One-Pot Synthesis of 4-Substituted 3,4-Dihydro-3-methoxyisocoumarins *via* Carboxylation of α-Substituted 2-Lithio-β-methoxystyrenes with Carbon Dioxide

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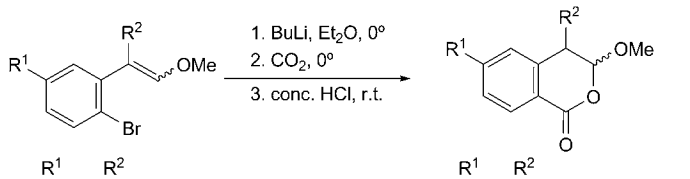
A new type of isocoumarins (=1*H*-isochromen-1-ones=1*H*-2-benzopyran-1-ones), 4-substituted 3,4-dihydro-3-methoxyisocoumarins **2**, can be obtained by a one-pot process from α-substituted 2-bromo-β-methoxystyrenes **1**. Thus, lithium 2-(1-aryl(or methyl)-2-methoxyethenyl)benzoates are conveniently generated *via* the Br/Li exchange between **1** and BuLi, followed by the action of CO_2 on the resulting α-substituted 2-lithio-β-methoxystyrenes. Upon treating with concentrated HCl at room temperature, these lithium benzoates undergo lactonization to provide the desired 3,4-dihydroisocoumarins **2** in relatively good yields.

Introduction. – The well-established biological activity [1] and occurrence in the nature [2] of compounds with the 3,4-dihydroisocoumarin skeleton have generated considerable interest in the development of new routes to this class of important heterocycles [3]. On the other hand, recent research in our laboratory has focused on the utilization of α-substituted 2-lithio-β-methoxystyrenes as intermediates for the construction of carbocyclic [4] and heterocyclic compounds [5][6]. In connection with our work in this area, we have undertaken a search for new approaches to 4-substituted isocoumarin (=1*H*-isochromen-1-one=1*H*-2-benzopyran-1-one) derivatives. We have found that 4-substituted 3,4-dihydro-3-methoxyisocoumarins **2** can be formed in satisfactory yields by the reaction of α-substituted 2-bromo-β-methoxystyrenes **1** with CO_2 or $(Boc)_2O$, followed by acid-mediated cyclization. Here, we describe the results of our investigation, which provide facile methods for the preparation of this new type of 3,4-dihydroisocoumarins. To the best of our knowledge, no procedure exists for their synthesis.

Results and Discussion. – The synthesis of 4-substituted 3,4-dihydro-3-methoxyisocoumarins **2** was accomplished as illustrated in *Scheme 1*. The starting materials, α-substituted 2-bromo-β-methoxystyrenes **1**, were synthesized by *Wittig* reaction of the respective 2-bromophenyl ketones according to our recently reported procedure [4][5]. Typically, treatment of 2-bromo-β-methoxy-α-phenylstyrene (**1a**) with BuLi at 0° for 1 h generated the corresponding 2-lithio intermediate, which was then allowed to react with CO_2 to give lithium 2-(2-methoxy-1-phenylethenyl)benzoates. Then, concentrated HCl was added to the resulting mixture. Under these acidic conditions,

the intermediate 2-(2-methoxy-1-phenylethenyl)benzoic acid formed by protonation of the lithium benzoate, underwent lactonization at a satisfactory rate at room temperature (1 h) to give the desired 3,4-dihydro-3-methoxy-4-phenylisocoumarin (**2a**) as a mixture of diastereoisomers in 70% yields as indicated in *Scheme 1*. The nine other α-substituted 2-bromo-β-methoxystyrenes **1b**–**1j** were subjected to the reactions under the above-mentioned conditions. The results are compiled in *Scheme 1*. Most of the dihydroisocoumarins could be obtained in fair yields. These methoxy lactones proved to be surprisingly stable and could be purified by preparative TLC on silica gel without difficulty. However, 3,4-dihydro-3-methoxy-4-(4-methoxyphenyl)isocoumarin (**2g**) could not be prepared; the action of concentrated HCl on the respective crude carboxylic acid resulted in decarboxylation, affording α-(4-methoxyphenyl)-β-methoxystyrene. 4-[1,1′-Biphenyl-4-yl]-3,4-dihydro-3-methoxyisocoumarin (**2h**) could not be obtained as well; the HCl conditions were found to be ineffective for the lactonization of the respective carboxylic acid, 2-[1-[1,1′-biphenyl-4-yl]-2-methoxyethenyl]benzoic acid. Unfortunately, reasons for these results are not clear.

