Supporting Information

Pt(IV)-Catalyzed Cyclization of Arene-Alkyne Substrates via Intramolecular Electrophilic Hydroarylation

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Systematic Screen: Lead Generation (HPLC analysis)

Reactions were conducted at 0.2 M with 5 mol% catalyst at room temperature in sealed vials unless otherwise noted. Reactions were conducted under argon only when air sensitive catalyst was used, otherwise reactions were carried out in the presence of air. After 12 hours, 30 μ L aliquots were taken from the reaction vessels and diluted to 1 ml with acetonitrile. 30 μ L of 0.1M 2,4-dihydroxyacetophenone was added as a internal standard. HPLC (HP 1100 series) analysis was carried out with a LiChrospher 100 RP-18e column using 45% acetonitrile and 65% water as an eluent: t_r = 2.1 (Std), t_r = 7.1 (**1**), t_r = 8.6 (**2a**).

Entry	Catalyst	Solvent	Yield 2a (%)	1 (%)
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1	GaCl ₃	toluene	3	103
2	AgBF ₄	CHCl ₃	0	96
3	AuCl ₃	toluene	6	82
4		CH ₃ CN	1	92
5	Pd ₂ (dba) ₃ /NaOAc ^a	HCO ₂ H	8	44
6	Pd(OAc) ₂ /NaOAc ^b	HCO ₂ H	18	25
7	Pd(CH ₃ CN) ₂ Cl ₂	CH ₂ Cl ₂	0	0
8		CH ₃ CN	0	56
9	Pd(OAc) ₂	CH ₂ Cl ₂	0	65
10		dioxane	0	53
11		CF ₃ CH ₂ OH	0	12
12		AcOH	0	67
13		TFA	0	trace
14	PtCl ₂	toluene	3	74
15		CH ₂ Cl ₂	trace	90
16		acetone	trace	90
17		CF ₃ CH ₂ OH	0	86
18		AcOH	3	85
19		TFA	0	0
20		THF	0	98
21		Dioxane	1	95
22	PtCl ₄	toluene	19	30
23		CH ₂ Cl ₂	32	7
24		acetone	10	30
25		CF ₃ CH ₂ OH	12	0
26		AcOH	18	17
27		TFA	0	0
28		THF	16	36
29		Dioxane	21	32
30	Na ₂ PdCl ₄	ClCH ₂ CH ₂ Cl	0	65
31		toluene	0	65
32		THF	0	57
33	Na ₂ PtCl ₆ • 6H ₂ O	ClCH ₂ CH ₂ Cl	0	103
34		toluene	0	83
35		THF	0	102
36	<i>trans</i> -Pt(NH ₃) ₂ Cl ₄	ClCH ₂ CH ₂ Cl	0	101
37		toluene	0	98

38		THF	0	108
39	Na ₂ PtCl ₄	ClCH ₂ CH ₂ Cl	1	97
40		toluene	0	103
41		THF	0	85
42	Rh ₂ (OAc) ₄	ClCH ₂ CH ₂ Cl	0	106
43		toluene	0	100
44		THF	0	112
45	RhCl ₃	ClCH ₂ CH ₂ Cl	0	110
46		toluene	0	112
47		THF	0	109
48	RuCl ₃ hydrate	ClCH ₂ CH ₂ Cl	0	107
49		toluene	0	101
50		THF	0	107
51	IrCl ₄ hydrate	ClCH ₂ CH ₂ Cl	0	109
52		toluene	0	103
53		THF	0	102
54	Cu(OTf) ₂	ClCH ₂ CH ₂ Cl	0	109
55		toluene	0	109
56		THF	0	101
57	NiCl ₂ •6H ₂ O	ClCH ₂ CH ₂ Cl	0	90
58		toluene	0	96
59		THF	0	81
60	Co(OAc) ₂ •4H ₂ O	ClCH ₂ CH ₂ Cl	0	51
61		toluene	0	107
62		THF	0	108
63	CoCl ₂ •6H ₂ O	ClCH ₂ CH ₂ Cl	0	101
64		toluene	0	107
65		THF	0	107
66	Sc(OTf) ₃	ClCH ₂ CH ₂ Cl	0	110
67		toluene	0	109
68		THF	0	87
69	Hf(Cl) ₄	ClCH ₂ CH ₂ Cl	0	98
70		toluene	0	92
71		THF	0	105
72	[Rh(Cod)Cl] ₂	ClCH ₂ CH ₂ Cl	0	85
73	[Rh(Cod)Cl] ₂ /Binap/AgSbF ₆	ClCH ₂ CH ₂ Cl	3	100
74	[Ir(Cod)Cl] ₂	ClCH ₂ CH ₂ Cl	0	98

75	[Ir(Cod)Cl] ₂ /Binap/AgSbF ₆	ClCH ₂ CH ₂ Cl	0	21
76	[RuCl ₂ (CO) ₃] ₂ /Ag(OTf)	toluene	2	94
77	Ruthenium Carbonyl	toluene	0	53
78	CuCl ^c	toluene	0	80

a. 2.5 mol % Pd₂(dba)₃/ 10 mol % NaOAc. b. 20 mol% NaOAc. c. 20 % CuCl.

