SUPPORTING INFORMATION

A Substructure Combination Strategy to Create Potent and Selective Transthyretin Kinetic Stabilizers that Prevent Amyloidogenesis and Cytotoxicity

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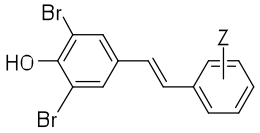
Figure S1. Purity of the stilbene-based TTR kinetic stabilizers.



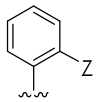
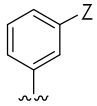
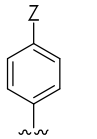
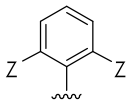
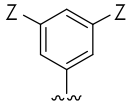
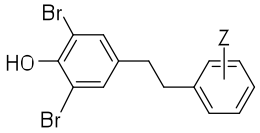
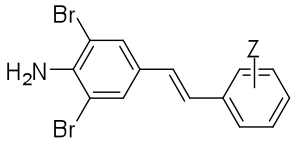
Z =	F **2**	Cl **3**	Br **4**	I **5**	CH_3 **6**	CF_3 **7**	CN **8**	OCH_3 **9**	OH **10**	$OCHF_2$ **11**	NO_2 **12**	NH_2 **13**	CO_2Me **14**	CO_2H **15**
 **a**	98%	96%	95%	94%	99%	97%	96%	99%	96%	97%	99%	96%	100%	100%
 **b**	94%	97%	97%	95%	99%	98%	97%	99%	99%	99%	95%	97%	99%	95%
 **c**	99%	97%	98%	94%	99%	99%	100%	99%	97%	98%	99%	95%	99%	100%
 **d**	97%	97%	99%		98%			97%						
 **e**	95%	99%	100%		99%	99%		99%	97%		100%			

Figure S2. Purity of the dihydrostilbene-based TTR kinetic stabilizers.



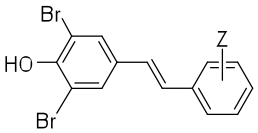
Z =	F **16**	Cl **17**	CH_3 **18**	CF_3 **19**	OCH_3 **20**	$OCHF_2$ **21**	NO_2 **22**	NH_2 **23**
a	97%	96%	99%	97%	99%	93%	99%	97%
b	98%	95%	99%	96%	99%	99%		98%
c	99%	98%	98%		99%	98%		98%
d	95%	98%	98%		99%			
e	99%		99%		96%			

Figure S3. Purity of amine-substituted-stilbene WT-TTR kinetic stabilizers **24b-e**.



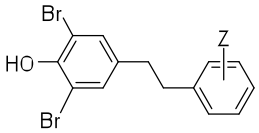
Z =	*m*-OCH_3	*o*-$(OCH_3)_2$	*m*-NH_2	*p*-NH_2
	24b	**24c**	**24d**	**24e**
	95%	95%	97%	98%

Figure S4. Evaluation of the fibril formation inhibition potency of stilbene-based WT-TTR kinetic stabilizers at equimolar concentrations of TTR and compound (3.6 μM).



	F **2**	Cl **3**	Br **4**	I **5**	CH_3 **6**	CF_3 **7**	CN **8**	OCH_3 **9**	OH **10**	$OCHF_2$ **11**	NO_2 **12**	NH_2 **13**	CO_2Me **14**	CO_2H **15**
a	17%	26%	26%	24%	17%	21%		15%	19%	21%		16%	21%	23%
b	23%	25%	24%	23%	15%	25%	23%	19%	20%	18%		15%	19%	19%
c	18%	28%	19%		22%			24%	15%			23%		19%
d	17%	18%	29%		23%			25%						
e	31%				16%			21%	21%					

Figure S5. Evaluation of the fibril formation inhibition potency of dihydrostilbene-based WT-TTR kinetic stabilizers at equimolar concentrations of TTR and compound (3.6 μM).



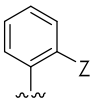
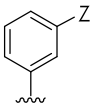
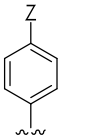
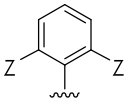
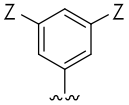
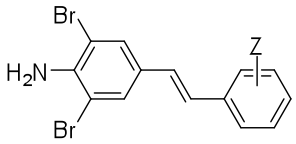
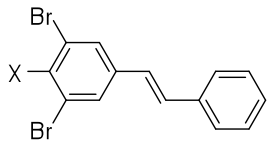
	F **16**	Cl **17**	CH_3 **18**	CF_3 **19**	OCH_3 **20**	$OCHF_2$ **21**	NO_2 **22**	NH_2 **23**
 **a**	25%	23%	25%	27%	22%	29%	25%	27%
 **b**	25%	22%	21%	24%	20%	22%		28%
 **c**	25%	30%	23%		21%	29%		25%
 **d**	23%	23%	22%		22%			
 **e**	26%		21%		23%			

Figure S6. Evaluation of the fibril formation inhibition potency of amine-substituted-stilbene WT-TTR kinetic stabilizers at equimolar concentrations of TTR and compound (3.6 μM).



	Z = *m*-OCH_3	*o*-$(OCH_3)_2$	*m*-NH_2	*p*-NH_2
% Fibril Formation	**24b** 18%	**24c** 21%	**24d** 22%	**24e** 19%

Figure S7. Evaluation of potential isosteres for the acidic phenol in the TTR fibril formation assay.



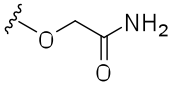
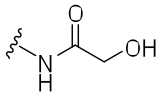
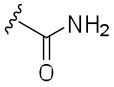
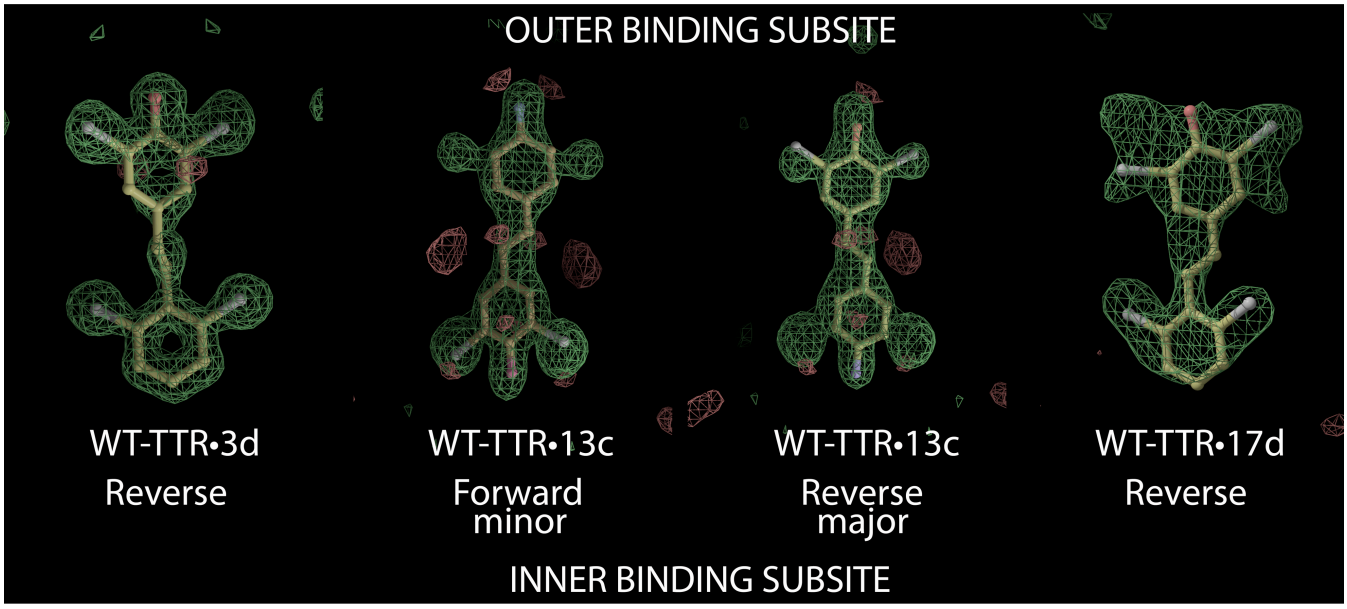
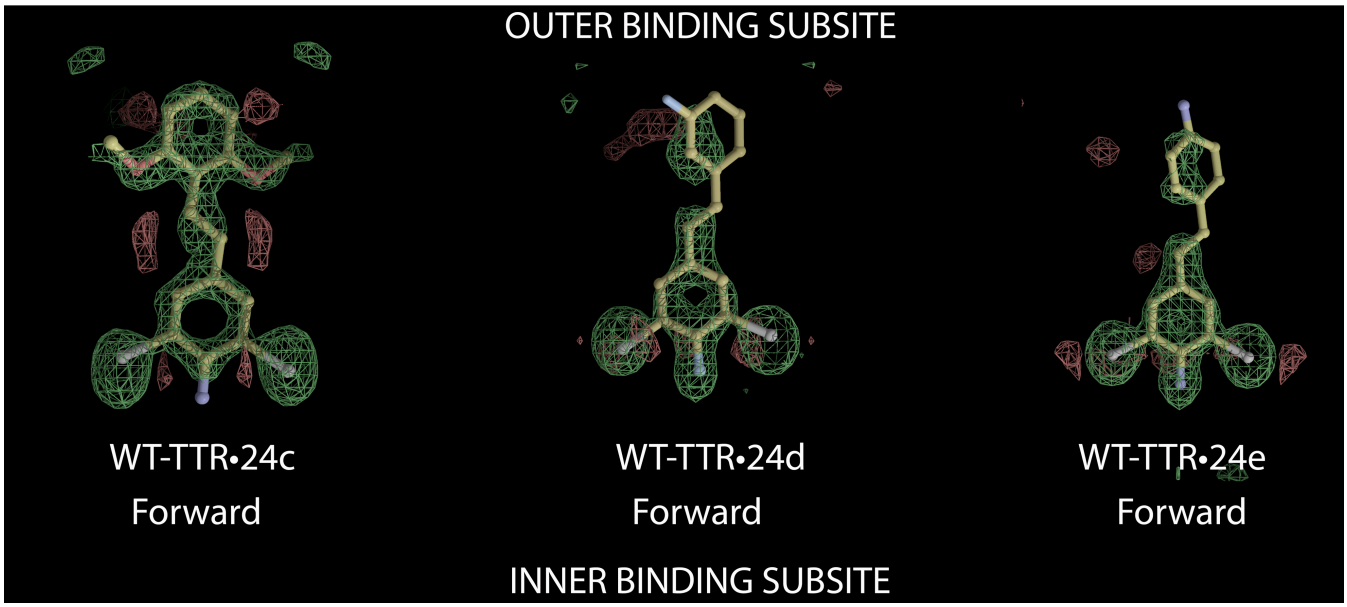
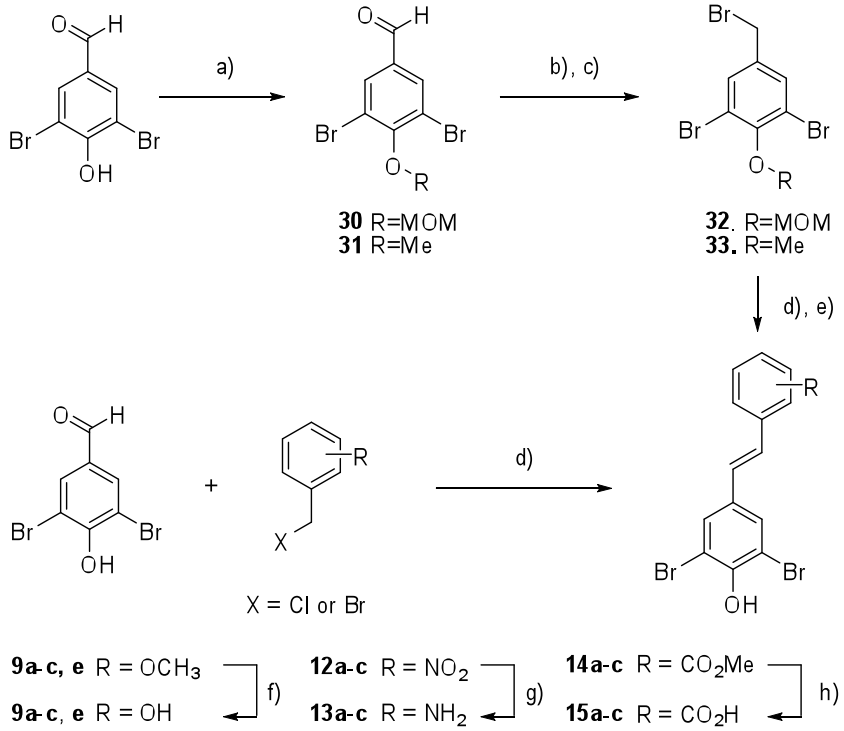
Cmpd	X	% Fibril Formation	Cmpd	X	% Fibril Formation
25		1%	**24a**		1%
26a		45%	**28**		71%
27a		69%	**29**		85%

Figure S8. Unbiased 2Fo-Fc electron density maps for **3d**, **13c** (both forward and reverse modes), **17d**, **24c**, **24d** and **24e** contoured at 3σ. The final models for the ligands are superimposed onto 2Fo-Fc density, with either forward or reverse subsite binding orientation indicated.