Scheme 1

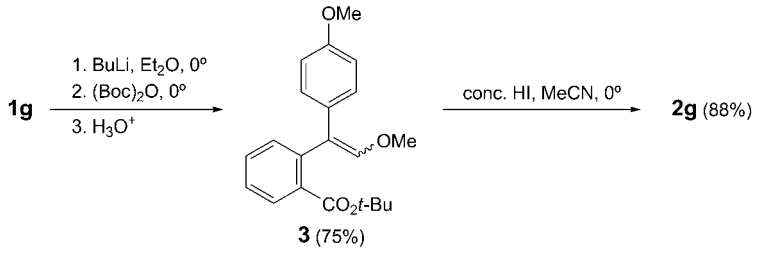


	R^1	R^2		R^1	R^2	
1a	H	Ph	**2a**	H	Ph	70%
1b	H	*m*-Tol	**2b**	H	*m*-Tol	71%
1c	H	*p*-Tol	**2c**	H	*p*-Tol	73%
1d	H	4-(*t*-Bu)–C_6H_4	**2d**	H	4-(*t*-Bu)–C_6H_4	60%
1e	H	4-Cl–C_6H_4	**2e**	H	4-Cl–C_6H_4	72%
1f	H	3-MeO–C_6H_4	**2f**	H	3-MeO–C_6H_4	70%
1g	H	4-MeO–C_6H_4	**2g**	H	4-MeO–C_6H_4	0%
1h	H	4-Ph–C_6H_4	**2h**	H	4-Ph–C_6H_4	0%
1i	MeO	Me	**2i**	MeO	Me	56%
1j	MeO	Ph	**2j**	MeO	Ph	60%

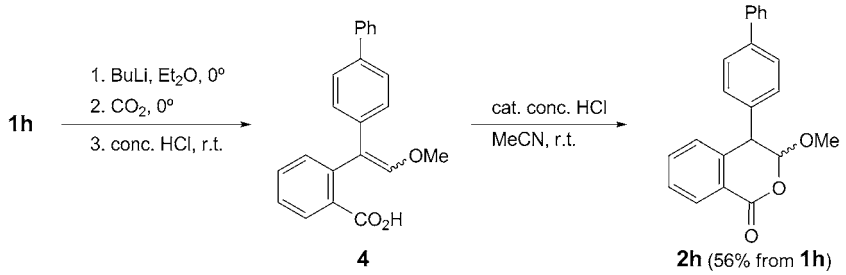
The transformation outlined in *Scheme 2* demonstrates the two-step synthesis of **2g** from 2-bromo-β-methoxy-α-(4-methoxyphenyl)styrene (**1g**). Thus, treatment of 2-lithio-β-methoxy-α-(4-methoxyphenyl)styrene, generated from **1g** as mentioned above, with $(Boc)_2O$ furnished *tert*-butyl 2-[2-methoxy-1-(4-methylphenyl)ethenyl]benzoate (**3**) in relatively good yield. Upon treating with an equimolar amount of concentrated HI at room temperature, lactonization of this ester proceeded smoothly in the expected fashion, and the desired product **2g** was obtained in good yield.

In *Scheme 3*, a procedure for the synthesis of **2h** is outlined. The mixture of α-[1,1′-biphenyl-4-yl]-2-lithio-β-methoxystyrene, generated from α-[1,1′-biphenyl-4-yl]-2-bromo-β-methoxystyrene (**1h**), with CO_2 was worked up as usual to afford crude 2-{1-[1,1′-biphenyl-4-yl]-2-methoxyvinyl}benzoic acid (**4**), which was then treated with a catalytic amount of concentrated HI in MeCN at room temperature to give the desired product **2h** in a reasonable overall yield from **1h**. All of the 3,4-dihydroisocoumarins **2** were obtained as diastereoisomeric mixtures.

Scheme 2



Scheme 3



The results of the study described here establish the utility of the carboxylation of α-substituted 2-lithio-β-methoxystyrenes, followed by acid-mediated lactonization, as a convenient method for the preparation of a new type of isocoumarins, *i.e.*, 4-substituted 3,4-dihydro-3-methoxyisocoumarins **2**. The ready availability of the starting materials and the simplicity of operations render this method attractive.