General Procedure for the cyclization using PtCl₄

A solution of the substrate and PtCl₄ (5 mol%) in dichloroethane (0.2 M) was stirred for the corresponding time and temperature under Ar until the substrate was completely consumed. The solvent was then evaporated and the residue was purified by column chromatography on silica gel by eluting EtOAc-hexane or CH₂Cl₂-hexane.

General Procedure for the cyclization using PtCl₂ in toluene¹

A solution of the substrate and PtCl₂ (5 mol%) in toluene (0.2 M) was stirred for the corresponding time and temperature under Ar. Then sat. NaHCO₃ solution was added and the crude product was extracted with ether, washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane or CH₂Cl₂-hexane.

General Procedure for the cyclization using PtCl₂ in aq. Acetone²

A solution of the substrate and PtCl₂ (5 mol%) in 5% aq. acetone (0.1 M) was stirred for the corresponding time at 60 °C under Ar. The solvent was then evaporated and the residue was purified by column chromatography on silica gel by eluting EtOAc-hexane.

General Procedure for the cyclization using GaCl₃³

A solution of the substrate and GaCl₃ (10 mol%) in toluene (0.2 M) was stirred for the corresponding time and temperature under Ar. Then sat. NaHCO₃ solution was added and the crude

product was extracted with ether, washed with brine, dried over MgSO_4 , and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane.

General Procedure for the cyclization using $\text{Pd}(\text{OAc})_2$ in TFA- CH_2Cl_2 ⁴

A solution of the substrate and $\text{Pd}(\text{OAc})_2$ (1-2 mol%) in TFA- CH_2Cl_2 (3:1, 0.2 M) was stirred for the corresponding time at rt under Ar. Brine was added and the crude product was extracted with ether. The ethereal layer was washed with brine, neutralized with sat. NaHCO_3 solution, dried over MgSO_4 , and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane.

General Procedure for the cyclization using $\text{Pd}(\text{OAc})_2$ in AcOH⁵

A solution of the substrate and $\text{Pd}(\text{OAc})_2$ (5 mol%) in AcOH (0.1 M) was stirred for the corresponding time at rt under Ar. Brine was added and the crude product was extracted with ether. The ethereal layer was washed with brine, neutralized with sat. NaHCO_3 solution, dried over MgSO_4 , and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane.

General Procedure for the cyclization using AuCl_3 ⁶

A solution of the substrate and AuCl_3 (10 mol%) in MeCN (0.2 M) was stirred for the corresponding time at 40 °C under Ar. The solvent was then evaporated and the residue was purified by column chromatography on silica gel by eluting EtOAc-hexane.

General Procedure for the cyclization using CuCl ⁷

A solution of the substrate and CuCl (10 mol%) in toluene (0.7 M) was refluxed for the corresponding time under Ar. Water was added and the crude product was extracted with CH_2Cl_2 ,

dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane.

General Procedure for the cyclization using Pd(OAc)₂ and NaOAc in HCO₂H⁸

A solution of the substrate, Pd(OAc)₂ (5 mol%), and NaOAc (20 mol%) in HCO₂H (0.2 M) was stirred for the corresponding time at rt under Ar. The mixture was diluted with CH₂Cl₂, washed with water, sat. NaHCO₃ solution, and brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane.

Compounds **1**⁹, **3**¹⁰, **4a**¹¹, **6a**¹¹, **6b**¹², **6c**¹³, **11**¹⁴, **12**¹⁴ are known and **2a** and **27** are commercially available.

Entry	Catalyst (mol%)	Solvent	Temp.	Time	Yields (%) ^a
			(°C)	(h)	2a : 2b : 2c (S.M.)
1	PtCl ₄ (3)	ClCH ₂ CH ₂ Cl	rt	24	55 : 0 : 0 (0)
2	PtCl ₂ (5)	Toluene	rt	24	6 : 0 : 0 (23)
3	GaCl ₃ (10)	Toluene	rt	24	0 : 0 : 0 (52)
4	Pd(OAc) ₂ (1)	TFA / CH ₂ Cl ₂	rt	24	0 : 0 : 0 (0)
5	Pd(OAc) ₂ (1)	TFA / CH ₂ Cl ₂	rt	1	9 : 0 : 0 (40)
6	Pd(OAc) ₂ (5) / NaOAc (20)	HCO ₂ H	rt	1	9 : 0 : 0 (6)
7	Pd(OAc) ₂ (5) / NaOAc (20)	HCO ₂ H	rt	24	9 : 0 : 0 (0)

a. Yields were determined by the mass recovery of the purified reaction mixture and the ratio was determined

by ^1H NMR of the mixture.

2H-Chromene (2a)

a colorless oil (SiO_2 , Hexanes : CH_2Cl_2 = 8 : 1)

HRFABMS m/z 131.0499 (M-H^+), calcd for $\text{C}_9\text{H}_7\text{O}$ 131.0497.