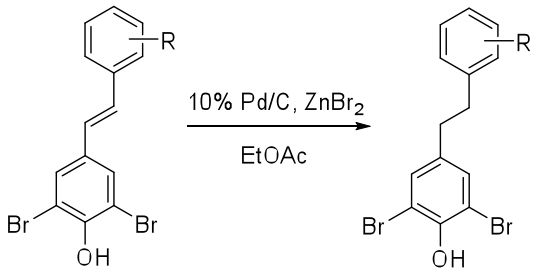


Scheme S1. Synthesis of stilbenes **2**-**15**.



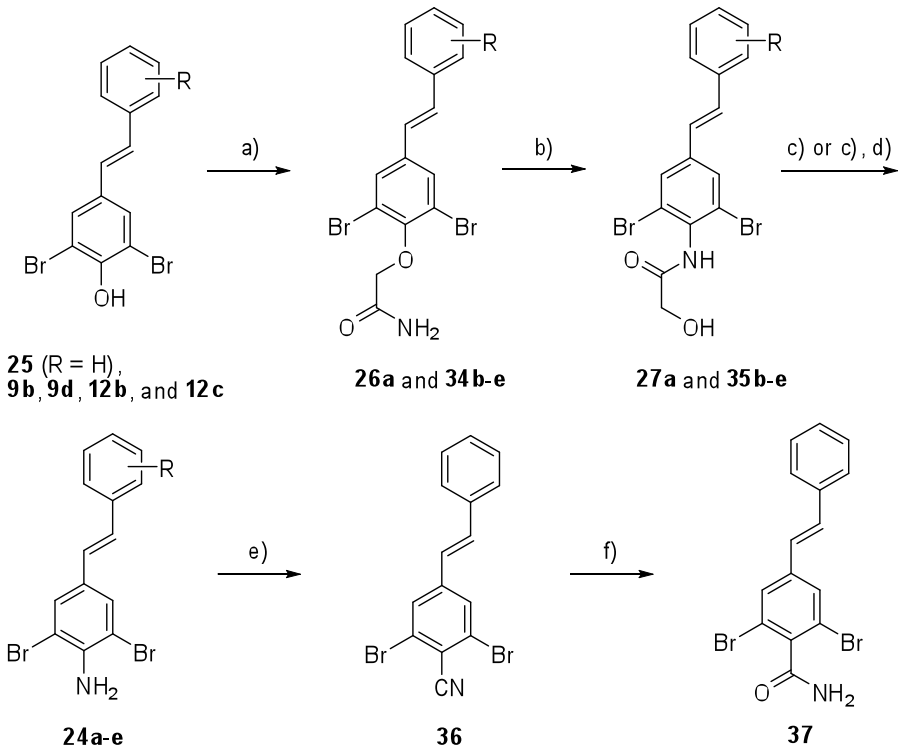
a) CH_3OCH_2Cl, DIEA, DCM for **30** or MeI, K_2CO_3, DMF for **31**; b) $NaBH_4$, MeOH; c) NBS, PPh_3, DCM for **32** or 48% HBr for **33**; d) $P(OEt)_3$, NaH, DMF, 150°C to r.t.; e) conc. HCl, MeOH, reflux for **8d** or 1M BBr_3 in DCM for **11e**; f) 1M BBr_3 in DCM, DCM; g) Sn dust, AcOH/HCl; h) 2N NaOH, MeOH

Scheme S2. Synthesis of dihydrostilbenes **16**-**23**.



16-**23**

Scheme S3. Synthesis of potential isosteres for the acidic phenol



25 (R = H), **9b**, **9d**, **12b**, and **12c**

26a and **34b-e**

27a and **35b-e**

24a-e

36

37

a) Bromoacetamide, K_2CO_3, DMF; b) NaOH, DMF; c) conc. HCl, 1,4-dioxane; d) Sn dust, AcOH/HCl for **24d** and **24e**; e) t-BuONO, HBF_4, KCN, CuCN, CH_3CN; f) KOH, t-BuOH

General Synthetic Methods. Unless otherwise indicated, all reactions were run under argon gas. Anhydrous solvents were obtained via passage through an activated alumina column and from commercial suppliers. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 500 MHz spectrometer. Chemical shifts are reported relative to internal $CDCl_3$ (Me_4Si, δ 0.0) and DMSO-d_6 (δ 2.50 for ^{1}H and δ 39.52 for ^{13}C). Reverse phase high performance liquid chromatography (RP-HPLC) was performed on a Waters 600 E multi-solvent delivery system, using a Waters 486 tunable absorbance detector, a 717 autosampler, and a ThermoHypersil Keystone Betabasic-18 column (150 Å pore size, 3 μm particle size, mobile phase A = 0.1% TFA in 94.9% H_2O + 5% CH_3CN, mobile phase B = 0.1% TFA in 94.9% CH_3CN + 5% H_2O). Final compound purities were determined by analytical RP-HPLC and were > 95% in purity (Figures S5-7). All mass spectrometry data were collected at The Scripps Research Institute Center for Mass Spectrometry (ESI-MS; Agilent Technologies, LC/MSD TOF G1969A and GC-MS; Agilent Technologies, 6850 Network GC System, 5973 Mass Selective Detector).

General Procedure for Horner-Wittig Reaction. Substituted benzyl bromide (1.2-2 equiv.) and triethylphosphite (1.4-2.4 equiv.) were heated to 150 °C for 3 h. The reaction mixture was cooled to 0 °C and then DMF was added. NaH (60% in oil, 1.8-3 equiv.) was added to the solution at 0 °C. After stirring for 20 min, the solution of aldehyde (1 equiv.) in DMF was added to the mixture dropwise at 0 °C. After 18 h, the mixture was diluted with EtOAc and the solution was washed with 10% citric acid and brine. After drying on Na_2SO_4, the organic layer was filtered and concentrated under reduced pressure. The compound was purified by column chromatography (Hexanes/EtOAc) or RP-HPLC. All compounds were characterized by ^{1}H, ^{13}C-NMR, and mass spectrometer.

3,5-dibromo-4-(methoxymethoxy)benzaldehyde (30). To a solution of 3,5-dibromo-4-hydroxy-benzaldehyde (5 g, 17.86 mmol) in 10 mL of CH_2Cl_2 was added DIEA (2.80 mL, 35.01 mmol). After 10 min, chloromethyl methyl ether (3.18 mL) was added to the reaction mixture at 0 °C and the mixture

was stirred for 3 h. The solution was washed with 5% citric acid and brine and dried with Na_2SO_4. The solution was filtered and concentrated. Compound **30** was purified by column chromatography (Hexanes/EtOAc = 8/1, 95%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.04 (s, 2H), 5.27 (s, 2H), 3.73 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 188.29, 156.76, 134.20, 133.95, 119.35, 100.06, 58.63.

3,5-dibromo-4-methoxybenzaldehyde (31). To a solution of 3,5-dibromo-4-hydroxybenzaldehyde (10 g, 35 mmol) and K_2CO_3 (7.26 g, 52.51 mmol) in 35 mL of DMF was added MeI (2.62 mL, 42.01 mmol) at room temperature. The reaction mixture was stirred overnight and diluted with EtOAc. The solution was washed with saturated $NaHCO_3$ and brine and dried with Na_2SO_4. The solution was filtered and concentrated. The residue was recrystallized (Hexanes/EtOAc) to give 3,5-dibromo-4-methoxybenzaldehyde **31** (8.61 g, 84%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.03 (s, 2H), 3.97 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 188.34, 159.11, 134.20, 133.88, 119.28, 60.86; ESI-MS: m/z (MH^+): 292.8807 (calc'd), 292.8816 (found).

1,3-dibromo-5-(bromomethyl)-2-(methoxymethoxy)benzene (32). To a solution of MOM protected compound **30** (4.97 g, 15.34 mmol) in 20 mL of MeOH was added $NaBH_4$ at room temperature. The reaction mixture was stirred for 1 h. After removal of solvent under reduced pressure, the residue was dissolved in EtOAc. The solution was washed with brine and dried with Na_2SO_4. The solution was filtered and concentrated. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 6/1) to give [3,5-dibromo-4-(methoxymethoxy)phenyl]-methanol (75%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.54 (s, 2H), 5.17 (s, 2H), 4.63 (d, *J*=5.9 Hz, 2H), 3.72 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 150.67, 139.65, 131.04, 118.38, 99.63, 63.34, 58.48; ESI-MS: m/z ($M+Na^+$): 346.8889 (calc'd), 346.8887 (found). To a solution of (3,5-dibromo-4-(methoxymethoxy)phenyl)-methanol (1 g, 3.07 mmol) and PPh_3 (1.22 g, 4.61 mmol) in 30 mL of DCM was added NBS (0.83 g, 4.61 mmol) at 0 °C. The reaction mixture was stirred for 30 min. After removal of solvent under reduced pressure, the

residue was dissolved in Et_2O. The solution was washed with brine and dried with $MgSO_4$. The solution was filtered and concentrated. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 7/1) to give **32** (1.1 g, 92%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.55 (s, 2H), 5.18 (s, 2H), 4.36 (s, 2H), 3.72 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 151.69, 136.35, 133.32, 118.43, 99.73, 58.51, 30.49; ESI-MS: m/z ($[M+Na]^+$): 408.8045 (calc'd), 408.8046 (found).

1,3-dibromo-5-(bromomethyl)-2-methoxybenzene (33). To a solution of 3,5-dibromo-4-methoxybenzaldehyde **31** (1 g, 3.4 mmol) in 6 mL of MeOH was added $NaBH_4$ (0.143 g, 3.74 mmol) at room temperature. The reaction mixture was stirred for 30 min. After removal of solvent under reduced pressure, the residue was dissolved in EtOAc. The solution was washed with brine and dried with Na_2SO_4. The solution was filtered and concentrated (99%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.51 (s, 2H), 4.62 (s, 2H), 3.87 (s, 3H). A solution of (3,5-dibromo-4-methoxyphenyl)methanol in 8 mL of 48% HBr was refluxed for 5 h. The reaction mixture was diluted with H_2O and extracted with Et_2O. The organic layer was washed with saturated $NaHCO_3$ and brine and dried with $MgSO_4$. The solution was filtered and concentrated. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9/1) to give **33** (1.1 g, 90%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.54 (s, 2H), 4.36 (s, 2H), 3.89 (s, 3H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 154.21, 136.19, 133.16, 118.21, 60.67, 30.60; GC-MS: m/z (M^+): 356 (calc'd), 356 (found).

Representative Procedure for Cleavage of Methyl Ether (10a). To a solution of **9a** (0.5 g, 1.302 mmol) in CH_2Cl_2 (9 mL) was added BBr_3 (6.61 mL, 1 M in DCM). The reaction mixture was stirred for 20 h at room temperature. The reaction was quenched carefully by addition of methanol and diluted with EtOAc. The solution was washed with saturated $NaHCO_3$ and brine and dried with Na_2SO_4. The solution was filtered and concentrated. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 8/1) to give **10a** (0.16 g, 34%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.61 (s, 2H), 7.47 (d,

J=7.8 Hz, 1H), 7.23 (d, *J*= 16.4 Hz, 1H), 7.15 (m, 1H), 6.92-6.96 (m, 2H), 6.79 (d, *J*=8.0 Hz, 1H), 5.87 (s, 1H), 5.02 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 153.03, 148.53, 133.07, 129.85, 128.95, 127.19, 126.53, 124.04, 123.74, 121.24, 115.96, 110.13; ESI-MS: m/z (MH^+): 368.9120 (calc'd), 368.9106 (found).