Experimental Part

General. All of the org. solvents used were dried on the appropriate drying agents and distilled under Ar prior to use. TLC: *Merck* silica gel *60 PF_{254}*. Column chromatography (CC): *Wako Gel C-200E.* M.p.: *Laboratory Devices MEL-TEMP II* melting-point apparatus; uncorrected. IR Spectra: *Shimadzu FTIR-8300* spectrometer. NMR Spectra (^{1}H: 500 and ^{13}C: 125 MHz): *JEOL ECP 500 FT NMR* spectrometer; in $CDCl_3$ with TMS as an internal reference. LR-MS (CI): *JEOL JMS AX 505 HA* spectrometer.

1-Bromo-2-(2-methoxyethenyl)benzenes **1a** [5], **1b**–**1d** [4], **1e** [5], **1f**–**1h** [4], and **1j** [5] were prepared by a previously reported procedure. BuLi was supplied by *Asia Lithium Corporation*. All other chemicals used in this study were commercially available.

1-Bromo-4-methoxy-2-(2-methoxy-1-methylethenyl)benzene (**1i**). This compound was prepared by the reaction of 1-(2-bromo-5-methoxyphenyl)ethanone with (methoxymethylene)(triphenyl)phosphorane under the conditions described in [5].

(*E*)-*Isomer*. Yield: 39%. Colorless oil. R_f (Et_2O/hexane 1:20) 0.51. IR (neat): 1667. ^{1}H-NMR: 1.94 (*d*, *J* = 1.4, 3 H); 3.69 (*s*, 3 H); 3.78 (*s*, 3 H); 6.03 (*q*, *J* = 1.4, 1 H); 6.66 (*dd*, *J* = 8.7, 3.2, 1 H); 6.74 (*d*, *J* = 3.2, 1 H); 7.42 (*d*, *J* = 8.7, 1 H). Anal. calc. for $C_{11}H_{13}BrO_2$ (257.12): C 51.38, H 5.10; found: C 51.58, H 5.08.

(*Z*)-*Isomer*. Yield: 32%. Colorless oil. R_f (Et_2O/hexane 1:20) 0.40. IR (neat). 1674. ^{1}H-NMR: 1.85 (*d*, *J* = 1.4, 3 H), 3.57 (*s*, 3 H); 3.78 (*s*, 3 H); 6.00 (*q*, *J* = 1.4, 1 H); 6.67 (*dd*, *J* = 8.7, 2.7, 1 H); 6.73 (*d*, *J* = 2.7, 3 H); 7.45 (*d*, *J* = 8.7, 1 H). Anal. calc. for $C_{11}H_{13}BrO_2$ (257.12): C 51.38, H 5.10; found: C 51.30, H 5.14.

3,4-Dihydro-3-methoxy-4-phenylisocoumarin (= *3,4-Dihydro-3-methoxy-4-phenyl-1*H-*2-benzopyran-1-one*; **2a**). *General Procedure.* To a stirred soln. of **1a** (0.31 g, 1.1 mmol) in Et_2O (6 ml) at 0° was added dropwise BuLi (1.6M in hexane; 1.1 mmol), and the mixture was stirred for 1.5 h at the same temp. A fine stream of CO_2 were passed through the resulting soln. for 30 min, and then 2 ml of conc. HCl were added. The resulting mixture was vigorously stirred for an additional hour. Five ml each of Et_2O and H_2O were added, and the layers were separated. The aq. layer was extracted with Et_2O (2 × 5 ml), and the combined extracts were washed with brine (10 ml), dried (Na_2SO_4), and evaporated. The residue was purified by prep. TLC (SiO_2) to afford **2a** (0.14 g, 50%) as a mixture of stereoisomers (*ca.* 6:4). Pale-yellow oil. R_f (AcOEt/hexane 1:5) 0.16. IR (neat): 1732. ^{1}H-NMR: 3.52 (*s*, 1.8 H); 3.56 (*s*, 1.2 H); 4.36 (*d*, *J* = 2.7, 0.4 H); 4.56 (*d*, *J* = 3.2, 0.6 H); 5.42 (*d*, *J* = 3.2, 0.6 H); 5.44 (*d*, *J* = 2.7, 0.4 H); 6.95 (*d*, *J* = 7.8, 0.6 H); 7.10 (*d*, *J* = 7.8, 1.2 H); 7.16 (*d*, *J* = 7.8, 0.4 H); 7.28–7.46 (*m*, 4.8 H); 7.49 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.6 H); 7.55 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.4 H); 8.17 (*dd*, *J* = 7.8, 1.4, 0.6 H); 8.20 (*d*, *J* = 7.8, 0.4 H). ^{13}C-NMR: 48.64; 48.77; 56.84; 57.20; 104.28; 106.07; 124.59; 125.06; 127.60; 127.65; 127.68; 127.91; 127.96; 128.32; 128.51; 128.77; 128.93; 129.83; 129.87; 130.56; 133.96; 134.37; 135.41; 138.13; 139.40; 139.98; 163.52; 164.03. MS: 255 (100, $[M+1]^+$). Anal. calc. for $C_{16}H_{14}O_3$ (254.28): C 75.57, H 5.55; found: C 75.40, H 5.59.