Entry	Catalyst (mol%)	Solvent	Temp. ($^{\circ}\text{C}$)	Time (h)	Yields (%) ^a 4a : 4b : 4c (S.M.)
1	PtCl_4 (5)	$\text{ClCH}_2\text{CH}_2\text{Cl}$	rt	24	67 : 0 : 0 (0)
2	PtCl_4 (5)	Dioxane ^b	rt	2	92 : 0 : 0 (0)
3	PtCl_4 (5)	Dioxane / H_2O^c	rt	2	83 : 0 : 0 (0)
4	PtCl_2 (5)	Toluene	rt	24	25 : 0 : 0 (61)
5	GaCl_3 (10)	Toluene	rt	24	46 : 0 : 0 (6)
6	$\text{Pd}(\text{OAc})_2$ (1)	TFA / CH_2Cl_2	rt	24	0 : 0 : 0 (0)
7	$\text{Pd}(\text{OAc})_2$ (1)	TFA / CH_2Cl_2	rt	1	0 : 0 : 10 (41)
8	$\text{Pd}(\text{OAc})_2$ (5) / NaOAc (20)	HCO_2H	rt	1	30 : 0 : <1 (18)
9	$\text{Pd}(\text{OAc})_2$ (5) / NaOAc (20)	HCO_2H	rt	24	4 : 0 : 6 (0)

a. Yields were determined by the mass recovery of the purified reaction mixture and the ratio was determined by ^1H NMR of the mixture. b. Reaction complete in < 30 min by HPLC. c. 0.5 % H_2O , reaction complete in approximately 120 min by HPLC.

4-Methyl-2H-chromene (4a)

a colorless oil (SiO_2 , Hexanes : CH_2Cl_2 = 8 : 1)

$\delta_{\text{H}}(\text{CDCl}_3, 300 \text{ MHz})$ 2.04 (q, J = 1.6 Hz, 3H), 4.77 (m, 2H), 5.59 (m, 1H), 6.83 (dd, J = 1.0, 7.8 Hz,

1H), 6.92 (td, $J = 1.2, 7.5$ Hz, 1H), 7.11-7.18 (m, 2H).

δ_{C} (CDCl₃, 75 MHz) 17.9, 65.4, 115.7, 118.3, 121.0, 123.4, 124.2, 128.9, 130.1, 154.1.

HRFABMS m/z 145.0642 (M-H)⁺, calcd for C₁₀H₉O 145.0653.

Entry	Catalyst (mol%)	Solvent	Temp.	Time (h)	Yields (%) ^a
			(°C)		6a : 6b : 6c (S.M.)
1	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	70	24	50 : 5 : 0 (0)
2	PtCl ₄ (5)	Dioxane	rt	5	57 : 28 : 0 (0)
3	PtCl ₂ (5)	Toluene	80	24	51 : 5 : 0 (0)
4	GaCl ₃ (10)	Toluene	80	24	39 : 2 : 0 (0)
5	Pd(OAc) ₂ (1)	TFA / CH ₂ Cl ₂	rt	24	0 : 0 : 0 (0)
6	Pd(OAc) ₂ (1)	TFA / CH ₂ Cl ₂	rt	1	0 : 0 : 67 (0)
7	Pd(OAc) ₂ (5) / NaOAc (20)	HCO ₂ H	rt	1	7 : 0 : 0 (46)
8	Pd(OAc) ₂ (5) / NaOAc (20)	HCO ₂ H	rt	24	23 : 5 : 0 (6)

a. Isolated yields.

4-Phenyl-2H-chromene (6a)

a pale yellow oil (SiO₂, Hexanes : CH₂Cl₂ = 12 : 1)

δ_{H} (CDCl₃, 500 MHz) 4.87 (d, $J = 3.8$ Hz, 2H), 5.81 (t, $J = 3.8$ Hz, 1H), 6.86 (t, $J = 7.5$ Hz, 1H), 6.91 (d, $J = 8.0$ Hz, 1H), 7.02 (d, $J = 7.6$ Hz, 1H), 7.17 (t, $J_{\text{av}} = 7.7$ Hz, 1H), 7.35-7.42 (m, 5H).

HRFABMS m/z 207.0824 (M-H)⁺, calcd for C₁₅H₁₁O 207.0810.

4-Phenyl-4H-chromene (6b)

a white solid (SiO₂, Hexanes : CH₂Cl₂ = 12 : 1)

δ_{H} (CDCl₃, 300 MHz) 4.69-4.71 (m, 1H), 5.02-5.06 (m, 1H), 6.67 (dd, J = 1.6, 6.7 Hz, 1H), 6.93-6.98 (m, 3H), 7.24-7.39 (m, 6H).

HRFABMS m/z 207.0811 (M-H)⁺, calcd for C₁₅H₁₁O 207.0810.

4-Phenylchroman (6c)

a colorless oil (SiO₂, Hexanes : CH₂Cl₂ = 12 : 1)

δ_{H} (CDCl₃, 500 MHz) 2.08-2.13 (m, 1H), 2.28-2.33 (m, 1H), 4.16-4.21 (m, 3H), 6.78-6.88 (m, 3H), 7.11-7.15 (m, 3H), 7.21-7.25 (m, 1H), 7.29-7.32 (m, 2H).

HRFABMS m/z 210.1055 (M)⁺, calcd for C₁₀H₉O 210.1045.