Representative Procedure for Reduction of Nitro Group (13a). To a suspension of **12a** (0.2 g, 0.501 mmol) in AcOH and HCl (2/0.2 mL, v/v) was added Sn powder (0.238 g, 2.005 mmol) and stirred for 3 h at room temperature. The mixture was diluted with EtOAc and neutralized by addition of saturated $NaHCO_3$. The solution was washed with saturated brine and dried with Na_2SO_4. The solution was filtered and concentrated. The residue was recrystallized (Hexanes/EtOAc) to give **13a** (0.17 g, 92%)**.** ^{1}H-NMR (500MHz, d_6-DMSO) δ 9.90 (s, 1H), 7.84 (s, 2H), 7.38 (d, *J*=7.7 Hz, 1H), 7.32 (d, *J*=16.1 Hz, 1H), 6.93-6.96 (m, 1H), 6.86 (d, *J*=16.1 Hz, 1H), 6.62 (d, *J*=8.0 Hz, 1H), 6.53 (dd, *J*=7.5 Hz, 1H), 5.40 (s, 2H); ^{13}C-NMR (125MHz, d_6-DMSO) δ149.27, 146.32, 132.86, 129.71, 128.43, 125.14, 124.32, 123.61, 120.22, 116.04, 115.39, 112.22; ESI-MS: m/z (MH^+): 367.9280 (calc'd), 367.9279 (found).

Representative Procedure for Hydrolysis of Methyl Ester (15a). To a solution of **14a** (0.2 g, 0.485 mmol) in MeOH (5 mL) was added 2 N NaOH (0.485 mL) at room temperature. This solution was stirred overnight. The mixture was diluted with EtOAc and acidified with 5% citric acid. The solution was washed with saturated brine and dried with Na_2SO_4. The solution was filtered and concentrated. The residue was recrystallized (Hexanes/EtOAc) to give **15a** (0.176 g, 92%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 13.01 (s, 1H), 10.10 (s, 1H), 7.85 (dd, *J*=1.3, 7.8 Hz, 1H), 7.78 (d, *J*=16.4 Hz, 1H), 7.73-7.76 (m, 3H), 7.57 (dd, *J*=7.6, 7.6 Hz, 1H), 7.38 (dd, *J*=7.5, 7.5 Hz, 1H), 7.03 (d, *J*=16.3 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 168.38, 150.15, 137.55, 132.02, 131.79, 130.21, 130.04, 129.61, 127.53, 127.39, 127.24, 126.552, 112.26; ESI-MS: m/z (MH^+): 396.9069 (calc'd), 396.9054 (found).

(*E*)-2,6-dibromo-4-styrylbenzonitrile (36). To a solution of **24a** (0.1 g, 0.283 mmol) in CH_3CN (2 mL) were slowly added HBF_4 (74 μL, 0.566 mmol) and *t*-BuONO (42 μL, 0.312 mmol) at 0 °C. The reaction mixture was stirred for 20 min. A solution of KCN (0.107 g, 1.613 mmol) and CuCN (0.072 g, 0.792 mmol) in H_2O (2 mL) was added to the above solution at 0 °C and stirred for 5 h. The mixture was diluted with EtOAc and H_2O. The organic layer was washed with saturated $NaHCO_3$ and saturated brine. After drying over Na_2SO_4, the solution was filtered and concentrated. The residue was subjected to preparative RP-HPLC and lyophilized to give **36**. ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.73 (s, 2H), 7.52 (d, *J*=7.3 Hz, 2H), 7.34-7.42 (m, 3H), 7.22 (d, *J*=16.3 Hz, 1H), 6.94 (d, *J*=16.3 Hz, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 143.96, 135.46, 135.01, 129.39, 129.21, 128.98, 127.19, 126.80, 124.15, 116.37, 116.17; ESI-MS: m/z (MH^+): 362 (calc'd), 362 (found).

(*E*)-2,6-dibromo-4-styrylbenzamide (37). A mixture of **36** (73 mg, 0.201 mmol) and powdered KOH (42 mg, 0.744 mmol) in 2 mL of *t*-BuOH was refluxed for 30 min. The reaction mixture was diluted with EtOAc and washed with brine. After drying over Na_2SO_4, the solution was filtered and concentrated. The purification was carried out on RP-HPLC and lyophilized to give **36** (71 mg, 93%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 8.03 (s, 1H), 7.91 (s ,2H), 7.74 (s, 1H), 7.61 (d, *J*=7.3 Hz, 2H), 7.46 (d, *J*=16.5 Hz, 1H), 7.40 (dd, *J*=7.6, 7.6 Hz, 2H), 7.30-7.33 (m, 1H), 7.22 (d, *J*=16.5 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 167.15, 140.25, 139.04, 136.23, 131.69, 128.92, 128.69, 128.30, 126.75, 124.84, 119.69; ESI-MS: m/z (MH^+): 379.9280 (calc'd), 379.9284 (found).

(*E*)-2,6-dibromo-4-(2-fluorostyryl)phenol (2a). Compound **2a** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-2-fluorobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.7/0.3) to give **2a** (90%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.61 (s, 2H), 7.51-7.54 (m, 1H), 7.21-7.25 (m,

1H), 7.05-7.15 (m, 3H), 6.97 (d, *J*=16.4 Hz, 1H), 5.90 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 161.42, 159.43, 148.86, 132.54, 129.99, 129.19, 129.12, 127.65, 127.61, 127.09, 124.48, 124.27, 121.63, 121.60, 115.98, 115.80, 110.19; ESI-MS: m/z (MH^+): 370.9077 (calc'd), 370.9073 (found).

(*E*)-2,6-dibromo-4-(3-fluorostyryl)phenol (2b). Compound **2b** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3-fluorobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **2b** (87%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.59 (s, 2H), 7.29-7.33 (m, 1H), 7.22 (d, *J*=7.8 Hz, 1H), 7.16 (d, *J*=10.1 Hz, 1H), 6.94-6.98 (m, 1H), 6.92 (d, *J*=16.3 Hz, 1H), 6.87 (d, *J*=16.3 Hz, 1H), 5.91 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 164.14, 162.18, 148.93, 139.03, 138.96, 132.13, 130.23, 130.16, 129.99, 129.93, 128.03, 126.66, 122.45, 114.85, 114.68, 112.87, 112.70, 110.23; ESI-MS: m/z ($[M-H]^-$): 368.8931 (calc'd), 368.8936 (found).

(*E*)-2,6-dibromo-4-(4-fluorostyryl)phenol (2c). Compound **2c** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-4-fluorobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **2c** (87%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.57 (s, 2H), 7.41-7.44 (m, 2H), 7.05 (dd, *J*=8.6, 8.6 Hz, 2H), 6.91 (d, *J*=16.3 Hz, 1H), 6.79 (d, *J*=16.3 Hz, 1H), 5.88 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 163.48, 161.51, 148.64, 132.84, 132.81, 132.49, 129.77, 128.05, 127.98, 125.10, 115.82, 115.65, 110.18; ESI-MS: m/z (MH^+): 370.9077 (calc'd), 370.9080 (found).

(*E*)-2,6-dibromo-4-(2,6-difluorostyryl)phenol (2d). Compound **2d** was prepared according to the general procedure for Horner-Wittig reaction from 2-(bromomethyl)-1,3-difluorobenzene and 3,5-dibromo-4-hydroxy-benzaldehyde. The residue was subjected to chromatography over silica gel (HexanesEtOAc = 9.5/0.5) to give **2d** (87%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.61 (s, 2H), 7.14-7.25 (m,

2H), 6.97 (d, *J*=16.7 Hz, 1H), 6.91 (dd, *J*=8.6, 8.6 Hz, 2H), 5.92 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 161.99, 161.93, 159.99, 159.93, 149.06, 132.76, 131.78, 131.71, 131.64, 130.05, 128.38, 128.29, 128.21, 115.72, 114.32, 114.20, 114.08, 111.73, 111.69, 111.56, 111.52, 110.21; ESI-MS: m/z (MH^+): 388.8983 (calc'd), 388.8971 (found).

(*E*)-2,6-dibromo-4-(3,5-difluorostyryl)phenol (2e). Compound **2e** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3,5-difluorobenzene and 3,5-dibromo-4-hydroxy-benzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **2e** (70%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.59 (s, 2H), 6.95-6.97 (m, 2H), 6.89 (d, *J*=16.2 Hz, 1H), 6.85 (d, *J*=16.2 Hz, 1H), 6.69-6.73 (m, 1H), 5.94 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 164.33, 164.23, 162.36, 162.25, 149.26, 140.12, 140.05, 139.97, 131.60, 130.17, 127.94, 127.04, 110.29, 109.18, 109.13, 109.02, 108.98, 103.30, 103.10, 102.90; ESI-MS: m/z ($[M-H]^-$): 386.8837 (calc'd), 386.8843 (found).

(*E*)-2,6-dibromo-4-(2-chlorostyryl)phenol (3a). Compound **3a** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-2-chlorobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **3a** (99%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.59-7.61 (m, 3H), 7.38 (dd, *J*=1.4, 7.9 Hz, 1H), 7.35 (d, *J*=16.2 Hz, 1H), 7.24-7.27 (m, 1H), 7.18-7.22 (m, 1H), 6.85 (d, *J*=16.2 Hz, 1H), 5.91 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.96, 134.74, 133.49, 132.34, 130.15, 129.89, 128.86, 127.90, 126.95, 126.37, 125.26, 110.19; ESI-MS: m/z (MH^+): 386.8781 (calc'd), 386.8766 (found).

(*E*)-2,6-dibromo-4-(3-chlorostyryl)phenol (3b). Compound **3b** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3-chlorobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc

= 9.5/0.5) to give **3b** (69%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.59 (s, 2H), 7.45 (dd, *J*=1.7, 1.7 Hz, 1H), 7.22-7.33 (m, 3H), 6.88 (s, 2H), 5.91 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.95, 138.56, 134.73, 132.10, 130.00, 129.95, 127.85, 127.76, 126.75, 126.28, 124.74, 110.22; ESI-MS: m/z (MH^+): 386.8781 (calc'd), 386.8772 (found).

(*E*)-2,6-dibromo-4-(4-chlorostyryl)phenol (3c). Compound **3c** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-4-chlorobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **3c** (68%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.58 (s, 2H), 7.38 (d, *J*=8.6 Hz, 2H), 7.32 (d, *J*=8.5 Hz, 2H), 6.90 (d, *J*=16.3 Hz, 1H), 6.84 (d, *J*=16.3 Hz, 1H), 5.89 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.80, 135.14, 133.59, 132.29, 129.88, 128.93, 127.93, 127.63, 125.92, 110.21; ESI-MS: m/z (MH^+): 386.8781 (calc'd), 386.8768 (found).

(*E*)-2,6-dibromo-4-(2,6-dichlorostyryl)phenol (3d). Compound **3d** was prepared according to the general procedure for Horner-Wittig reaction from 2-(bromomethyl)-1,3-dichlorobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **3d** (99%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.63 (s, 2H), 7.35 (d, *J*=8.0 Hz, 2H), 7.12 (dd, *J*=8.0, 8.0 Hz, 1H), 6.97 (s, 2H), 5.93 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 149.23, 134.56, 133.93, 133.76, 132.00, 130.17, 128.63, 128.36, 123.10, 110.21; ESI-MS: m/z ($[M-H]^-$): 418.8246 (calc'd), 418.8245 (found).

(*E*)-2,6-dibromo-4-(3,5-dichlorostyryl)phenol (3e). Compound **3e** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3,5-dichlorobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **3e** (64%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.59 (s, 2H), 7.33 (d, *J*=1.8

Hz, 2H), 7.25 (dd, *J*=1.8, 1.8 Hz, 1H), 6.90 (d, *J*= 16.2 Hz, 1H), 6.82 (d, *J*= 16.2 Hz, 1H), 5.94 (s, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 150.52, 140.68, 134.30, 131.14, 130.35, 128.67, 126.47, 125.49, 124.69, 112.20; ESI-MS: m/z ([M-H]$^-$): 418.8246 (calc'd), 418.8244 (found).

(*E*)-2,6-dibromo-4-(2-bromostyryl)phenol (4a). Compound **4a** was prepared according to the general procedure for Horner-Wittig reaction from 1-bromo-2-(bromomethyl)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.6/0.4) to give **4a** (96%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.61 (s, 2H), 7.57-7.59 (m, 2H), 7.29-7.32 (m, 2H), 6.81 (d, *J*=16.2 Hz, 1H), 5.92 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.98, 136.48, 133.14, 132.27, 130.16, 129.12, 128.11, 127.95, 127.60, 126.62, 124.15, 110.21; ESI-MS: m/z (MH^+): 430.8276 (calc'd), 430.8279 (found).