3,4-Dihydro-3-methoxy-4-(3-methylphenyl)isocoumarin (= *3,4-Dihydro-3-methoxy-4-(3-methylphenyl)-1*H-*2-benzopyran-1-one*; **2b**). A mixture of stereoisomers (*ca.* 1:1). Yellow oil. R_f (AcOEt/hexane 1:5) 0.32. IR (neat): 1732, 1605. ^{1}H-NMR: 2.31 (*s*, 1.5 H); 2.36 (*s*, 1.5 H); 3.52 (*s*, 1.5 H); 3.56 (*s*, 1.5 H); 4.32 (*d*, *J* = 2.3, 0.5 H); 4.52 (*d*, *J* = 3.2, 0.5 H); 5.42 (*d*, *J* = 3.2, 0.5 H); 5.44 (*d*, *J* = 2.7, 0.5 H); 6.88–6.97 (*m*, 1.5 H); 7.08–7.22 (*m*, 3 H); 7.26 (*dd*, *J* = 7.8, 7.3, 0.5 H); 7.39–7.46 (*m*, 1 H), 7.49 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.5 H); 7.55 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.5 H); 8.17 (*dd*, *J* = 7.8, 1.4, 0.5 H); 8.20 (*dd*, *J* = 7.8, 1.4, 0.5 H). ^{13}C-NMR: 21.39; 21.43; 48.62; 48.80; 56.85; 57.24; 104.38; 106.13; 124.57; 125.07; 125.38; 127.58; 127.60; 127.71; 127.87; 128.42; 128.48; 128.74; 128.81; 128.83; 128.99; 129.83; 129.87; 131.23; 133.95; 134.37; 135.34; 138.12; 138.18; 138.70; 139.55; 140.11; 163.59; 164.09. MS: 269 (100, $[M+1]^+$). Anal. calc. for $C_{17}H_{16}O_3$ (268.31): C 76.10, H 6.01; found: C 75.83, H 6.25.

3,4-Dihydro-3-methoxy-4-(4-methylphenyl)isocoumarin (= *3,4-Dihydro-3-methoxy-4-(4-methylphenyl)-1*H-*2-benzopyran-1-one*; **2c**). A mixture of stereoisomers (*ca.* 1:1). Pale-yellow oil. R_f (AcOEt/hexane 1:20) 0.34. IR (neat): 1732, 1602. ^{1}H-NMR: 2.32 (*s*, 1.5 H); 2.37 (*s*, 1.5 H); 3.51 (*s*, 1.5 H); 3.56 (*s*, 1.5 H); 4.32 (*d*, *J* = 2.7, 0.5 H); 4.52 (*d*, *J* = 3.2, 0.5 H); 5.40 (*d*, *J* = 3.2, 0.5 H); 5.42 (*d*, *J* = 2.7, 0.5 H); 6.96–7.00 (*m*, 1.5 H); 7.12–7.22 (*m*, 3.5 H); 7.39–7.45 (*m*, 1 H); 7.49 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.5 H); 7.54 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.5 H); 8.16 (*d*, *J* = 7.8, 0.5 H); 8.19 (*d*, *J* = 7.8, 0.5 H). ^{13}C-NMR: 20.99; 21.11; 48.33; 48.45; 56.88; 57.25; 104.45; 106.21; 124.60; 125.11; 127.57; 127.69; 127.86; 128.21; 128.76; 129.29; 129.66; 129.84; 129.89; 130.45; 132.37; 133.95; 134.37; 135.19; 137.49; 137.75; 139.72; 140.24; 163.59; 164.10. MS: 269 (100, $[M+1]^+$). Anal. calc. for $C_{17}H_{16}O_3$ (268.31): C 76.10, H 6.01; found: C 76.01, H 6.03.