Entry	Catalyst (mol%)	Solvent	Temp.	Time	Yields (%) ^a
			(°C)	(h)	8a : 8b : 8c (S.M.)
1	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	70	24	54 : 0 : 0 (0)
2	PtCl ₂ (5)	Toluene	80	24	<1 : 0 : 0 (85)
3	GaCl ₃ (10)	Toluene	80	24	0 : 0 : 0 (92)
4	Pd(OAc) ₂ (1)	TFA / CH ₂ Cl ₂	50	24	59 : 0 : 0 (0)
5	Pd(OAc) ₂ (5) / NaOAc (20)	HCO ₂ H	rt	24	0 : 0 : 0 (0)

a. Isolated yields.

2H-Chromene-4-carboxylic acid methyl ester (8a)

a pale yellow oil (SiO₂, Hexanes : EtOAc = 6 : 1)

δ_{H} (CDCl₃, 300 MHz) 3.86 (s, 3H), 4.83 (d, J = 4.1 Hz, 2H), 6.81-6.87 (m, 2H), 6.96 (t, J = 7.4 Hz, 1H), 7.18 (t, J = 7.4 Hz, 1H), 7.89 (d, J = 7.8 Hz, 1H).

δ_{C} (CDCl₃, 75 MHz) 52.0, 64.6, 116.2, 119.5, 121.6, 126.3, 127.2, 129.8, 131.8, 154.1, 165.2.

ν_{max} (NaCl)/cm⁻¹ 1734, 1617, 1506, 1256, 1030.

HRFABMS m/z 189.0567 (M-H)⁺, calcd for C₁₁H₉O₃ 189.0552.

2,4-Dimethyl-2H-chromene (10)

a colorless oil (SiO₂, Hexanes : CH₂Cl₂ = 8 : 1)

Isolated in 82% yield in 89% ee as determined by HPLC analysis (Chiraicel OD, 5% *i*-POH in Hexanes, 225nm) t_{r} = 15.6 (major), t_{r} = 16.9 (minor); $[\alpha]_{\text{D}}^{22}$ -131.3 (c = 0.5, CHCl₃).

δ_{H} (CDCl₃, 300 MHz) 1.41 (d, J = 6.6, 3H), 2.01 (t, J = 1.6 Hz, 3H), 4.91 (m, 1H), 5.44 (m, 1H), 6.78 (d, J = 7.8 Hz, 1H), 6.87 (dt, J = 1.2, 7.5 Hz, 1H), 7.08-7.14 (m, 2H).

δ_{C} (CDCl₃, 125 MHz) 17.9, 21.3, 71.2, 115.9, 120.8, 123.4, 123.6, 128.9, 129.4, 153.6.

ν_{max} (NaCl)/cm⁻¹ 2974, 1605, 1487, 1451, 1223, 1045.

HRFABMS m/z 159.0816 (M-H)⁺, calcd for C₁₁H₁₁O 159.0810.

Entry	Catalyst (mol%)	Solvent	Temp. (°C)	Time (h)	Yields (%) ^a 12 : 12' (S.M.)
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1	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	rt	3.5	74 : 0 (0)
2	PtCl ₄ (1)	ClCH ₂ CH ₂ Cl	rt	24	77 : 0 (0)
3	PtCl ₄ (5)	Dioxane	rt	0.5	87 : 9 (0)
4	PtCl ₄ (1)	Dioxane	rt	1	86 : 10 (0)
5	PtCl ₂ (5)	Toluene	rt	13	84 : 0 (0)
6	GaCl ₃ (10)	Toluene	rt	24	15 : 0 (18)
7	Pd(OAc) ₂ (1)	TFA / CH ₂ Cl ₂	rt	0.33	0 : 0 (18)

a. Isolated yields.

4,5,7-Trimethyl-2H-chromene (12)

a colorless oil (SiO₂, Hexanes : CH₂Cl₂ = 8 : 1)

δ_{H} (CDCl₃, 300 MHz) 2.18 (q, J = 0.6 Hz, 3H), 2.24 (s, 3H), 2.43 (s, 3H), 4.41-4.43 (m, 2H), 5.64-5.66 (m, 1H), 6.57 (s, 1H), 6.59 (s, 1H).

δ_{C} (CDCl₃, 75 MHz) 21.0, 22.5, 22.9, 64.3, 114.8, 119.7, 122.0, 126.1, 132.6, 134.9, 138.4, 155.7.

HRFABMS m/z 173.0973 (M-H)⁺, calcd for C₁₂H₁₃O 173.0966.

4,5,7-Trimethyl-4H-chromene (12')

a colorless oil (SiO₂, Hexanes : CH₂Cl₂ = 8 : 1)

δ_{H} (CDCl₃, 300 MHz) 1.22 (d, J = 6.7 Hz, 3H), 2.25 (s, 6H), 3.41 (quintet, J_{av} = 6.3 Hz, 1H), 5.04 (t, J_{av} = 5.6 Hz, 1H), 6.50 (d, J = 6 Hz, 1H), 6.91 (s, 1H), 6.99 (s, 1H).

δ_{C} (CDCl₃, 75 MHz) 18.3, 20.8, 22.4, 25.8, 107.5, 114.6, 121.7, 126.2, 136.3, 136.5, 139.7, 151.3.