(*E*)-2,6-dibromo-4-(3-bromostyryl)phenol (4b). Compound **4b** was prepared according to the general procedure for Horner-Wittig reaction from 1-bromo-3-(bromomethyl)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **4b** (71%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.61 (dd, *J*=1.7, 1.7 Hz, 1H), 7.58 (s, 2H), 7.22 (dd, *J*=7.8, 7.8 Hz, 1H), 7.35 -7.40 (m, 2H), 6.87(s, 2H), 5.91 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.96, 138.81, 132.08, 130.75, 130.22, 130.01, 129.23, 127.64, 126.79, 125.18, 122.95, 110.23; ESI-MS: m/z ([M-H]$^-$): 428.8131 (calc'd), 428.8131 (found).

(*E*)-2,6-dibromo-4-(4-bromostyryl)phenol (4c). Compound **4c** was prepared according to the general procedure for Horner-Wittig reaction from 1-bromo-4-(bromomethyl)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **4c** (63%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.57 (s, 2H), 7.47 (d, *J*=8.5 Hz, 2H), 7.31 (d, *J*=8.5 Hz, 2H), 6.87 (s, 2H), 5.89 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.82, 135.56, 132.25, 131.87,

129.89, 127.96, 127.92, 126.02, 121.74, 110.21; ESI-MS: m/z ([M-H]$^-$): 428.8131 (calc'd), 428.8141 (found).

(*E*)-2,6-dibromo-4-(2,6-dibromostyryl)phenol (4d). Compound **4d** was prepared according to the general procedure for Horner-Wittig reaction from 1,3-dibromo-2-(bromomethyl)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 8/1) to give **4d** (94%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.16 (s, 1H), 7.85 (s, 2H), 7.72 (d, *J*=7.9 Hz, 2H), 7.15 (dd, *J*=8.0, 8.0 Hz, 1H), 7.04 (d, *J*=16.6 Hz, 1H), 6.75 (d, *J*=16.6 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 150.62, 137.51, 133.46, 132.30, 130.61, 130.24, 130.09, 126.78, 123.48, 112.21; ESI-MS: m/z ([M-H]$^-$): 506.7236 (calc'd), 506.7237 (found).

(*E*)-2,6-dibromo-4-(3,5-dibromostyryl)phenol (4e). Compound **4e** was prepared according to the general procedure for Horner-Wittig reaction from 1,3-dibromo-5-(bromomethyl)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 8/1) to give **4e** (90%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.16 (s, 1H), 7.79 (s, 2H), 7.77 (d, *J*=1.6 Hz, 2H), 7.68 (dd, *J*=1.6, 1.6 Hz, 1H), 7.31 (d, *J*=16.4 Hz, 1H), 7.17 (d, *J*=16.4 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 150.51, 141.22, 131.74, 131.15, 130.36, 128.62, 127.90, 125.31, 122.75, 112.20; ESI-MS: m/z ([M-H]$^-$): 506.7236 (calc'd), 506.7240 (found).

(*E*)-2,6-dibromo-4-(2-iodostyryl)phenol (5a). Compound **5a** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-2-iodobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **5a** (86%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.86 (dd, *J*=1.1, 7.9 Hz, 1H), 7.60 (s, 2H), 7.53 (dd, *J*=1.4, 7.8 Hz, 1H), 7.33 (dd, *J*=7.8, 7.8 Hz, 1H), 7.14 (d, *J*=16.0 Hz, 1H), 6.94-6.97 (m, 1H), 6.72 (d, *J*=16.0 Hz, 1H), 5.91 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.95, 139.69, 139.66, 132.90, 132.17,

130.13, 129.28, 128.46, 128.29, 126.23, 110.22, 100.40; ESI-MS: m/z (MH^+): 478.8138 (calc'd), 478.8134 (found).

(*E*)-2,6-dibromo-4-(3-iodostyryl)phenol (5b). Compound **5b** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3-iodobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **5b** (64%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.82 (dd, *J*=1.6, 1.6 Hz, 1H), 7.58-7.60 (m, 3H), 7.40 (d, *J*=7.8 Hz, 1H), 7.08 (dd, *J*=7.8, 7.8 Hz, 1H), 6.87 (d, *J*=16.3 Hz, 1H), 6.83 (d, *J*=16.3 Hz, 1H), 5.91 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.95, 138.89, 136.71, 135.27, 132.11, 130.37, 129.99, 127.54, 126.67, 125.75, 110.23, 94.79; ESI-MS: m/z ($[M-H]^-$): 476.7992 (calc'd), 476.7993 (found).

(*E*)-2,6-dibromo-4-(4-iodostyryl)phenol (5c). Compound **5c** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-4-iodobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **5c** (58%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.68 (d, *J*=8.3 Hz, 2H), 7.58 (s, 2H), 7.19 (d, *J*=8.3 Hz, 2H), 6.87 (s, 2H), 5.90 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.85, 137.83, 136.15, 132.23, 129.92, 128.14, 128.08, 126.12, 110.22, 93.24; ESI-MS: m/z ($[M-H]^-$): 476.7992 (calc'd), 476.7995 (found).

(*E*)-2,6-dibromo-4-(2-methylstyryl)phenol (6a). Compound **6a** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-2-methylbenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **6a** (76%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.60 (s, 2H), 7.51-7.53 (m, 1H), 7.17-7.21 (m, 4H), 6.79 (d, *J*=16.1 Hz, 1H), 5.88 (s, 1H), 2.43 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.58, 135.88,

135.68, 132.97, 130.48, 129.85, 127.88, 127.08, 126.65, 126.24, 125.28, 110.14, 19.94; ESI-MS: m/z (MH^+): 366.9328 (calc'd), 366.9320 (found).

(*E*)-2,6-dibromo-4-(3-methylstyryl)phenol (6b). Compound **6b** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3-methylbenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **6b** (71%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.58 (s, 2H), 7.23-7.28 (m, 3H), 7.08 (d, *J*=6.5 Hz, 1H), 6.92 (d, *J*=16.3 Hz, 1H), 6.86 (d, *J*=16.3 Hz, 1H), 5.86 (s, 1H), 2.37 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.51, 138.30, 136.56, 132.75, 129.77, 129.37, 128.80, 128.63, 127.19, 125.09, 123.69, 110.13, 21.42; ESI-MS: m/z (MH^+): 366.9328 (calc'd), 366.9323 (found).

(*E*)-2,6-dibromo-4-(4-methylstyryl)phenol (6c). Compound **6c** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-4-methylbenzeneand 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **6c** (88%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.57 (s, 2H), 7.35 (d, *J*=8.1 Hz, 1H), 7.16 (d, *J*=8.0 Hz, 2H), 6.93 (d, *J*=16.3 Hz, 1H), 6.82 (d, *J*=16.3 Hz, 1H), 5.85 (s, 1H), 2.36 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.40, 137.96, 133.85, 132.87, 129.69, 129.46, 129.22, 126.42, 124.32, 110.13, 21.26; ESI-MS: m/z (MH^+): 366.9328 (calc'd), 366.9311 (found).

(*E*)-2,6-dibromo-4-(2,6-dimethylstyryl)phenol (6d). Compound **6d** was prepared according to the general procedure for Horner-Wittig reaction from 2-(bromomethyl)-1,3-dimethylbenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **6d** (79%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.57 (s, 2H), 7.05-7.10 (m, 3H), 6.97 (d, *J*=16.6 Hz, 1H), 6.40 (d, *J*=16.6 Hz, 1H), 5.88 (s, 1H), 2.34 (s, 6H); ^{13}C-NMR (125MHz,

$CDCl_3$) δ 148.62, 136.21, 136.17, 132.83, 130.78, 129.63, 127.94, 127.60, 126.98, 110.15, 21.04; ESI-MS: m/z (MH^+): 380.9484 (calc'd), 380.9474 (found).

(*E*)-2,6-dibromo-4-(3,5-dimethylstyryl)phenol (6e). Compound **6e** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3,5-dimethylbenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 8/1) to give **6e** (91%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.57 (s, 2H), 7.09 (s, 2H), 6.83-6.92 (m, 3H), 5.86 (s, 1H), 2.33 (s, 6H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.46, 138.20, 136.53, 132.86, 129.78, 129.74, 129.48, 124.91, 124.43, 110.13, 21.28; ESI-MS: m/z (MH^+): 380.9484 (calc'd), 380.9484 (found).

(*E*)-2,6-dibromo-4-(2-(trifluoromethyl)styryl)phenol (7a). Compound **7a** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-2-(trifluoromethyl)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **7a** (60%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.69 (d, *J*=7.9 Hz, 1H), 7.67 (d, *J*=7.9 Hz, 1H), 7.60 (s, 2H), 7.54 (dd, *J*=7.6, 7.6 Hz, 1H), 7.37 (dd, *J*=7.6, 7.6 Hz, 1H), 7.29-7.32 (m, 1H), 6.86 (d, *J*=16.0 Hz, 1H), 5.94 (s, 1H);^{13}C-NMR (125MHz, $CDCl_3$) δ 149.18, 135.73, 132.11, 131.95, 130.27, 129.45, 127.73, 127.55, 127.49, 126.98, 126.07, 126.03, 125.98, 125.94, 125.42, 124.92, 123.24, 110.25; ESI-MS: m/z (MH^+): 420.9045 (calc'd), 420.9029 (found).

(*E*)-2,6-dibromo-4-(3-(trifluoromethyl)styryl)phenol (7b). Compound **7b** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3-(trifluoromethyl)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **7b** (79%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.61-7.62 (m, 3H), 7.51 (d, *J*=7.7 Hz, 1H), 7.46 (dd, *J*=7.7, 7.7 Hz, 1H), 6.97 (d, *J*=16.3 Hz, 1H), 6.93 (d, *J*=16.3 Hz,

1H), 5.92 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 149.07, 137.42, 131.94, 130.05, 129.54, 129.21, 127.63, 127.16, 125.11, 124.40, 124.37, 123.06, 123.03, 122.95, 110.25; ESI-MS: m/z (MH^+): 420.9045 (calc'd), 420.9034 (found).

(*E*)-2,6-dibromo-4-(4-(trifluoromethyl)styryl)phenol (7c). Compound **7c** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-4-(trifluoromethyl)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **7c** (79%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.60-7.61 (m, 4H), 7.55 (d, *J*=8.3 Hz, 2H), 6.97 (s, 2H), 5.93 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 149.16, 140.08, 131.91, 130.14, 129.74, 129.48, 127.81, 127.64, 126.57, 125.73, 125.70, 125.18, 123.02, 110.27; ESI-MS: m/z ($[M-H]^-$): 418.8899 (calc'd), 418.8897 (found).

(*E*)-4-(3,5-bis(trifluoromethyl)styryl)-2,6-dibromophenol (7e). Compound **7e** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3,5-bis(trifluoromethyl)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **7e** (82%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.88 (s, 2H), 7.75 (s, 1H), 7.65 (s, 2H), 7.05 (d, *J*=16.3 Hz, 1H), 7.00 (d, *J*=16.3 Hz, 1H), 5.98 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 149.60, 138.76, 132.30, 132.04, 131.23, 130.34, 129.20, 126.13, 126.02, 124.33, 122.16, 121.14, 121.111, 121.08, 110.39, 99.59; ESI-MS: m/z ($[M-H]^-$): 486.8773 (calc'd), 486.8772 (found).

(*E*)-2-(3,5-dibromo-4-hydroxystyryl)benzonitrile (8a). Compound **8a** was prepared according to the general procedure for Horner-Wittig reaction from 2-(bromomethyl)benzonitrile and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 6/1) to give **8a** (71%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.25 (s, 1H), 7.91 (d, *J*=8.0 Hz, 1H), 7.83-

7.85 (m, 3H), 7.72 (dd, *J*=7.7, 7.7 Hz, 1H), 7.46 (dd, *J*=7.6, 7.6 Hz, 1H), 7.38 (d, *J*=16.2, 1H), 7.28 (d, *J*=16.2 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 150.92, 139.71, 133.31, 133.18, 130.84, 130.76, 130.57, 128.08, 125.75, 123.46, 117.71, 112.24, 109.84; ESI-MS: m/z (MH^+): 377.9124 (calc'd), 377.9118 (found).

(*E*)-3-(3,5-dibromo-4-hydroxystyryl)benzonitrile (8b). Compound **8b** was prepared according to the general procedure for Horner-Wittig reaction from 3-(bromomethyl)benzonitrile and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 6/1) to give **8b** (96%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.67 (d, *J*=7.9 Hz, 1H), 7.61 (s, 2H), 7.54 (d, *J*=7.7 Hz, 1H), 7.46 (dd, *J*=7.8, 7.8 Hz, 1H), 6.95 (d, *J*=16.3 Hz, 1H), 6.91 (d, *J*=16.3 Hz, 1H), 5.96 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 149.31, 137.93, 131.61, 131.01, 130.49, 130.16, 129.81, 129.57, 127.97, 126.71, 118.60, 113.07, 110.31; ESI-MS: m/z (MH^+): 377.9124 (calc'd), 377.9126 (found).