4-[4-(1,1-Dimethylethyl)phenyl]-3,4-dihydro-3-methoxyisocoumarin (= *4-[4-(*tert-*Butyl)phenyl]-3,4-dihydro-3-methoxy-1*H-*2-benzopyran-1-one*; **2d**). A mixture of stereoisomers (*ca.* 3:2). Colorless oil. R_f (AcOEt/hexane 1:10) 0.35. IR (neat): 1732, 1605. ^{1}H-NMR: 1.28 (*s*, 3.6 H); 1.34 (*s*, 5.4 H); 3.52 (*s*, 1.8 H); 3.56 (*s*, 1.2 H); 4.33 (*d*, *J* = 2.3, 0.4 H); 4.53 (*d*, *J* = 3.2, 0.6 H); 5.41 (*d*, *J* = 3.2, 0.6 H); 5.44 (*d*, *J* = 2.3, 0.4 H); 6.97 (*d*, *J* = 7.8, 0.6 H); 7.01 (*d*, *J* = 8.2, 0.8 H); 7.18 (*d*, *J* = 7.8, 0.4 H); 7.24 (*d*, *J* = 8.7, 1.2 H); 7.32 (*d*, *J* = 8.2, 0.8 H); 7.37–7.40 (*m*, 1.8 H); 7.43 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.4 H); 7.48 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.6 H); 7.55 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.4 H); 8.16 (*dd*, *J* = 7.8, 1.4, 0.6 H); 8.19 (*dd*, *J* = 7.8, 1.4, 0.4 H). ^{13}C-NMR: 31.22; 31.29; 34.44; 34.51; 48.16; 48.37; 56.82; 57.20; 104.46; 106.17; 124.63; 125.10; 125.46; 125.86; 127.52; 127.71; 127.84; 127.90; 128.84; 129.79; 129.84; 130.18; 132.25; 133.90; 134.33; 135.12; 139.58; 140.27; 150.59; 150.81; 163.56; 164.10. MS: 311 (100, $[M+1]^+$). Anal. calc. for $C_{20}H_{22}O_3$ (310.39): C 77.39, H 7.14; found: C 77.10, H 7.18.

4-(4-Chlorophenyl)-3,4-dihydro-3-methoxyisocoumarin (= *4-(4-Chlorophenyl)-3,4-dihydro-3-methoxy-1*H-*2-benzopyran-1-one*; **2e**). A mixture of stereoisomers (*ca.* 3:2). Pale-yellow oil. R_f (Et_2O/hexane 1:1) 0.45. IR (neat): 1732. ^{1}H-NMR: 3.52 (*s*, 1.8 H); 3.56 (*s*, 1.2 H); 4.33 (*d*, *J* = 2.7, 0.4 H); 4.54 (*d*, *J* = 3.2, 0.6 H); 5.39 (*d*, *J* = 3.2, 0.6 H); 5.40 (*d*, *J* = 2.7, 0.4 H); 6.94 (*d*, *J* = 7.8, 0.6 H); 7.05 (*d*, *J* = 8.2, 1.2 H); 7.14 (*d*, *J* = 7.8, 0.4 H); 7.26 (*d*, *J* = 8.2, 0.8 H); 7.30 (*d*, *J* = 8.2, 0.8 H); 7.35 (*d*, *J* = 8.2, 1.2 H); 7.43 (*dd*, *J* = 7.8, 7.3, 0.6 H); 7.46 (*dd*, *J* = 7.8, 7.3, 0.4 H); 7.51 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.6 H); 7.57 (*ddd*, *J* = 7.8, 7.3,

1.4, 0.4 H); 8.17 (*d*, *J* = 7.8, 0.6 H), 8.21 (*d*, *J* = 7.8, 0.4 H). ^{13}C-NMR: 48.15; 48.17; 56.92; 57.24; 103.92; 105.79; 124.59; 125.08; 127.56; 127.86; 128.16; 128.65; 128.75; 129.16; 129.73; 130.01; 130.08; 131.90; 133.76; 134.02; 134.03; 134.09; 134.49; 136.65; 139.01; 139.49; 163.27; 163.76. MS: 289 (100, $[M+1]^+$). Anal. calc. for $C_{16}H_{13}ClO_3$ (288.73): C 66.56, H 4.54; found: C 66.60, H 4.57.