ν_{max} (NaCl)/cm⁻¹ 2961, 2924, 2856, 1670, 1576, 1456, 1297.

HRFABMS m/z 173.0970 (M-H)⁺, calcd for C₁₂H₁₃O 173.0966.

Entry	Catalyst (mol%)	Solvent	Temp. (°C)	Time (h)	Yields (%) ^a (14a : 14b) : 14c : 13
1	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	rt	1.5	69 (90 : 10) : 3 : 0
2	PtCl ₄ (2)	ClCH ₂ CH ₂ Cl	rt	6	67 (90 : 10) : trace : 0
3	PtCl ₄ (1)	ClCH ₂ CH ₂ Cl	rt	24	65 (91 : 9) : trace : 16
4	PtCl ₄ (5)	Dioxane	rt	1	68 (82 : 18) : 9 : 0
5	PtCl ₄ (3)	Dioxane	rt	52	47 (82 : 18) : 5 : 18
6	PtCl ₂ (5)	Toluene	80	0.5	70 (88 : 12) : 3 : 0
7	GaCl ₃ (10)	Toluene	80	24	3 (100 : 0) : 0 : 16 (16d : 31%)
8	Pd(OAc) ₂ (2)	TFA / CH ₂ Cl ₂	rt	7	0 : 0 : 0 (15 : 72%, 16a : trace)

a. Isolated yields.

(4-Methyl-2H-chromen-7-yl)carbamic acid tert-butyl ester (14a)

a yellow oil (SiO₂, EtOAc : hexane = 1 : 8)

δ_{H} (CDCl₃, 300 MHz) 1.49 (s, 9H), 1.95 (q, J = 1.7 Hz, 3H), 4.68 (sextet, J = 1.7 Hz, 2H), 5.44, (tq, J = 1.7, 3.5 Hz, 1H), 6.47 (br s, 1H), 6.81 (d, J = 2.2 Hz, 1H), 6.89 (dd, J = 2.1, 8.3 Hz, 1H), 7.01 (d, J = 8.3 Hz, 1H).

δ_{C} (CDCl₃, 75 MHz) 17.8, 28.3, 65.5, 80.5, 105.9, 110.8, 116.5, 119.5, 123.9, 129.9, 139.0, 152.5, 154.81.

ν_{max} (NaCl)/cm⁻¹ 3335, 1726, 1705, 1619, 1588, 1524, 1235, 1160.

HRFABMS m/z 260.1298 (M-H)⁺, calcd for C₁₅H₁₈NO₃ 260.1287.

(4-Methyl-2H-chromen-5-yl)carbamic acid tert-butyl ester (14b)

a yellow oil (SiO₂, EtOAc : hexane = 1 : 8)

δ_{H} (CDCl₃, 400 MHz) 1.49 (s, 9H), 2.13 (q, J = 1.4 Hz, 3H), 4.45 (dq, J = 1.4, 4.5 Hz, 2H), 5.67 (tq, J = 1.4, 4.5 Hz, 1H), 6.26 (br s, 1H), 6.72 (d, J = 8.0 Hz, 1H), 6.81 (dd, J = 1.4, 8.1 Hz, 1H), 7.08 (t, J = 8.0 Hz, 1H).

$\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 20.7, 28.5, 64.4, 80.5, 113.2, 115.6, 118.4, 120.6, 129.4, 133.7, 139.2, 152.2, 155.8.

$\nu_{\text{max}}(\text{NaCl})/\text{cm}^{-1}$ 3339, 1733, 1718, 1700, 1606, 1522, 1249, 1145.

HRFABMS m/z 260.1278 (M-H)⁺, calcd for C₁₅H₁₈NO₃ 260.1287.

(4-Methyl-4H-chromen-5-yl)carbamic acid tert-butyl ester (14c)

a yellow oil (SiO₂, EtOAc : hexane = 1 : 8)

$\delta_{\text{H}}(\text{CDCl}_3, 300 \text{ MHz})$ 1.27 (d, $J = 6.7 \text{ Hz}$, 3H), 1.51 (s, 9H), 3.40 (dq, $J = 5.3, 6.6 \text{ Hz}$, 1H), 4.99 (dd, $J = 5.2, 6.0 \text{ Hz}$, 1H), 6.17 (br s, 1H), 6.49 (dd, $J = 0.5, 6.1 \text{ Hz}$, 1H), 6.65 (dd, $J = 1.1, 8.2 \text{ Hz}$, 1H), 7.11 (t, $J = 8.1 \text{ Hz}$, 1H), 7.49 (d, $J = 8.1 \text{ Hz}$, 1H).

$\delta_{\text{C}}(\text{CDCl}_3, 75 \text{ MHz})$ 24.1, 24.5, 28.3, 80.7, 106.2, 112.3, 116.6, 116.8, 127.4, 135.8, 139.6, 151.4, 153.0.

$\nu_{\text{max}}(\text{NaCl})/\text{cm}^{-1}$ 3333, 1708, 1588, 1523, 1260, 1159.

HRFABMS m/z 260.1291 (M-H)⁺, calcd for C₁₅H₁₈NO₃ 260.1287.