(*E*)-4-(3,5-dibromo-4-hydroxystyryl)benzonitrile (8c). Compound **8c** was prepared according to the general procedure for Horner-Wittig reaction from 4-(bromomethyl)benzonitrile and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 6/1) to give **8c** (87%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.18 (s, 1H), 7.86 (s, 2H), 7.82 (d, *J*=8.3 Hz, 2H), 7.72 (d, *J*=8.3 Hz, 2H), 7.33 (s, 2H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 150.59, 141.60, 132.51, 131.19, 130.49, 129.15, 126.89, 126.72, 118.89, 112.22, 109.37; ESI-MS: m/z (MH^+): 377.9124 (calc'd), 377.9118 (found).

(*E*)-2,6-dibromo-4-(2-methoxystyryl)phenol (9a). Compound **9a** was prepared according to the general procedure for Horner-Wittig reaction from 1-(chloromethyl)-2-methoxybenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel

(Hexanes/EtOAc = 9.5/0.5) to give **9a** (89%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.60 (s, 2H), 7.51 (dd, *J*=1.6, 7.7 Hz, 1H), 7.31 (d, *J*=16.4 Hz, 1H), 7.23-7.27 (m, 1H), 7.96 (dd, *J*=7.5, 7.5 Hz, 1H), 6.89-6.92 (m, 2H), 5.85 (s, 1H), 3.89 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 156.94, 148.34, 133.35, 129.82, 129.02, 126.49, 125.75, 125.69, 124.19, 120.75, 110.94, 110.07, 55.48; ESI-MS: m/z (MH^+): 382.9277 (calc'd), 382.9266 (found).

(*E*)-2,6-dibromo-4-(3-methoxystyryl)phenol (9b). Compound **9b** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3-methoxybenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was recrystallized (Hexanes/EtOAc) to give **9b** (75%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.60 (s, 2H), 7.28 (dd, *J*=8.0, 8.0 Hz, 1H), 7.07 (d, *J*=7.7 Hz, 1H), 7.00 (m, 1H), 6.94 (d, *J*=16.2 Hz, 1H), 6.88 (d, *J*=16.3 Hz, 1H), 6.82 (m, 1H), 5.89 (s, 1H), 3.84 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 159.91, 148.66, 138.08, 132.57, 129.87, 129.73, 129.19, 125.65, 119.21, 113.66, 111.77, 110.17, 55.26; ESI-MS: m/z (MH^+): 382.9277 (calc'd), 382.9263 (found).

(*E*)-2,6-dibromo-4-(4-methoxystyryl)phenol (9c). Compound **9c** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-4-methoxybenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9/1) to give **9c** (85%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.57 (s, 2H), 7.41 (d, *J*=8.7 Hz, 2H), 6.89-6.93 (m, 3H), 6.75 (d, *J*=16.2 Hz, 1H), 5.85 (s, 1H), 3.83 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 159.55, 148.24, 133.03, 129.53, 129.42, 128.83, 127.75, 123.19, 114.20, 110.12, 55.33; ESI-MS: m/z (MH^+): 382.9277 (calc'd), 382.9266 (found).

(*E*)-2,6-dibromo-4-(2,6-dimethoxystyryl)phenol (9d). MOM protected **9d** was prepared according to the general procedure for Horner-Wittig reaction from **32** and 2,6-dimethoxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9/1) to give MOM protected

9d (83%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.66 (s, 2H), 7.36 (d, *J*=16.6 Hz, 1H), 7.40 (d, *J*=16.6 Hz, 1H), 7.18 (dd, *J*=8.4, 8.4 Hz, 1H), 6.58 (d, *J*=8.4 Hz, 2H), 5.17 (s, 2H), 3.89 (s, 6H), 3.72 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 158.74, 149.80, 138.50, 130.28, 128.78, 128.58, 121.95, 118.37, 113.93, 103.89, 99.62, 58.43, 55.76.

*MOM deprotection of MOM protected **9d***; to a solution of MOM protected **9d** (0.4 g, 0.873 mmol) in 3 mL of MeOH was added a catalytic amount of concentrated HCl. The reaction mixture was refluxed for 1 h. After cooling and removal of solvent under reduced pressure, the residue was dissolved in EtOAc. The solution was washed with brine and dried with Na_2SO_4. The solution was filtered and concentrated. The residue was recrystallized (Hexanes/EtOAc) to give **9d** (84%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.61 (s, 2H), 7.39 (d, *J*=16.6 Hz, 1H), 7.31 (d, *J*=16.6 Hz, 1H), 7.18 (dd, *J*=8.4, 8.4 Hz, 1H), 6.59 (d, *J*=8.4 Hz, 2H), 5.82 (s, 1H), 3.90 (s, 6H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 158.65, 147.98, 134.74, 129.67, 128.92, 128.49, 120.44, 114.13, 109.99, 103.94, 55.79; ESI-MS: m/z (MH^+): 412.9382 (calc'd), 412.9371 (found).

(*E*)-2,6-dibromo-4-(3,5-dimethoxystyryl)phenol (9e). Compound **9e** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3,5-dimethoxybenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was recrystallized (Hexanes/EtOAc) to give **9e** (79%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.04 (s, 1H), 7.80 (s, 2H), 7.15 (s, 2H), 6.74 (d, *J*=2.2 Hz, 2H), 6.41 (dd, *J*=2.2, 2.2 Hz, 1H), 3.77 (s, 6H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 160.51, 149.92, 138.78, 131.84, 129.96, 128.45, 125.87, 112.25, 104.34, 99.82, 55.07; ESI-MS: m/z (MH^+): 412.9382 (calc'd), 412.9372 (found).

(*E*)-2,6-dibromo-4-(3-hydroxystyryl)phenol (10b). Compound **10b** was prepared according to the general procedure for cleavage of methyl ether from **9b**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 5/1) to give **10b** (97%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.00 (s,

1H), 9.42 (s, 1H), 7.81 (s, 2H), 7.12-7.17 (m, 2H), 6.98-7.04 (m, 2H), 6.93 (dd, *J*=1.9, 1.9 Hz, 1H), 6.68 (dd, *J*=2.0, 8.0 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 157.47, 149.79, 138.07, 131.99, 129.91, 129.47, 128.69, 125.11, 117.35, 114.81, 112.97, 112.24; ESI-MS: m/z (MH^+): 368.9120 (calc'd), 368.9116 (found).

(*E*)-2,6-dibromo-4-(4-hydroxystyryl)phenol (10c). Compound **10c** was prepared according to the general procedure for cleavage of methyl ether from **9c**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 5/1) to give **10c** (75%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 9.90 (s, 1H), 9.57 (s, 1H), 7.73 (s, 2H), 7.38 (d, *J*=8.6 Hz, 2H), 7.10 (d, *J*=16.4 Hz, 1H), 6.86 (d, *J*=16.4 Hz, 1H), 6.76 (d, *J*=8.6 Hz, 2H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 157.25, 149.26, 132.58, 129.37, 128.57, 127.78, 127.73, 121.99, 115.42, 112.29; ESI-MS: m/z (MH^+): 368.912 (calc'd), 368.9106 (found).

(*E*)-5-(3,5-dibromo-4-hydroxystyryl)benzene-1,3-diol (10e). Compound **10e** was prepared according to the general procedure for cleavage of methyl ether from **9e**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 2/1) to give **10e** (90%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 9.97 (s, 1H), 9.24 (s, 2H), 7.79 (s, 2H), 7.03 (d, *J*=16.3 Hz, 1H), 6.91 (d, *J*=16.3 Hz, 1H), 6.41 (d, *J*=2.1 Hz, 2H), 6.15 (dd, *J*=2.1, 2.1 Hz, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 158.38, 149.72, 138.47, 132.03, 129.90, 129.05, 124.81, 112.24, 104.62, 102.33; ESI-MS: m/z (MH^+): 384.9069 (calc'd), 384.9074 (found).

(*E*)-2,6-dibromo-4-(2-(difluoromethoxy)styryl)phenol (11a). Compound **11a** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-2-(difluoromethoxy)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **11a** (95%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.60-7.63 (m, 3H), 7.21-7.29 (m, 3H), 7.14 (d, *J*=8.0 Hz, 1H), 6.92 (d, *J*=16.4 Hz, 1H), 6.54 (t,

J=73.8 Hz, 1H), 5.91 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 148.92, 148.64, 132.47, 130.08, 129.03, 128.98, 127.71, 126.68, 125.76, 122.41, 119.66, 118.40, 116.33, 114.27, 110.19; ESI-MS: m/z (MH^+): 418.9088 (calc'd), 418.9069 (found).

(*E*)-2,6-dibromo-4-[3-(difluoromethoxy)styryl]phenol (11b). Compound **11b** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3-(difluoromethoxy)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **11b** (88%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.16 (s, 1H), 7.85 (s, 2H), 7.72 (d, *J*=7.9 Hz, 2H), 7.15 (dd, *J*=8.0, 8.0 Hz, 1H), 7.04 (d, *J*=16.6 Hz, 1H), 6.75 (d, *J*=16.6 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 150.62, 137.51, 133.46, 132.30, 130.61, 130.24, 130.09, 126.78, 123.48, 112.21; ESI-MS: m/z ($[M-H]^-$): 506.7236 (calc'd), 506.7237 (found).

(*E*)-2,6-dibromo-4-[4-(difluoromethoxy)styryl]phenol (11c). Compound **11c** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-4-(difluoromethoxy)benzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **11c** (92%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.58 (s, 2H), 7.45 (d, *J*=8.6 Hz, 2H), 7.11 (d, *J*=8.6 Hz, 2H), 6.92 (d, *J*=16.3 Hz, 1H), 6.82 (d, *J*=16.3 Hz, 1H), 6.59 (t, *J*=73.8 Hz, 1H), 5.89 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 150.73, 148.74, 134.03, 132.38, 129.83, 127.90, 127.79, 125.61, 119.81, 117.86, 115.80, 113.73, 110.20; ESI-MS: m/z ($[M-H]^-$): 416.8943 (calc'd), 416.8944 (found).

(*E*)-2,6-dibromo-4-(2-nitrostyryl)phenol (12a). Compound **12a** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-2-nitrobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc =

8/1) to give **12a** (77%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.98 (dd, *J*=1.3, 8.2 Hz, 1H), 7.69 (dd, *J*=1.1, 7.9 Hz, 1H), 7.62-7.59 (m, 3H), 7.46 (d, *J*=16.0 Hz, 1H), 7.41-7.44 (m, 1H), 6.86 (d, *J*=16.1 Hz, 1H), 6.00 (s, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 149.43, 147.92, 133.20, 132.44, 131.73, 130.44, 128.31, 128.12, 124.88, 124.17, 110.27; ESI-MS: m/z (MH^+): 397.9022 (calc'd), 397.9012 (found).

(*E*)-2,6-dibromo-4-(3-nitrostyryl)phenol (12b). Compound **12b** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-3-nitrobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 5/1) to give **12b** (70%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.15 (s, 1H), 8.39 (dd, *J*=1.9, 1.9 Hz, 1H), 8.08-8.11 (m, 1H), 7.99 (d, *J*=7.9 Hz, 1H), 7.87 (s, 2H), 7.67 (dd, *J*=7.9, 7.9 Hz, 1H), 7.41 (d, *J*=16.5 Hz, 1H), 7.37 (d, *J*=16.5 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 150.44, 148.23, 138.79, 132.33, 131.26, 130.39, 130.09, 128.27, 126.18, 121.85, 120.52, 112.21; ESI-MS: m/z ($[M-H]^-$): 395.8876 (calc'd), 395.8876 (found).

(*E*)-2,6-dibromo-4-(4-nitrostyryl)phenol (12c). Compound **12c** was prepared according to the general procedure for Horner-Wittig reaction from 1-(bromomethyl)-4-nitrobenzene and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 5/1) to give **12c** (47%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.22 (s, 1H), 8.23 (d, *J*=8.8 Hz, 2H), 7.89 (s, 2H), 7.79 (d, *J*=8.8 Hz, 2H), 7.40 (s, 2H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 150.78, 146.06, 143.77, 131.09, 130.66, 130.18, 127.05, 126.28, 123.96, 112.21; ESI-MS: m/z (MH^+): 397.9022 (calc'd), 397.9017 (found).