3,4-Dihydro-3-methoxy-4-(3-methoxyphenyl)isocoumarin (= *3,4-Dihydro-3-methoxy-4-(3-methoxyphenyl)-1*H-*2-benzopyran-1-one*; **2f**). A mixture of stereoisomers (*ca.* 4:1). Yellow oil. R_f (AcOEt/hexane 3:10) 0.32. IR (neat): 1732. ^{1}H-NMR: 3.52 (*s*, 2.4 H); 3.56 (*s*, 0.6 H); 3.75 (*s*, 0.6 H); 3.79 (*s*, 2.4 H); 4.32 (*d*, *J* = 2.3, 0.2 H); 4.54 (*d*, *J* = 2.3, 0.8 H); 5.42 (*d*, *J* = 2.3, 0.8 H); 5.45 (*d*, *J* = 2.3, 0.2 H); 6.64–6.82 (*m*, 1 H); 6.89–6.93 (*m*, 2 H); 6.97 (*d*, *J* = 7.8, 0.8 H); 7.09–7.31 (*m*, 1.4 H); 7.39–7.56 (*m*, 1.8 H); 8.16 (*d*, *J* = 7.8, 0.8 H); 8.19 (*d*, *J* = 7.8, 0.2 H). ^{13}C-NMR: 48.61; 48.77; 55.16; 55.19; 56.86; 57.22; 104.26; 106.00; 112.62; 113.28; 114.56; 116.31; 120.59; 122.94; 124.55; 125.03; 127.61; 127.67; 127.94; 128.77; 129.48; 129.83; 129.88; 129.97; 133.96; 134.37; 136.91; 139.30; 139.69; 139.86; 159.63; 159.93; 163.47; 163.97. MS: 285 (100, $[M+1]^+$). Anal. calc. for $C_{17}H_{16}O_4$ (284.31): C 71.82, H 5.67; found: C 71.58, H 5.80.

3,4-Dihydro-3,6-dimethoxy-4-methylisocoumarin (= *3,4-Dihydro-3,6-dimethoxy-4-methyl-1*H-*2-benzopyran-1-one*; **2i**). A mixture of stereoisomers (*ca.* 3:2). Pale-yellow solid. M.p. 75–85° (after purification by PLC on SiO_2). IR (KBr): 1728, 1715. ^{1}H-NMR: 1.357 (*d*, *J* = 6.9, 1.2 H); 1.364 (*d*, *J* = 6.9, 1.8 H); 3.05–3.10 (*m*, 0.6 H); 3.27–3.29 (*m*, 0.4 H); 3.55 (*s*, 1.8 H); 3.57 (*s*, 1.2 H); 3.87 (*s*, 1.8 H); 3.88 (*s*, 1.2 H); 5.16 (*d*, *J* = 2.3, 0.6 H); 5.25 (*d*, *J* = 3.2, 0.4 H); 6.73 (*d*, *J* = 2.3, 0.6 H), 6.77 (*d*, *J* = 2.3, 0.4 H); 6.88 (*dd*, *J* = 8.7, 2.3, 1 H); 8.05 (*d*, *J* = 8.7, 1 H). ^{13}C-NMR: 13.25; 19.01; 36.32; 37.84; 55.48 (2 overlapped Cs); 56.76; 57.12; 104.55; 106.12; 111.51; 112.13; 112.64; 113.25; 116.21; 116.91; 132.41; 132.51; 143.95; 144.92; 153.23; 153.95; 154.22; 154.26. MS: 223 (100, $[M+1]^+$). Anal. calc. for $C_{12}H_{14}O_4$ (222.24): C 64.85, H 6.35; found: C 64.81, H 6.43.

3,4-Dihydro-3,6-dimethoxy-4-phenylisocoumarin (= *3,4-Dihydro-3,6-dimethoxy-4-phenyl-1*H-*2-benzopyran-1-one*; **2j**). A mixture of diastereoisomers (*ca.* 7:3). Pale-yellow oil. R_f (AcOEt/hexane 1:5) 0.50. IR (neat): 1728, 1607. ^{1}H-NMR: 3.51 (*s*, 0.9 H); 3.56 (*s*, 2.1 H); 3.75 (*s*, 0.9 H); 3.80 (*s*, 2.1 H); 4.29 (*d*, *J* = 2.8, 0.7 H); 4.51 (*s*, 0.3 H); 5.39 (*s*, 0.3 H); 5.40 (*d*, *J* = 2.8, 0.7 H); 6.42 (*d*, *J* = 2.7, 0.3 H); 6.62 (*d*, *J* = 2.3, 0.7 H); 6.90 (*dd*, *J* = 8.7, 2.7, 0.3 H); 6.94 (*dd*, *J* = 8.7, 2.3, 0.7 H); 7.12 (*d*, *J* = 8.7, 1 H); 7.28–7.38 (*m*, 4 H); 8.12 (*d*, *J* = 8.7, 0.3 H); 8.15 (*d*, *J* = 8.7, 0.7 H). ^{13}C-NMR: 49.07; 49.11; 55.44; 55.50; 56.85; 57.22; 104.09; 105.86; 113.01; 113.16; 113.31; 114.16; 117.22; 117.66; 127.74; 128.01; 128.32; 128.55; 128.97; 130.58; 132.30; 132.34; 135.41; 138.13; 141.73; 142.45; 163.33; 163.87; 164.14; 164.39. MS: 285 (100, $[M+1]^+$). Anal. calc. for $C_{17}H_{16}O_4$ (284.31): C 71.82, H 5.67; found: C 71.70, H 5.54.

