H, 7.27.

3'-(3-Hydroxy-3-methylbutynyl)-4'-methoxymethoxyacetophenone (2d). A brown oil, 86% yield (chloroform:acetone=10:1 as a solvent for chromatography). ^1H NMR(60 MHz; $CDCl_3$): δ 1.65(6H, s, Me), 2.53(3H, s, Ac), 3.25(1H, br s, OH), 3.52(3H, s, OMe), 5.29(2H, s, OCH_2), 7.09(1H, d, J=8 Hz, 5'-H), 7.83(1H, dd, J=2, 8 Hz, 6'-H), 7.94(1H, d, J=2 Hz, 2'-H). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.53; H, 6.90.

2-Benzyloxy-1-(3-hydroxy-3-methylbutynyl)-4-methoxybenzene (2f). mp 72-73°C, 80% yield (from hexane), pale brown needles (chloroform:acetone=20:1 as a solvent for chromatography). ^1H NMR(60 MHz; $CDCl_3$): δ 1.61(6H, s, 2 x Me), 2.38(1H, s, OH), 3.76(3H, s, OMe), 5.09(2H, s, OCH_2), 6.42(1H, dd, J=2, 8 Hz, 5-H), 6.47(1H, d, J=2 Hz, 3-H), 7.20-7.65(6H, m, 6-H and 5 x Ar-*H*). Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 77.25; H, 6.89.

1-(3-Hydroxy-3-methylbutynyl)-4-methoxy-2-methoxymethoxybenzene (2g). A brown oil, 95% yield (chloroform:acetone=10:1 as a solvent for chromatography). ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.62(6H, s, 2 x Me), 2.70(1H, s, OH), 3.52(3H, s, *CH_2OMe*), 3.78(3H, s, Ar-*OMe*), 5.23(2H, s, OCH_2), 6.50(1H, dd, J=2, 8 Hz, 5-H), 6.65(1H, d, J=2 Hz, 3-H), 7.29(1H, d, J=8 Hz, 6-H). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 66.95; H, 7.21.

General synthesis of 4-bromo-2,2-dimethylchromenes (3) from *o*-(3-hydroxy-3-methylbutynyl)phenols (2)

To a solution of **2** (23 mmol) in dichloromethane (300 mL), was added boron tribromide (1-4 mol equiv., a 1.32 mol dm^{-3} solution in dichloromethane) at -70−25°C and stirred for 5−15 min. The reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was washed with 5% aqueous sodium hydrogen carbonate and water, and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the resulting compound was purified by column chromatography to give 4-bromo-2,2-dimethylchromenes (**3**).

4-Bromo-2,2-dimethylchromene (3a). A pale yellow oil (hexane:chloroform=5:1 as a solvent for chromatography). ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.42(6H, s, 2 x Me), 5.90(1H, s, 3-H), 6.55-7.42(4H, m, 4 x Ar-*H*). Anal. Calcd for $C_{11}H_{11}OBr$: C, 55.25; H, 4.62. Found: C, 55.20; H, 4.62.

4-Bromo-2,2,6-trimethylchromene[5] (3b). A pale yellow oil (hexane:chloroform=5:1 as a solvent for chromatography). ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.42(6H, s, 2 x Me), 2.28(3H, s, Ar-*Me*), 5.97(1H, s, 3-H), 6.64(1H, d, J=8 Hz, 8-H), 6.98(1H, dd, J=2, 8 Hz, 7-H), 7.19(1H, d, J=2 Hz, 5-H). Anal. Calcd for $C_{12}H_{13}OBr$: C, 56.94; H, 5.18. Found: C, 57.14; H, 5.16.

6-Acetyl-4-bromo-2,2-dimethylchromene (3c). Compound (**3c**) was prepared in 30% yield from **2c** and in 52% yield from **2d** as pale yellow needles (chloroform as a solvent for chromatography), mp 79-81°C (from methanol). ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.46(6H, s, 2 x Me), 2.57(3H, s, Ac), 5.96(1H, s, 3-H), 6.70(1H, d, J=8 Hz, 8-H), 7.70(1H, d, J=2, 8 Hz, 7-H), 7.92(1H, d, J=2 Hz, 5-H). Anal. Calcd for $C_{13}H_{13}O_2Br$: C, 55.54; H, 4.66. Found: C, 55.78; H, 4.58.

6-Acetyl-4-bromo-7-hydroxy-2,2-dimethylchromene (3d). To a solution of **2e** (5.0 g, 12 mmol) in dichloromethane (100 mL), was added boron tribromide-dichloromethane (36 mL, 4 equiv. mol) at 0°C and stirred for 5 min. After the usual work-up, the resulting compound was purified by chromatography ($CHCl_3$) to yield **3d** (1.9 g, 54%) as a major product, 2',4'-dihydroxy-5'-(3-hydroxy-3-methyl-1-butynyl)acetophenone (**4**) (0.43 g, 18%) and 2',4'-dihydroxy-5'-(3-methyl-3-buten-1-ynyl)acetophenone (**5**) (0.35 g, 14%) as minor products.