(*E*)-2,6-dibromo-4-(3,5-dinitrostyryl)phenol (12e). Methyl protected **12e** was prepared according to the general procedure for Horner-Wittig reaction from **33** and 3,5-dinitrobenzaldehyde. The purification was carried out on RP-HPLC and lyophilized to give methyl protected **12e** (34%). ^{1}H-

NMR (500MHz, $CDCl_3$) δ 8.92 (dd, *J*=2.0, 2.0 Hz, 1H), 8.63 (d, *J*=2.0 Hz, 1H), 7.72 (s, 2H), 7.20 (d, *J*=16.3 Hz, 1H), 7.12 (d, *J*=16.3 Hz, 1H), 3.93 (s, 3H). Compound **12e** was prepared according to the general procedure for cleavage of methyl ether from methyl protected **12e**. The purification was carried out by RP-HPLC, which after lyophilization afforded **12e** (89%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.29 (s, 1H), 8.77 (d, *J*=2.0Hz, 2H), 8.66 (dd, *J*=2.0, 2.0 Hz, 1H), 7.90 (s, 2H), 7.62 (d, *J*=16.5 Hz, 1H), 7.54 (d, *J*=16.5 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 151.01, 148.48, 140.68, 130.78, 130.70, 125.79, 124.50, 116.36, 112.21; ESI-MS: m/z ($[M-H]^-$): 440.8727 (calc'd), 440.8725 (found).

(*E*)-4-(3-aminostyryl)-2,6-dibromophenol (13b). Compound **13b** was prepared according to the general procedure for reduction of nitro group from **12b**. The residue was recrystallized (Hexanes/EtOAc) to give **13b** (82%)**.** ^{1}H-NMR (500MHz, DMSO-d_6) δ 7.78 (s, 2H), 7.06 (d, *J*=16.4 Hz, 1H), 7.01 (dd, *J*=7.6, 7.6 Hz, 1H), 6.93 (d, *J*=16.4 Hz, 1H), 6.71-6.73 (m, 2H), 6.47-6.49 (m, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 149.65, 148.68, 137.18, 132.14, 129.76, 129.39, 128.96, 124.27, 114.38, 113.70, 112.25, 111.64; ESI-MS: m/z (MH^+): 367.9280(calc'd), 367.9280 (found).

(*E*)-4-(4-aminostyryl)-2,6-dibromophenol (13c). Compound **13c** was prepared according to the general procedure for reduction of nitro group from **12c**. The residue was recrystallized (Hexanes/EtOAc) to give **13c** (84%)**.** ^{1}H-NMR (500MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.68 (s, 2H), 7.23 (d, *J*=8.5 Hz, 2H), 7.01 (d, *J*=16.3 Hz, 1H), 6.75 (d, *J*=16.3 Hz, 1H), 6.54 (d, *J*=8.5 Hz, 2H), 5.31 (s, 2H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 148.83, 148.74, 133.09, 129.28, 129.01, 127.54, 124.37, 119.60, 113.72, 112.35; ESI-MS: m/z (MH^+): 367.9280 (calc'd), 367.9274 (found).

(*E*)-methyl 2-(3,5-dibromo-4-hydroxystyryl)benzoate (14a). Compound **14a** was prepared according to the general procedure for Horner-Wittig reaction from methyl 2-(bromomethyl)benzoate[1] and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel

(Hexanes/EtOAc = 8/1) and HPLC to separate **14a** and (*E*)-ethyl 2-(3,5-dibromo-4-hydroxystyryl)-benzoate (by-product). ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.11 (s, 1H), 7.83 (d, *J*=7.8 Hz, 1H), 7.76-7.78 (m, 3H), 7.71 (d, *J*=16.3 Hz, 1H), 7.60 (dd, *J*=7.6, 7.6 Hz, 1H), 7.40 (dd, *J*=7.6, 7.6 Hz, 1H), 7.05 (d, *J*=16.3 Hz, 1H), 3.87 (s, 3H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 167.10, 150.23, 137.64, 132.17, 131.86, 130.13, 130.03, 128.49, 128.03, 127.46, 126.65, 112.25, 52.16; ESI-MS: m/z (MH^+): 410.9226 (calc'd), 410.9242 (found).

(*E*)-methyl 3-(3,5-dibromo-4-hydroxystyryl)benzoate (14b). Compound **14b** was prepared according to the general procedure for Horner-Wittig reaction from methyl 3-(bromomethyl)benzoate and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 8/1) and HPLC to separate **14b** and (*E*)-ethyl 3-(3,5-dibromo-4-hydroxystyryl)-benzoate (by-product). ^{1}H-NMR (500MHz, $CDCl_3$) δ 8.16 (dd, *J*=1.5, 1.5 Hz, 1H), 7.92-7.94 (m, 1H), 7.61-7.64 (m, 3H), 7.43 (dd, *J*=7.7, 7.7 Hz, 1H), 6.98 (s, 2H), 3.94 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 166.87, 148.91, 136.99, 132.23, 130.80, 130.70, 129.98, 128.83, 128.12, 127.44, 126.57, 110.24, 52.23; ESI-MS: m/z (MH^+): 410.9226 (calc'd), 410.9216 (found).

(*E*)-methyl 4-(3,5-dibromo-4-hydroxystyryl)benzoate (14c). Compound **14c** was prepared according to the general procedure for Horner-Wittig reaction from methyl 4-(bromomethyl)benzoate and 3,5-dibromo-4-hydroxybenzaldehyde. The residue was subjected to chromatography over silica gel (Hexane/EtOAc = 8/1) and preparative HPLC to separate **14c** and (*E*)-ethyl 4-(3,5-dibromo-4-hydroxystyryl)- benzoate (by-product). ^{1}H-NMR (500MHz, $CDCl_3$) δ 8.03 (d, *J*=8.4 Hz, 2H), 7.63 (s, 2H), 7.52 (d, *J*=8.4 Hz, 2H), 6.99 (s, 2H), 5.94 (s, 1H), 3.93 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 166.75, 149.13, 141.08, 132.07, 130.15, 130.09, 129.27, 128.12, 127.83, 126.32, 110.28, 52.12; ESI-MS: m/z (MH^+): 410.9226 (calc'd), 410.9209 (found).

(*E*)-3-(3,5-dibromo-4-hydroxystyryl)benzoic acid (15b). Compound **15b** was prepared according to the general procedure for hydrolysis of methyl ester from **14b**. The residue was recrystallized (Hexanes/EtOAc) to give **15b** (84%)**.** ^{1}H-NMR (500MHz, DMSO-d_6) δ 13.01 (s, 1H), 10.06 (s, 1H), 8.13 (s, 1H), 7.87 (s, 2H), 7.79-7.83 (m, 2H), 7.50 (dd, *J*=7.7, 7.7 Hz, 1H), 7.33 (d, *J*=16.5 Hz, 1H), 7.23 (d, *J*=16.5 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 167.10, 150.06, 137.21, 131.72, 131.19, 130.35, 130.16, 128.89, 128.21, 127.52, 127.07, 126.44, 112.22; ESI-MS: m/z (MH^+): 396.9069 (calc'd), 396.9068 (found).

(*E*)-4-(3,5-dibromo-4-hydroxystyryl)benzoic acid (15c). Compound **15c** was prepared according to the general procedure for hydrolysis of methyl ester from **14c**. The residue was recrystallized (Hexanes/EtOAc) to give **16c** (80%)**.** ^{1}H-NMR (500MHz, DMSO-d_6) δ 10.12 (s, 1H), 7.93 (d, *J*=8.4 Hz, 2H), 7.86 (s, 2H), 7.66 (d, *J*=8.4 Hz, 2H), 7.32 (d, *J*=16.5 Hz, 1H), 7.27 (d, *J*=16.5 Hz, 1H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 166.93, 150.35, 141.18, 131.49, 130.32, 129.65, 129.36, 127.93, 127.37, 126.27, 112.24; ESI-MS: m/z (MH^+): 396.9069 (calc'd), 396.9068 (found).

Representative Procedure for Reduction of Olefin (16a). To a solution of **2a** (0.2 g, 0.538 mmol) and 10% Pd/C (69 mg, 0.065 mmol) in EtOAc (8 mL) was added $ZnBr_2$ (0.13 g, 0.591 mmol). The mixture was stirred for 1 h under H_2 gas. The solution was filtered and concentrated. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.5) to give **16a** (754%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.24 (s, 2H), 7.17-7.21 (m, 1H), 7.00-7.10 (m, 3H), 5.74 (s, 1H), 2.87-2.90 (m, 2H), 2.78-2.81 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 162.06, 160.12, 147.58, 136.10, 131.89, 130.66, 130.62, 128.04, 127.97, 127.67, 127.54, 123.98, 115.40, 115.23, 109.54, 35.00, 31.14; ESI-MS: m/z ($[M-H]^-$): 370.9088 (calc'd), 370.9084 (found).

2,6-dibromo-4-(3-fluorophenethyl)phenol (16b). Compound **16b** was prepared according to the general procedure for reduction of olefin from **2b**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.5) to give **16b** (74%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.22-7.25 (m, 3H), 6.88-6.92 (m, 2H), 6.84-6.86 (m, 1H), 5.75 (s, 1H), 2.84-2.88 (m, 2H), 2.78-2.82 (m ,2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 163.88, 161.92, 147.64, 143.30, 143.24, 135.84, 131.86, 129.89, 129.82, 124.09, 115.32, 115.15, 113.19, 113.02, 109.59, 37.35, 36.07; ESI-MS: m/z ($[M-H]^-$): 370.9088 (calc'd), 370.9084 (found).

2,6-dibromo-4-(4-fluorophenethyl)phenol (16c). Compound **16c** was prepared according to the general procedure for reduction of olefin from **2c**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **16c** (65%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.21 (s, 2H), 7.06-7.08 (m, 2H), 6.95-6.98 (m, 2H), 5.74 (s, 1H), 2.82-2.85 (m, 2H), 2.76-2.79 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 162.40, 160.46, 147.58, 136.34, 136.00, 131.89, 129.82, 129.75, 115.27, 115.11, 109.55, 36.83, 36.51; ESI-MS: m/z ($[M-H]^-$): 370.9088 (calc'd), 370.9081 (found).

2,6-dibromo-4-(2,6-difluorophenethyl)phenol (16d). Compound **16d** was prepared according to the general procedure for reduction of olefin from **2d**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.2) to give **16d** (35%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.26 (s, 2H), 7.13-7.19 (m, 1H), 6.82-6.7 (m, 2H), 5.75 (s, 1H), 2.89-2.92 (m,2H), 2.75-2.78 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 162.43, 162.36, 160.47, 160.40, 147.67, 135.80, 131.87, 127.88, 127.80, 127.72, 116.43, 116.27, 116.11, 111.17, 111.12, 111.00, 110.95, 109.53, 34.15, 24.27; ESI-MS: m/z ($[M-H]^-$): 388.8994 (calc'd), 388.8986 (found).

2,6-dibromo-4-(3,5-difluorophenethyl)phenol (16e). Compound **16e** was prepared according to the general procedure for reduction of olefin from **2e**. The residue was subjected to chromatography

over silica gel (Hexanes/EtOAc = 10/0.5) to give **16e** (64%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.23 (s, 2H), 6.64-6.67 (m, 3H), 5.76 (s, 1H), 2.83-2.86 (m, 2H), 2.77-2.81 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 164.05, 163.95, 162.08, 161.98, 147.78, 144.64, 144.57, 135.34, 131.81, 111.28, 111.24, 111.13, 111.08, 109.67, 101.93, 101.73, 101.53, 37.30, 35.68; ESI-MS: m/z ($[M-H]^-$): 388.8994 (calc'd), 388.8988 (found).

2,6-dibromo-4-(2-chlorophenethyl)phenol (17a). Compound **17a** was prepared according to the general procedure for reduction of olefin from **3a**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.5) to give **17a** (77%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.35-7.37 (m, 1H), 7.26 (s, 2H), 7.16-7.18 (m, 2H), 7.10-7.12 (m, 1H), 5,75 (s, 1H), 2.95-2.98 (m, 2H), 2.78-2.82 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.60, 138.32, 136.09, 133.86, 131.92, 130.52, 129.60, 127.77, 126.82, 109.55, 35.71, 34.55; ESI-MS: m/z ($[M-H]^-$): 386.8792 (calc'd), 386.8799 (found).