Entry	Catalyst (mol%)	Solvent	Temp. (°C)	Time (h)	Yields (%) ^a (16a : 16b) : 16c : 16d : 15
1	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	70	48	34 (47 : 53) : 7 : 0 : 11
2	PtCl ₄ (5)	Dioxane	70	90	25 (25 : 75) : 4 : 0 : 15
3	PtCl ₂ (5)	Toluene	80	46	30 (63 : 37) : 4 : 0 : 40
4	GaCl ₃ (10)	Toluene	80	46	2 (56 : 44) : trace : 15 : 7
5	Pd(OAc) ₂ (2)	TFA / CH ₂ Cl ₂	rt	7	trace (100 : 0) : 0 : 0 : 76

a. Isolated yields.

4-Methyl-2H-chromen-7-ylamine (16a)

a yellow oil (SiO₂, EtOAc : hexane = 1 : 3)

δ_{H} (CDCl₃, 400 MHz) 1.95 (q, J = 1.6 Hz, 3H), 3.43 (br s, 2H), 4.66 (sextet, J = 1.6 Hz, 2H), 5.35 (tq, J = 1.6, 3.6 Hz, 1H), 6.14 (d, J = 2.3 Hz, 1H), 6.21 (dd, J = 2.3, 8.0 Hz, 1H), 6.92 (d, J = 8.0 Hz, 1H).

δ_{C} (CDCl₃, 100 MHz) 18.1, 65.6, 102.3, 107.6, 114.2, 115.6, 124.4, 130.2, 147.2, 155.2.

ν_{max} (NaCl)/cm⁻¹ 3460, 3372, 3223, 1623, 1509, 1179, 810.

HRFABMS m/z 162.0927 (M+H)⁺, calcd for C₁₀H₁₂NO 162.0919.

4-Methyl-2H-chromen-5-ylamine (16b)

a yellow oil (SiO₂, EtOAc : hexane = 1 : 5)

δ_{H} (CDCl₃, 300 MHz) 2.22 (q, J = 2.0 Hz, 3H), 3.83 (br s, 2H), 4.42 (dq, J = 2.0, 6.0 Hz, 2H), 5.57 (tq, J = 2.0, 6.0 Hz, 1H), 6.25 (dd, J = 1.4, 10.6 Hz, 1H), 6.34 (dd, J = 1.4, 10.6 Hz, 1H), 6.91 (t, J = 10.6 Hz, 1H).

δ_{C} (CDCl₃, 75 MHz) 21.2, 64.4, 106.8, 110.6, 112.4, 119.0, 129.2, 130.6, 144.0, 156.4.

ν_{max} (NaCl)/cm⁻¹ 3452, 3377, 3233, 1640, 1621, 1599, 1462, 1223, 1131, 772.

HRFABMS m/z 162.0931 (M+H)⁺, calcd for C₁₀H₁₂NO 162.0919.

4-Methylenechroman-5-ylamine (16c)

a yellow oil (SiO₂, EtOAc : hexane = 1 : 5) **16c** was isomerised to **16b** slowly even at 4 °C.

δ_{H} (CDCl₃, 300 MHz) 2.59 (t, J = 5.7 Hz, 2H), 4.28 (t, J = 5.7 Hz, 2H), 5.17 (d, J = 1.1 Hz, 1H), 5.50 (s, 1H), 6.25 (dd, J = 1.1, 8.0 Hz, 1H), 6.26 (dd, J = 1.2, 8.1 Hz, 1H), 6.91 (t, J = 8.0 Hz, 1H).

4-Methylchroman-7-ylamine (16d)

a yellow oil (SiO₂, EtOAc : hexane = 1 : 3)

δ_{H} (CDCl₃, 300 MHz) 1.25 (d, J = 6.9 Hz, 3H), 1.64 (m, 1H), 2.01 (m, 1H), 2.83 (sextet, J = 6.6 Hz,

1H), 3.36 (br s, 1H), 4.12 (m, 2H), 6.14, (d, $J = 2.4$ Hz, 1H), 6.25 (dd, $J = 2.4, 8.1$ Hz, 1H), 6.92 (d, $J = 8.1$ Hz, 1H).

δ_{C} (CDCl₃, 75 MHz) 22.2, 27.9, 30.7, 64.0, 103.0, 108.3, 118.4, 129.2, 145.3, 155.0.

ν_{max} (NaCl)/cm⁻¹ 3447, 3368, 3220, 1629, 1508, 1172, 1131.

HRFABMS m/z 163.0987 (M)⁺, calcd for C₁₀H₁₃NO 163.0997.