1,1-Dimethylethyl 2-[2-Methoxy-1-(4-methoxyphenyl)ethenyl]benzoate (= tert-*Butyl 2-[2-Methoxy-1-(4-methoxyphenyl)ethenyl]benzoate*; **3**). To a stirred soln. of 1-lithio-2-[2-methoxy-1-(4-methoxyphenyl)ethenyl]benzene, generated from **1g** (0.18 g, 0.55 mmol) and BuLi (1.65M in hexane; 0.55 mmol), as described for the preparation of **2a**, in Et_2O (5 ml) at 0° was added $(Boc)_2O$ (0.12 g, 0.55 mmol). After 20 min, H_2O (15 ml) was added, and the mixture was extracted with Et_2O (3 × 10 ml). The combined extracts were washed with H_2O and then brine (15 ml each), and dried (Na_2SO_4). After evaporation of the solvent, the residue was purified by CC (SiO_2) to afford **3** (0.13 g, 68%) as a mixture of stereoisomers ((*E*)/(*Z*) = *ca.* 3:2). An anal. specimen of each isomer was obtained by fractional CC.

*Data of (*E*)-***3***.* Colorless oil. R_f (THF/hexane 1:20) 0.38. IR (neat): 1709, 1634, 1607. ^{1}H-NMR: 1.28 (*s*, 9 H); 3.76 (*s*, 3 H); 3.77 (*s*, 3 H); 6.12 (*s*, 1 H); 6.80 (*d*, *J* = 9.2, 2 H); 7.24 (*dd*, *J* = 7.8, 1.4, 1 H); 7.33 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.35 (*d*, *J* = 9.2, 2 H); 7.40 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.65 (*dd*, *J* = 7.8, 1.4, 1 H). Anal. calc. for $C_{21}H_{24}O_4$ (340.41): C 74.09, H 7.11; found: C 73.96, H 7.15.

*Data of (Z)-***3***.* Colorless oil. R_f (THF/hexane 1:20) 0.25. IR (neat) 1711, 1641, 1606. ^{1}H-NMR: 1.37 (*s*, 9 H); 3.67 (*s*, 3 H); 3.76 (*s*, 3 H); 6.49 (*s*, 1 H); 6.78 (*d*, *J* = 9.2, 2 H); 7.07 (*d*, *J* = 9.2, 2 H); 7.21 (*dd*, *J* = 7.8, 1.4, 1 H); 7.31 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.43 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.76 (*dd*, *J* = 7.8, 1.4, 1 H). Anal. calc. for $C_{21}H_{24}O_4$ (340.41): C 74.09, H 7.11; found: C 73.87, H 7.15.

3,4-Dihydro-3-methoxy-4-(4-methoxyphenyl)isocoumarin (= *3,4-Dihydro-3-methoxy-4-(4-methoxyphenyl)-1*H-*2-benzopyran-1-one*; **2g**). To a stirred soln. of **3** (86 mg, 0.25 mmol) in MeCN (2 ml) at 0° was added conc. HI (32 mg, 0.25 mmol). After stirring for 3 h, sat. aq. $NaHCO_3$ (10 ml) was added, and MeCN was removed by evaporation. The mixture was extracted with AcOEt (3 × 5 ml), and the combined extracts were washed with brine (5 ml) and dried (Na_2SO_4). After evaporation of the solvent,