2,6-dibromo-4-(3-chlorophenethyl)phenol (17b). Compound **17b** was prepared according to the general procedure for reduction of olefin from **3b**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.5) to give **17b** (77%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.23 (s, 2H), 7.19-7.21 (m, 2H), 7.15 (s, 1H), 6.99-7.01 (m, 1H), 5.75 (s, 1H), 2.82-2.86 (m, 2H), 2.77-2.81 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.67, 142.76, 135.79, 134.23, 131.87, 129.68, 128.54, 126.63, 126.43, 109.61, 37.33, 36.13; ESI-MS: m/z ($[M-H]^-$): 386.8792 (calc'd), 386.8786 (found).

2,6-dibromo-4-(4-chlorophenethyl)phenol (17c). Compound **17c** was prepared according to the general procedure for reduction of olefin from **3c**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.5) to give **17c** (70%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.24 (d, *J*=8.3 Hz, 2H), 7.21 (s, 2H), 7.05 (d, *J*=8.3 Hz, 2H), 5.74 (s, 1H), 2.81-2.85 (m, 2H), 2.76-2.79 (m, 2H); ^{13}C-NMR

(125MHz, $CDCl_3$) δ 147.61, 139.15, 135.85, 131.95, 131.86, 129.74, 128.53, 109.57, 36.94, 36.23; ESI-MS: m/z ($[M-H]^-$): 386.8792 (calc'd), 386.8785 (found).

2,6-dibromo-4-(2,6-dichlorophenethyl)phenol (17d). Compound **17d** was prepared according to the general procedure for reduction of olefin from **3d**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **17d** (37%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.33 (s, 2H), 7.30 (d, *J*=8.0 Hz, 2H), 7.10 (dd, *J*=8.0, 8.0 Hz, 1H), 5.77 (s, 1H), 3.13-3.16 (m, 2H), 2.73-2.76 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.73, 136.66, 135.94, 135.31, 131.90, 128.24, 127.98, 109.61, 33.39, 32.77; ESI-MS: m/z ($[M-H]^-$): 420.8403 (calc'd), 420.8409 (found).

2,6-dibromo-4-(2-methylphenethyl)phenol (18a). Compound **18a** was prepared according to the general procedure for reduction of olefin from **6a**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **18a** (62%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.24 (s, 2H), 7.12-7.15 (m, 3H), 7.06-7.08 (m, 1H), 5.74 (s, 1H), 2.82-2.86 (m, 2H), 2.73-2.76 (m, 2H), 2.29 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.53, 138.99, 136.54, 135.77, 131.83, 130.29, 128.83, 126.35, 126.06, 109.54, 35.23, 35.16, 19.24; ESI-MS: m/z ($[M-H]^-$): 366.9339 (calc'd), 366.9340 (found).

2,6-dibromo-4-(3-methylphenethyl)phenol (18b). Compound **18b** was prepared according to the general procedure for reduction of olefin from **6b**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **18b** (56%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.24 (s, 2H), 7.18 (dd, *J*=7.5, 7.5 Hz, 1H), 7.03 (d, *J*=7.5 Hz, 1H), 6.94-6.97 (m, 2H), 5.73 (s, 1H), 2.77-2.83 (m, 4H), 2.33 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.48, 140.78, 138.03, 136.49, 131.89, 129.24, 128.35, 126.92, 125.38, 109.51, 99.58, 37.68, 36.52, 21.39; ESI-MS: m/z (MNa^+): 390.9304 (calc'd), 390.9305 (found).

2,6-dibromo-4-(4-methylphenethyl)phenol (18c). Compound **18c** was prepared according to the general procedure for reduction of olefin from **6c**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.5) to give **18c** (71%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.24 (s, 2H), 7.10 (d, *J*= 8.1 Hz, 2H), 7.03 (d, *J*=8.1 Hz, 2H), 5.73 (s, 1H), 2.77-2.83 (m, 4H), 2.32 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.46, 137.74, 136.49, 135.66, 131.87, 129.11, 128.26, 109.51, 37.23, 36.56, 20.99; ESI-MS: m/z ($[M-H]^-$): 366.9339 (calc'd), 366.9342 (found).

2,6-dibromo-4-(2,6-dimethylphenethyl)phenol (18d). Compound **18d** was prepared according to the general procedure for reduction of olefin from **6d**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **18d** (33%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.26 (s, 2H), 7.02-7.04 (m, 3H), 5.75 (s, 1H), 2.84-2.88 (m, 2H), 2.62-2.66 (m, 2H), 2.32 (s, 6H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.60, 137.57, 136.76, 135.98, 131.68, 128.28, 126.10, 109.63, 33.80, 31.75, 19.78; ESI-MS: m/z ($[M-H]^-$): 380.9495 (calc'd), 380.9481 (found).

2,6-dibromo-4-(3,5-dimethylphenethyl)phenol (18e). Compound **18e** was prepared according to the general procedure for reduction of olefin from **6e**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **18e** (64%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.25 (s, 2H), 6.86 (s, 1H), 6.78 (s, 2H), 5.73 (s, 1H), 2.77 (s, 1H), 2.29 (s, 6H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.46, 140.80, 137.95, 136.62, 131.89, 127.80, 126.23, 109.49, 37.66, 36.60, 21.26; ESI-MS: m/z (MH^+): 404.9460 (calc'd), 404.9466 (found).

2,6-dibromo-4-[2-(trifluoromethyl)phenethyl]phenol (19a). Compound **19a** was prepared according to the general procedure for reduction of olefin from **7a**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.3) to give **19a** (68%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.48 (d, *J*=7.6 Hz, 1H), 7.39-7.42 (m, 2H), 7.30 (d, *J*=7.6 Hz, 1H), 7.23 (s, 2H), 5.76 (s, 1H),

2.91-2.94 (m, 3H), 2.81-2.84 (m, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.73, 141.61, 135.60, 131.88, 131.83, 130.93, 130.67, 128.87, 125.21, 125.15, 125.12, 125.09, 123.18, 123.14, 123.05, 109.64, 37.48, 36.16; ESI-MS: m/z ($[M-H]^-$): 420.9056 (calc'd), 420.9059 (found).

2,6-dibromo-4-[3-(trifluoromethyl)phenethyl]phenol (19b). Compound **19b** was prepared according to the general procedure for reduction of olefin from **7b**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.5) to give **19b** (70%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.48 (d, *J*=7.8 Hz, 1H), 7.38-7.41 (m, 2H), 7.30 (d, *J*=7.8 Hz, 1H), 7.23 (s, 2H), 5.76 (s, 1H), 2.90-2.94 (m, 2H), 2.80-2.84 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.73, 141.61, 135.60, 131.88, 131.83, 130.92, 130.67, 128.87, 125.21, 125.14, 125.11, 123.14, 109.63, 37.48, 36.16; ESI-MS: m/z (MH^+): 420.9056 (calc'd), 420.9061 (found).

2,6-dibromo-4-(2-methoxyphenethyl)phenol (20a). Compound **20a** was prepared according to the general procedure for reduction of olefin from **9a**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **20a** (63%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.25 (s, 2H), 7.20 (dd, *J*=7.8, 7.8 Hz, 1H), 7.05 (d, *J*=7.4 Hz, 1H), 6.85-6.88 (m, 2H), 5.71 (s, 1H), 3.82 (s, 3H), 2.83-2.86 (m, 2H), 2.75-2.78 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 157.37, 147.29, 137.08, 131.92, 129.88, 129.25, 127.47, 120.40, 110.26, 109.37, 55.21, 34.79, 32.30; ESI-MS: m/z (MNa^+): 406.9253 (calc'd), 406.9245 (found).

2,6-dibromo-4-(3-methoxyphenethyl)phenol (20b). Compound **20b** was prepared according to the general procedure for reduction of olefin from **9b**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **20b** (31%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.24 (s, 2H), 7.21 (dd, *J*=7.9, 7.9 Hz, 1H), 6.73-6.77 (m, 2H), 6.69 (s, 1H), 5.74 (s, 1H), 3.79 (s, 3H), 2.7-2.85 (m,

4H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 159.70, 147.53, 142.43, 136.33, 131.90, 129.43, 120.81, 114.24, 111.51, 109.53, 55.18, 37.73, 36.32; ESI-MS: m/z (MH^+): 384.9433 (calc'd), 384.9433 (found).

2,6-dibromo-4-(4-methoxyphenethyl)phenol (20c). Compound **20c** was prepared according to the general procedure for reduction of olefin from **9c**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **20c** (45%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.22 (s, 2H), 7.04 (d, *J*=8.5 Hz, 2H), 6.83 (d, *J*=8.5 Hz, 2H), 5.73 (s, 1H), 3.79 (s, 3H), 2.76-2.81 (m, 4H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 158.03, 147.46, 136.44, 132.89, 131.92, 129.33, 113.87, 109.51, 55.28, 36.79, 36.71; ESI-MS: m/z (MH^+): 384.9433 (calc'd), 384. 9389(found).

2,6-dibromo-4-(2,6-dimethoxyphenethyl)phenol (20d). Compound **20d** was prepared according to the general procedure for reduction of olefin from **9d**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **20d** (53%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.28 (s, 2H), 7.14 (dd, *J*=8.3, 8.3 Hz, 1H), 6.53 (d, *J*=8.3 Hz, 2H), 5.69 (s, 1H), 3.78 (s, 6H), 2.87-2.90 (m, 2H), 2.64-2.67 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 158.19, 147.05, 137.74, 131.98, 127.11, 117.40, 109.13, 103.56, 55.62, 33.82, 24.68; ESI-MS: m/z (MH^+): 414.9539 (calc'd), 414.9540 (found).

2,6-dibromo-4-(3,5-dimethoxyphenethyl)phenol (20e). Compound **20e** was prepared according to the general procedure for reduction of olefin from **9e**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.5) to give **20e** (66%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.25 (s, 2H), 6.33 (dd, *J*=2.2, 2.2 Hz, 1H), 6.30 (d, *J*=2.2 Hz, 2H), 5.75 (s, 1H), 3.77 (s, 6H), 2.80 (s, 4H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 160.82, 147.52, 143.17, 136.28, 131.89, 109.51, 106.52, 98.16, 55.27, 37.95, 36.19; ESI-MS: m/z ($[M-H]^-$): 412.9393 (calc'd), 412.9395 (found).

2,6-dibromo-4-[2-(difluoromethoxy)phenethyl]phenol (21a). Compound **21a** was prepared according to the general procedure for reduction of olefin from **11a**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.3) to give **21a** (65%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.21-7.25 (m, 3H), 7.11-7.15 (m, 2H), 7.07-7.09 (m, 1H), 6.49 (t, *J*=74.1 Hz, 1H), 5.74 (s, 1H), 2.88-2.91 (m, 2H), 2.76-2.79 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 149.62, 147.57, 136.16, 132.18, 131.89, 130.80, 127.77, 125.39, 118.45, 118.39, 116.33, 114.28, 109.53, 34.99, 32.09; ESI-MS: m/z ($[M-H]^-$): 418.9099 (calc'd), 418.9095 (found).

2,6-dibromo-4-[3-(difluoromethoxy)phenethyl]phenol (21b). Compound **21b** was prepared according to the general procedure for reduction of olefin from **11b**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.5) to give **21b** (67%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.28 (d, J=7.9 Hz, 1H), 7.22 (s, 2H), 6.96-6.99 (m, 2H), 6.89 (s, 1H), 6.48 (t, *J*=74.1 Hz, 1H), 5.75 (s, 1H), 2.85-2.88 (m, 2H), 2.78-2.82 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 151.32, 147.66, 143.00, 135.78, 131.88, 129.78, 125.51, 119.62, 118.01, 117.23, 115.95, 113.88, 109.58, 37.41, 36.10; ESI-MS: m/z ($[M-H]^-$): 418.9099 (calc'd), 418.9097 (found).

2,6-dibromo-4-[4-(difluoromethoxy)phenethyl]phenol (21c). Compound **21c** was prepared according to the general procedure for reduction of olefin from **11c**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 10/0.5) to give **21c** (71%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.21 (s, 2H), 7.11 (d, *J*=8.5 Hz, 2H), 7.04 (d, *J*=8.5 Hz, 2H), 6.48 (t, *J*=74.1 Hz, 1H), 5.75 (s, 1H), 2.83-2.87 (m, 2H), 2.77-2.80 (m, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 149.57, 147.61, 138.00, 135.90, 131.88, 129.72, 119.67, 118.07, 116.01, 113.94, 109.57, 36.87, 36.35; ESI-MS: m/z ($[M-H]^-$): 418.9099 (calc'd), 418.9102 (found).