Entry	Catalyst (mol%)	Solvent	Temp. (°C)	Time (h)	Yields (%) ^a (18a : 18b) : 18c : 18d : 18
1	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	70	0.5	68 (96 : 4) : trace : trace : 0
2	PtCl ₄ (1)	ClCH ₂ CH ₂ Cl	70	6.5	65 (98 : 2) : trace : 0 : 6
3	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	rt	1.5	66 (88 : 12) : 3 : 2 : 0
4	PtCl ₄ (1)	ClCH ₂ CH ₂ Cl	rt	6.5	58 (88 : 12) : 0 : 1 : 0
5	PtCl ₄ (5)	Dioxane	70	0.5	58 (66 : 34) : 6 : trace : 0
6	PtCl ₄ (5)	Dioxane	rt	1	57 (61 : 39) : 7 : 1 : 0
7	PtCl ₂ (5)	Toluene	80	8	58 (96 : 4) : 0 : 0 : 0
8	GaCl ₃ (10)	Toluene	80	0.5	25 (81 : 19) : 0 : 7 : 0
9	Pd(OAc) ₂ (2)	TFA / CH ₂ Cl ₂	rt	25	0 : 0 : 2 : 10

a. Yields were determined by the mass recovery of the purified reaction mixture and the ratio was determined by ¹H NMR of the mixture.

7-Bromo-4-methyl-2H-chromene (**18a**) & 5-Bromo-4-methyl-2H-chromene (**18b**)

The mixture of **18a** and **18b** was obtained as a colorless oil (SiO₂, EtOAc : hexane = 1 : 50).

18a : δ_{H} (CDCl₃, 300 MHz) 1.99 (q, $J = 1.7$ Hz, 3H), 4.73 (sextet, $J = 1.8$ Hz, 2H), 5.55 (tq, $J = 1.7$,

3.5 Hz, 1H), 6.92 (d, J = 1.9 Hz, 1H), 6.95 (d, J = 8.2 Hz, 1H), 7.00 (dd, J = 1.8, 8.2 Hz, 1H).

δ_{C} (CDCl₃, 75 MHz) 17.8, 65.8, 118.6, 118.9, 121.6, 123.2, 124.1, 124.6, 129.5, 154.9.

18b : δ_{H} (CDCl₃, 300 MHz) 2.34 (q, J = 1.5 Hz, 3H), 4.45 (dq, J = 1.5, 4.6 Hz, 2H), 5.78 (tq, J = 1.5, 4.6 Hz, 1H), 6.83 (dd, J = 1.4, 8.0 Hz, 1H), 6.94 (t, J = 8.0 Hz, 1H), 7.17 (dd, J = 1.4, 7.9 Hz, 1H).

δ_{C} (CDCl₃, 75 MHz) 22.0, 64.4, 115.7, 119.7, 121.6, 122.2, 127.9, 129.2, 132.0, 157.0.

ν_{max} (NaCl)/cm⁻¹ 1594, 1485, 1223, 1084, 1006, 815.

HRFABMS m/z 222.9749 (M-H)⁺, calcd for C₁₀H₈⁷⁹BrO 222.9759.

5-Bromo-4-methyl-4H-chromene (18c)

The ¹H NMR spectrum of **18c** was obtained from a mixture of **18a/18b** and **18c**.

δ_{H} (CDCl₃, 300 MHz) 1.29 (d, J = 6.7 Hz, 3H), 3.53 (dq, J = 5.4, 6.6 Hz, 1H), 5.08 (dd, J = 5.4, 5.8 Hz, 1H), 6.47 (d, J = 5.9 Hz, 1H), 6.83 (dd, J = 1.4, 8.0 Hz, 1H), 6.98 (t, J = 8.0 Hz, 1H), 7.23 (dd, J = 1.4, 7.9 Hz, 1H).

7-Bromo-4-methyl-chroman (18d)

The ¹H and ¹³C NMR spectrum of **18d** were obtained from a mixture of **18a/18b** and **18d**.

δ_{H} (CDCl₃, 400 MHz) 1.28 (d, J = 7.1 Hz, 3H), 1.68 (m, 1H), 2.04 (m, 1H), 2.87 (sextet, J = 6.6 Hz, 1H), 4.16 (m, 2H), 6.93 (m, 1H), 6.96 (m, 2H).

δ_{C} (CDCl₃, 100 MHz) 22.2, 28.4, 30.1, 64.1, 119.6, 119.7, 123.0, 126.5, 129.7, 154.9.

Entry	Catalyst (mol%)	Solvent	Temp. (°C)	Time (h)	Yields (%) ^a (20a : 20b) : (20c : 20d) : 19
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1	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	70	2	82 (78 : 22) : 0 : 0
2	PtCl ₂ (5)	Toluene	80	15	66 (82 : 18) : 0 : 0
3	GaCl ₃ (10)	Toluene	80	20	44 (60 : 40) : 8 : 0
4	Pd(OAc) ₂ (2)	TFA / CH ₂ Cl ₂	rt	11	0 : 42 (67 : 33) : 0
5	CuCl (10)	Toluene	reflux	24	- ^b

a. Yields were determined by the mass recovery of the purified reaction mixture and the ratio was determined by ¹H NMR of the mixture. b. No reaction.

7-Methoxy-4-methyl-2H-quinoline-1-carboxylic acid methyl ester (20a) & 5-Methoxy-4-methyl-2H-quinoline-1-carboxylic acid methyl ester (20b)

The mixture of **20a** and **20b** was obtained as a colorless oil (SiO₂, EtOAc : hexane = 1 : 5).