6-Acetyl-4-bromo-7-hydroxy-2,2-dimethylchromene (3d). mp 142-144°C (from hexane) as pale yellow needles. ^{1}H NMR(400 MHz; $CDCl_3$): δ 1.47(6H, s, 2 x Me), 2.60(3H, s, Ac), 5.97(1H, s, 3-H), 6.33(1H, s, 8-H), 7.74(1H, s, 5-H), 12.77(1H, s, 7-OH). Anal. Calcd for $C_{13}H_{13}O_3Br$: C, 52.55; H, 4.41. Found: C, 52.36; H, 4.32.

2',4'-Dihydroxy-5'-(3-hydroxy-3-methylbutynyl)acetophenone (4). mp 148-150°C (from dichloromethane) as colorless needles. ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.53(6H, s, 2 x Me), 2.54(3H, s, Ac), 6.33(1H, s, 3'-H), 7.80(1H, s, 6'-H), 12.70(1H, s, 2'-OH). Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found: C, 66.56; H, 5.74.

2',4'-Dihydroxy-5'-(3-methyl-3-buten-1-ynyl)acetophenone (5). mp 110-112°C (from hexane) as colorless needles. ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.99(3H, s, Me), 2.54(3H, s, Ac), 5.24-5.46(2H, m, $=CH_2$), 6.30(1H, br s, 4'-OH), 6.41(1H, s, 3'-H), 7.67(1H, s, 6'-H), 12.57(1H, s, 2'-OH). Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 71.93; H, 5.55.

Additional synthesis of 6-acetyl-4-bromo-7-hydroxy-2,2-dimethylchromene (3d). A mixture of 2',4'-dihydroxy-5'-(3-hydroxy-3-methylbutynyl)acetophenone (0.1 g, 0.43 mmol) and BBr_3-CH_2Cl_2 (0.33 mL, 1 equiv. mol) in CH_2Cl_2 (80 mL) was stirred for 10 min at rt. After the usual work-up, the resulting compound was purified by chromatography (hexane:ethyl acetate=2:1) to yield **3d** (0.101 g, 80%), mp 142-144°C (from hexane) as pale yellow needles.

6-Acetyl-4-bromo-7-methoxy-2,2-dimethylchromene (3e). A mixture of **3d** (1.5 g, 5.1 mmol) and dimethyl sulfate (0.76 g, 6.1 mmol) in the presence of potassium carbonate (1.4 g, 10 mmol) in acetone (50 mL) was stirred for 1.5 h at 70°C. After the usual work-up, the resulting compound was purified by column chromatography (hexane-ethyl acetate=2:1) to give **3e** (1.5 g, 95%), mp 80-81°C as colorless needles. ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.43(6H, s, 2 x Me), 2.52(3H, s, Ac), 3.82(3H, s, OMe), 5.82(1H, s, 3-H), 6.29(1H, s, 8-H), 7.77(1H, s, 5-H). Anal. Calcd for $C_{14}H_{15}O_3Br$: C, 54.04; H, 4.86. Found: C, 54.21; H, 4.78.

4-Bromo-7-methoxy-2,2-dimethylchromene (3f). Compound (**3f**) was prepared in 48% yield from **2f** and in 58% yield from **2g** as a colorless oil (chloroform as a solvent for chromatography). ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.42(6H, s, 2 x Me), 3.77(3H, s, OMe), 5.83(1H, s, 3-H), 6.35(1H, d, J=2 Hz, 8-H), 6.45(1H, dd, J=2, 8 Hz, 6-H), 7.29(1H, d, J=8 Hz, 5-H). Anal. Calcd for $C_{12}H_{13}O_2Br$: C, 53.55; H, 4.87. Found: C, 53.42; H, 4.83.

General procedure for electroreduction of 3

Nonaqueous acetonitrile solutions were prepared from the pre-deoxygenated acetonitrile and tetraethylammonium *p*-toluenesulufonate(Et_4NOTs) or tetrabutylammonium perchlorate (Bu_4ClO_4).[13] Et_4NOTs and Bu_4ClO_4 were recrystalyllized three times from ethyl acetate-metanol and ethyl acetate respectively and dried *in vacuo* at 80°C for three days.

Polarography. Polarography at a dropping mercury electrode was carried out, using the same experimental set-up and procedures as reported in the preceding paper.[13] All the polarograms were taken in MeCN containing 0.1 mol dm^{-3} Bu_4ClO_4, all the potentials being quoted against a Ag/0.1 mol dm^{-3} $AgNO_3$ in MeCN reference electrode (Ag/Ag^+), unless noted otherwise.