2,6-dibromo-4-(2-nitrophenethyl)phenol (22a). Compound **22a** was prepared according to the general procedure for reduction of olefin from **12a**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 7/1) to give **22a** (36%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.97 (d, *J*=8.2 Hz, 1H), 7.52 (dd, *J*=7.5, 7.5 Hz, 1H), 7.39 (dd, *J*=7.5, 7.5 Hz, 1H), 7.29 (s, 2H), 7.24-7.26 (m, 1H), 5.77 (s, 1H), 3.10-3.14 (m, 2H), 2.84-2.87 (m,2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 149.19, 147.80, 135.83, 135.57, 133.09, 132.19, 131.96, 127.54, 124.98, 109.68, 35.59, 35.51; ESI-MS: m/z (MNa^+): 421.8998 (calc'd), 421.8999 (found).

4-(2-aminophenethyl)-2,6-dibromophenol (23a). Compound **23a** was prepared according to the general procedure for reduction of nitro group from **22a**. The residue was recrystallized (Hexanes/EtOAc) to give **23a** (98%)**.** ^{1}H-NMR (500MHz, DMSO-d_6) δ 9.61 (s, 1H), 7.48 (s, 2H), 6.87-6.91 (m 2H), 6.61 (d, *J*=7.7 Hz, 1H), 6.46 (dd, *J*=7.3, 7.3 Hz, 1H), 4.91 (s, 2H), 2.68-2.71 (m, 2H), 2.62-2.66 (m ,2H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 148.39, 145.97, 136.62, 132.04, 129.08, 126.53, 124.13, 115.96, 114.49, 111.64, 32.71, 32.61; ESI-MS: m/z (MH^+): 369.9437 (calc'd), 369.9439 (found).

4-(3-aminophenethyl)-2,6-dibromophenol (23b). Compound **23b** was prepared according to the general procedure for reduction of olefin from **12b**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **23b** (29%)**.** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.25 (s, 2H), 7.07 (dd, *J*=7.7, 7.7 Hz, 1H), 6.53-6.56 (m, 2H), 6.49 (s, 1H), 2.75-2.78 (m, 4H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 147.46, 146.44, 142.09, 136.51, 131.86, 129.36, 118.73, 115.18, 113.07, 109.51, 37.68, 36.30; ESI-MS: m/z (MH^+): 369.9437 (calc'd), 369.9432 (found).

4-(4-aminophenethyl)-2,6-dibromophenol (23c). Compound **23c** was prepared according to the general procedure for reduction of olefin from **12c**. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9.5/0.5) to give **23c** (40%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 7.39 (s, 2H),

7.21 (d, *J*=8.3 Hz, 2H), 7.07 (d, *J*=8.3 Hz, 2H), 2.74-2.83 (m, 4H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 148.37, 146.40, 136.44, 131.91, 128.63, 127.92, 113.77, 111.65, 36.09, 35.68; ESI-MS: m/z (MH^+): 369.9437 (calc'd), 369.9441 (found).

Representative Procedure for O-Alkylation (26a). To a solution of (*E*)-2,6-dibromo-4-styrylphenol **25** (1.5 g, 4.24 mmol) and K_2CO_3 (1.41 g, 10.17 mmol) in 10 mL of DMF was added bromoacetamide (0.716 g, 5.08 mmol). The reaction mixture was heated to 60 °C. After 2 h, the mixture was diluted with EtOAc. The organic layer was washed with H_2O, 5% citric acid, and brine. The solution was washed with saturated brine and dried with Na_2SO_4. The solution was filtered and concentrated. The solid was washed with cold Hexanes and EtOAc mixture (5/1) to get pure **26a** (quantitative). ^{1}H-NMR (500MHz, DMSO-d_6) δ 7.94 (s, 2H), 7.58 (d, *J*=7.4 Hz, 3H), 7.53 (s, 1H), 7.36-7.41 (m, 3H), 7.30 (dd, *J*=7.3, 7.3 Hz, 1H), 7.19 (d, *J*=16.5 Hz, 1H), 4.33 (s, 2H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 168.62, 150.21, 136.91, 136.39, 130.85, 130.29, 128.65, 128.06, 126.59, 124.78, 117.67, 70.59; ESI-MS: m/z (MH^+): 409.9386 (calc'd), 409.9380 (found).

(*E*)-2-(2,6-dibromo-4-(3-methoxystyryl)phenoxy)acetamide (34b); (85%), ^{1}H-NMR (500MHz, DMSO-d_6) δ 7.93 (s, 2H), 7.60 (s, 1H), 7.52 (s, 1H), 7.35 (d, *J*=16.4 Hz, 1H), 7.30 (dd, *J*=8.1, 8.1 Hz, 1H), 7.21 (d, *J*=16.4 Hz, 1H), 7.15-7.17 (m, 2H), 6.86-6.88 (m, 1H), 4.33 (s, 2H), 3.79 (s, 3H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 168.62, 159.45, 150.23, 137.84, 136.87, 130.77, 130.30, 129.64, 125.08, 119.19, 117.67, 113.89, 111.64, 70.59, 54.96; ESI-MS: m/z (MH^+): 439.9491 (calc'd), 439.9494 (found).

(*E*)-2-(2,6-dibromo-4-(2,6-dimethoxystyryl)phenoxy)acetamide (34c); (95%), ^{1}H-NMR (500MHz, DMSO-d_6) δ 7.79 (s, 2H), 7.58 (s, 1H), 7.52 (s, 1H), 7.42 (d, *J*=16.6 Hz, 1H), 7.53 (d, *J*=16.6 Hz, 1H), 7.24 (dd, *J*=8.4, 8.4 Hz, 1H), 6.70 (d, *J*=8.4 Hz, 2H), 4.32 (s, 2H), 3.85 (s, 6H); ^{13}C-NMR (125MHz,

DMSO-d_6) δ 168.63, 158.23, 149.86, 138.45, 129.70, 129.25, 127.89, 121.95, 117.66, 112.80, 104.05, 70.60, 55.71; ESI-MS: m/z (MH^+): 469.9597 (calc'd), 469.9604 (found).

(*E*)-2-(4-(3-aminostyryl)-2,6-dibromophenoxy)acetamide (34d); (95%), ^{1}H-NMR (500MHz, DMSO-d_6) δ 8.42 (s, 1H), 8.12-8.14 (m, 1H), 7.99-8.02 (m, 3H), 7.69 (dd, *J*=7.9, 7.9 Hz, 1H), 7.53-7.59 (m, 3H), 7.43 (d, *J*=16.5 Hz, 1H), 4.34 (s, 2H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 168.57, 150.74, 148.21, 138.35, 136.24, 132.62, 130.71, 130.16, 128.58, 127.65, 122.33, 120.81, 117.73, 70.59; ESI-MS: m/z (MH^+): 454.9237 (calc'd), 454.9248 (found).

(*E*)-2-(4-(4-aminostyryl)-2,6-dibromophenoxy)acetamide (34e); (96%), ^{1}H-NMR (500MHz, DMSO-d_6) δ 8.24 (d, *J*=8.9 Hz, 2H), 8.00 (s, 2H), 7.60 (s, 1H), 7.51-7.54 (m, 2H), 7.44 (d, *J*=16.5 Hz, 1H), 4.34 (s, 2H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 168.57, 151.00, 146.40, 143.25, 136.07, 130.96, 129.46, 128.67, 127.41, 123.97, 117.79, 70.58; ESI-MS: m/z (MH^+): 454.9237 (calc'd), 454.9231 (found).

Representative Procedure for Smiles Rearrangment and Hydrolysis (27a and 24a). A mixture of **26a** (1.5 g, 3.65 mmol) and NaOH (0.75 g, 18.244 mmol) in 15 mL of DMF was stirred for 3 h at room temperature. The reaction mixture was diluted with EtOAc and washed with 5% citric acid and brine. After drying over Na_2SO_4, the solution was filtered and concentrated. The residue was recrystallized (Hexanes/EtOAc) to give **27a** (1.33 g, 89%). ^{1}H-NMR (500MHz, DMSO-d_6) δ 9.66 (s, 1H), 7.96 (s, 2H), 7.61 (d, *J*=7.3 Hz, 2H), 7.39-7.45 (m, 3H), 7.31 (dd, *J*=7.3, 7.3 Hz, 1H), 7.23 (d, *J*=16.5 Hz, 1H), 7.56 (s, 1H), 4.04 (s, 2H)); ^{13}C-NMR (125MHz, DMSO-d_6) δ 170.85, 139.09, 136.32, 134.26, 131.36, 129.38, 128.67, 128.19, 126.70, 124.88, 124.46, 61.39; ESI-MS: m/z (MH^+): 409.9386 (calc'd), 409.9386 (found). A mixture of **27a** (1.2 g, 2.92 mmol) in 9 mL of conc. HCl and 9 mL of 1,4-dioxane was refluxed for 3 h. The reaction mixture was diluted with EtOAc and neutralized by addition

of NaOH and washed with saturated $NaHCO_3$ and brine. After drying over Na_2SO_4, the solution was filtered and concentrated. The residue was subjected to chromatography over silica gel (Hexanes/EtOAc = 9/1) to give **24a** (0.92 g, 89%). ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.53 (s, 2H), 7.44 (d, *J*=7.5 Hz, 2H), 7.34 (dd, *J*=7.5, 7.5 Hz, 2H), 7.24 (m, 1H), 6.89 (d, *J*=16.3 Hz, 1H), 6.84 (d, *J*=16.3 Hz, 1H), 4.59 (s, 2H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 141.16, 137.03, 129.73, 129.57, 128.67, 127.54, 127.36, 126.30, 125.92, 108.94; ESI-MS: m/z (MH^+): 351.9331 (calc'd), 351.9333 (found).

(*E*)-2,6-dibromo-4-(3-methoxystyryl)aniline (24b); (94% in 2 steps), ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.55 (s, 2H), 7.24-7.27 (m, 1H), 7.05 (d, *J*=7.7 Hz, 1H), 6.98-6.99 (m, 1H), 6.88 (d, *J*=16.4 Hz, 1H), 6.85 (d, *J*=16.4 Hz, 1H), 6.79-6.82 (m, 1H), 4.61 (s, 2H), 3.84 (s, 3H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 159.86, 141.21, 138.49, 129.77, 129.63, 129.45, 127.24, 126.24, 119.02, 113.25, 111.53, 108.92, 55.21; ESI-MS: m/z (MH^+): 381.9437 (calc'd), 381.9431 (found).

(*E*)-2,6-dibromo-4-(2,6-dimethoxystyryl)aniline (24c); (60% in 2 steps), ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.56 (s, 2H), 7.36 (d, *J*=16.6 Hz, 1H), 7.24 (d, *J*=16.6 Hz, 1H), 7.15 (dd, *J*=8.3, 8.3 Hz, 1H), 6.58 (d, *J*=8.3 Hz, 2H), 4.54 (s, 2H), 3.89 (s, 6H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 158.52, 140.55, 131.74, 129.61, 128.02, 118.62, 114.50, 109.02, 103.96, 55.78; ESI-MS: m/z (MH^+): 411.9542 (calc'd), 411.9542 (found).

(*E*)-4-(3-aminostyryl)-2,6-dibromoaniline (24d); (97% in 2 steps), ^{1}H-NMR (500MHz, DMSO-d_6) δ 8.35 (dd, *J*=1.9, 1.9 Hz, 1H), 8.05-8.07 (m, 1H), 7.95-7.97 (m, 1H), 7.77 (s, 2H), 7.64 (dd, *J*=8.0, 8.0 Hz, 1H), 7.31 (d, *J*=16.5 Hz, 1H), 7.28 (d, *J*=16.5 Hz, 1H), 5.59 (s, 2H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 148.22, 142.60, 139.15, 132.05, 130.21, 130.00, 128.78, 127.34, 123.97, 121.39, 120.21, 107.73; ESI-MS: m/z (MH^+): 396.9182 (calc'd), 396.9185 (found).

(*E*)-4-(4-aminostyryl)-2,6-dibromoaniline (24e); (94% in 2 steps), ^{1}H-NMR (500MHz, DMSO-d_6) δ 8.21 (d, *J*=8.9 Hz, 2H), 7.76 (d, *J*=8.9 Hz, 2H), 7.35 (d, *J*=16.4 Hz, 1H), 7.28 (d, *J*=16.4 Hz, 1H), 5.67 (s, 2H); ^{13}C-NMR (125MHz, DMSO-d_6) δ 145.67, 144.22, 142.97, 130.81, 130.52, 127.13, 126.68, 124.02, 123.94, 107.69; ESI-MS: m/z (MH^+): 396.9182 (calc'd), 396.9180 (found).

1. Dvornikovs, V.; Smithrud, D. B., *J. Org. Chem.* **2002,** *67*, 2160-2167.