the residue was purified by PLC (SiO_2) to give **2g** (62 mg, 88%) as a mixture of diastereoisomers ((*E*)/(*Z*) = *ca.* 3:2). Pale-yellow solid. M.p. 80–83°. IR (KBr): 1732, 1611. ^{1}H-NMR: 3.52 (*s*, 1.2 H); 3.56 (*s*, 1.8 H); 3.78 (*s*, 1.8 H); 3.83 (*s*, 1.2 H); 4.30 (*d*, *J* = 2.7, 0.6 H); 4.52 (*d*, *J* = 3.2, 0.4 H); 5.39 (*d*, *J* = 3.2, 0.4 H); 5.40 (*d*, *J* = 2.7, 0.6 H); 6.85 (*d*, *J* = 9.2, 1.2 H); 6.91 (*d*, *J* = 8.7, 0.8 H); 6.96 (*d*, *J* = 7.8, 0.4 H); 7.01 (*d*, *J* = 9.2, 1.2 H); 7.16 (*d*, *J* = 7.8, 0.6 H); 7.25 (*d*, *J* = 8.7, 0.8 H); 7.39–7.45 (*m*, 1 H); 7.49 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.4 H); 7.55 (*ddd*, *J* = 7.8, 7.3, 1.4, 0.6 H); 8.16 (*dd*, *J* = 7.8, 1.4, 0.4 H); 8.19 (*dd*, *J* = 7.8, 1.4, 0.6 H). ^{13}C-NMR: 47.87; 47.95; 55.20; 55.21; 56.83; 57.20; 104.46; 106.23; 113.93; 114.32; 124.54; 125.07; 127.31; 127.52; 127.62; 127.80; 128.72; 129.36; 129.77; 129.84; 130.19; 131.61; 133.92; 134.34; 139.81; 140.34; 159.01; 159.29; 163.56; 164.04. MS: 285 (100, $[M+1]^+$). Anal. calc. for $C_{17}H_{16}O_4$ (284.31): C 71.82, H 5.67; found: C 71.70, H 5.94.

4-[1,1′-Biphenyl-4-yl]-3,4-dihydro-3-methoxyisocoumarin (= *4-[1,1′-Biphenyl-4-yl]-3,4-dihydro-3-methoxy-1*H*-2-benzopyran-1-one*; **2h**). 1-{1-[1,1′-Biphenyl-4-yl]-2-methoxyethenyl}-2-bromobenzene (0.20 g, 0.55 mmol) was treated successively with BuLi (1.6M in hexane, 0.55 mmol) and CO_2 gas as described for the preparation of **2a**. The resulting mixture was worked up as described for the preparation of **3**. The crude product **4** (0.18 g) was dissolved in MeCN (2 ml) and treated with a drop of conc. HI at r.t. for 20 min under stirring. Sat. aq. $NaHCO_3$ (10 ml) was added, and MeCN was removed by evaporation. The resulting mixture was extracted with AcOEt (3 × 5 ml), and the combined extracts were washed with H_2O (10 ml) and dried (Na_2SO_4). After evaporation of the solvent, the residue was purified by CC (SiO_2; AcOEt/hexane 1:5) to afford **2h** (66 mg, 55%). Mixture of diastereoisomers ((*E*)/(*Z*) *ca.* 7:3). Pale-yellow solid. M.p. 52–55°. IR (KBr): 1732, 1603. ^{1}H-NMR: 3.55 (*s*, 0.9 H); 3.59 (*s*, 2.1 H); 4.41 (*d*, *J* = 2.7, 0.7 H); 4.61 (*d*, *J* = 2.7, 0.3 H); 5.46 (*d*, *J* = 2.7, 0.3 H), 5.48 (*d*, *J* = 2.7, 0.7 H); 7.02–7.62 (*m*, 12 H); 8.19 (*dd*, *J* = 7.8, 1.4, 0.3 H); 8.22 (*dd*, *J* = 7.8, 1.4, 0.7 H). ^{13}C-NMR: 48.38; 48.48; 56.91; 57.28; 104.29; 106.45; 124.63; 125.10; 127.01; 127.03; 127.22; 127.42; 127.45; 127.67; 127.70; 127.74; 128.00; 128.10; 128.75; 128.78; 129.91; 129.97; 130.97 (2 overlapped Cs); 134.03; 134.44; 137.13 (2 overlapped Cs); 139.40; 139.96; 140.33; 140.49; 140.69; 140.84; 163.52; 164.03. MS: 331 (100, $[M+1]^+$). Anal. calc. for $C_{22}H_{18}O_3$ (330.38): C 79.98, H 5.49; found: C 79.74, H 5.60.

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