Macroelectrolysis. In the controlled potential macroelectrolysis of **3**, mercury pool (*ca.* 7 cm^2) was used as the working electrode, Et_4NOTs as the supporting electrolyte, and benzoic acid as the proton donor. The controlled potential macroelectrolysis in a three-compartment cell and the work-up after the electrolysis were carried out according to the procedures as reported in the preceding paper.[14] After the usual work-up, the resulting compounds were purified by column chromatography on silica gel to give 2,2-dimethylchromenes (**6**). Macroelectrolysis of **3e** in the presence of acetic anhydride was also carried out by the same procedure as described above.

2,2-Dimethylchromene[15] (6a). oil (chloroform:hexane=1:1 as a solvent for chromatography). ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.40(6H, s, 2 x Me), 5.50(1H, d, J=10 Hz, 3-H), 6.24(1H, d, J=10 Hz, 4-H), 6.62-7.15(4H, m, 4 x Ar-*H*).

2,2,6-Trimethylchromene[16] (6b). oil (hexane-ethyl acetate=5:1 as a solvent for chromatography). ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.42(6H, s, 2 x Me), 2.23(3H, s, Me), 5.58(1H, d, J=10 Hz, 3-H), 6.29(1H, d, J=10 Hz, 4-H), 6.68(1H, d, J=8 Hz, 8-H), 6.78(1H, d, J=2 Hz, 5-H), 6.92(1H, dd, J=2, 8 Hz, 7-H).

6-Acetyl-2,2-dimethylchromene (6c). oil ($CHCl_3$ as a solvent for chromatography). ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.47(6H, s, 2 x Me), 2.54(3H, s, Ac), 5.69(1H, d, J=10 Hz, 3-H), 6.40(1H, d, J=10 Hz, 4-H), 6.82(1H, d, J=8 Hz, 8-H), 7.69 (1H, d, J=2 Hz, 5-H), 7.78(1H, dd, J=2, 8 Hz, 7-H). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.27; H, 7.00.

6-Acetyl-7-methoxy-2,2-dimethylchromene[17] (6e). oil (hexane-ethyl acetate=2:1 as a solvent for chromatography). ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.41(6H, s, 2 x Me), 2.51(3H, s, Ac), 3.80(3H, s, OMe), 5.44(1H, d, J=10 Hz, 3-H), 6.21(1H, d, J=10 Hz, 4-H), 6.29(1H, s, 8-H), 7.42(1H, s, 5-H).

7-Methoxy-2,2-dimethylchromene (Precocene I)[18] (6f). oil (hexane-ethyl acetate=5:1 as a solvent for chromatography). ^{1}H NMR(60 MHz; $CDCl_3$): δ 1.42(6H, s, 2 x Me), 3.77(3H, s, OMe), 5.42 (1H, d, J=10 Hz, 3-H), 6.27(1H, d, J=10 Hz, 4-H), 6.37(1H, d, J=2 Hz, 8-H), 6.41(1H, dd, J=2, 8 Hz, 6-H), 6.88(1H, d, J=8 Hz, 5-H).

Crystal data of 3d

$C_{13}H_{13}O_3Br$, MW=297.2, Triclinic, a=8.724(3), b=10.220(4), c=8.238(2) Å, α=108.18(3), β=114.54(2), γ=68.70(3)°, V=611.2(4) Å^3 (by least-squares refinement on diffractometer angles for 25 automatically centered reflections, λ=1.54178 Å), space group $P1$, Z=2, Dx=1.61g cm^{-3}. colorless prisms, Crystal dimensions: 0.20x0.20x0.30 mm, μ(Cu-Kα)=45.49 cm^{-1}.

Data collection and processing

The data were collected using the ω-2θ scan technique to a maximum 2θ value of 120.1° by a Rigaku AFC7R diffractometer with graphite monochromated Cu-Kα radiation. Scans of (1.78+0.30 tan θ)° were made at a speed of 16.0°/min (in omega). Of the 1959 reflections which were collected, 1819 were unique (R_{int}=0.034). The intensities of three representative reflection were measured after every 150 reflections. No decay correction was applied. The linear absorption coefficient, μ, for Cu-Kα radiation is 45.5 cm^{-1}. An empirical absorption correction based on azimuthal scans of several reflections was applied which resulted in transmission factors ranging from 0.79 to 1.00. The data were corrected for Lorentz and polarization effects. A correction for secondary extinction was applied (coefficient=7.22358e-07).

Structure analysis and refinement

The structure was solved by direct method[19] and expanded using Fourier technique.[20] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares refinements was based on 1646 observed reflections (I>3.00 σ(I)). The weighting scheme was based on counting statistics and included a factor (p=0.007) to downweight the intense reflections. Plots of $\Sigma\,\omega(|Fo|-|Fc|)^2$ versus |Fo|, reflection order in data collection, sin θ/λ and various classes of indices showed no unusual trends. Neutral atom scattering factors were taken from Cromer and Waber.[21] Final R and R_w values are 0.046 and 0.045. All calculation were performed using the teXan[22] crystallographic software package of Molecular Structure Corporation.

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