δ_{H} (CDCl₃, 400 MHz) **20a** : 2.00 (d, J = 1.5 Hz, 3H), 3.77 (s, 3H), 3.80 (s, 3H), 4.28 (dd, J = 1.7, 4.2 Hz, 2H), 5.65 (m, 1H), 6.66 (dd, J = 2.6, 8.6 Hz, 1H), 7.14 (d, J = 8.6 Hz, 1H), 7.19 (br s, 1H). **20b** : 2.18 (d, J = 1.5 Hz, 3H), 3.74 (s, 3H), 3.80 (s, 3H), 4.10 (dd, J = 1.7, 4.2 Hz, 2H), 5.75 (m, 1H), 6.7 (m, 2H), 7.14(m, 1H).

δ_{C} (CDCl₃, 100 MHz) the mixture of **20a** & **20b** : 18.6, 22.1, 42.6, 43.4, 53.0, 53.1, 55.4, 55.5, 107.8, 109.5, 109.7, 116.9, 119.1, 122.5, 123.0, 1234.0, 127.1, 131.2, 132.6, 137.4, 138.3, 154.2, 154.4, 156.37, 158.42 (One carbon is missing due to overlapping).

ν_{max} (NaCl)/cm⁻¹ 1708, 1615, 1445, 1216, 1040.

HRFABMS m/z 232.0991 (M-H)⁺, calcd for C₁₃H₁₄NO₃ 232.0974.

7-Methoxy-4-methyl-3,4-dihydro-2H-quinoline-1-carboxylic acid methyl ester (20c) & 5-Methoxy-4-methyl-3,4-dihydro-2H-quinoline-1-carboxylic acid methyl ester (20d)

The mixture of **20c** and **20d** was obtained as a pale yellow oil (SiO₂, EtOAc : hexane = 1 : 5).

δ_{H} (CDCl₃, 400 MHz) **20c** : 1.25 (d, J = 7.0 Hz, 3H), 1.58 (m, 1H), 2.02 (m, 1H), 2.82 (m, 1H), 3.74 (m, 2H), 3.77 (s, 3H), 3.78 (s, 3H), 6.62 (dd, J = 2.6, 8.5 Hz, 1H), 7.06 (d, J = 8.7 Hz, 1H), 7.30 (br s, 1H). **20d** : 1.17 (d, J = 7.0 Hz, 3H), 1.74 (m, 1H), 1.92 (m, 1H), 3.25 (m, 1H), 3.65 (m, 2H), 3.76

(s, 3H), 3.80 (s, 3H), 6.58 (d, $J = 8.3$ Hz, 1H), 7.09 (t, $J = 8.3$ Hz, 1H), 7.31 (br s, 1H).

δ_{C} (CDCl₃, 100 MHz) the mixture of **20c** & **20d** : 20.3, 21.5, 25.6, 30.3, 30.6, 31.7, 41.6, 43.2, 53.0, 53.0, 55.4, 55.5, 105.5, 108.8, 110.1, 116.3, 123.3, 125.7, 126.9, 127.5, 138.0, 138.1, 155.0, 155.1, 156.6, 157.3.

ν_{max} (NaCl)/cm⁻¹ 1700, 1506, 1438, 1338, 1259, 1049.

HRFABMS m/z 235.1213 (M)⁺, calcd for C₁₃H₁₇NO₃ 235.1208.

Entry	Catalyst (mol%)	Solvent	Temp. (°C)	Time (h)	Yields (%) ^a 22 (S.M.)
1	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	70	5.5	78 (0)
2	PtCl ₄ (17)	ClCH ₂ CH ₂ Cl	rt	27	89 (0)
3	PtCl ₂ (5)	Toluene	80	24	13 (56)
4	GaCl ₃ (10)	Toluene	80	24	6 (90)
5	Pd(OAc) ₂ (1)	TFA / CH ₂ Cl ₂	rt	0.66	72 (0)

a. Isolated yields.

5,7-Dimethyl-2H-chromene-4-carboxylic acid methyl ester (**22**)

a pale yellow oil (SiO₂, Hexanes : EtOAc = 6 : 1)

δ_{H} (CDCl₃, 300 MHz) 2.17 (s, 3H), 2.27 (s, 3H), 3.82 (s, 3H), 4.54 (s, $J = 4.6$ Hz, 2H), 6.53 (t, $J = 4.6$ Hz, 1H), 6.64 (s, 1H), 6.65 (s, 1H).

δ_{C} (CDCl₃, 75 MHz) 20.4, 21.3, 52.1, 63.8, 114.5, 117.8, 125.4, 128.5, 130.4, 139.8, 155.5, 168.1.

ν_{max} (NaCl)/cm⁻¹ 1731, 1615, 1436, 1264, 1460.

HRFABMS m/z 217.0886 (M-H)⁺, calcd for C₁₃H₁₃O₃ 217.0865.

Entry	Catalyst (mol%)	Solvent	Temp. (°C)	Time (h)	Yields (%) ^a 24 (S.M.)
1	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	70	36	73 (0)
2	PtCl ₄ (5)	Dioxane	70	26	52 (0)
3	PtCl ₂ (5)	Toluene	80	41	28 (56)
4	GaCl ₃ (10)	Toluene	80	41	29 (61)
5	Pd(OAc) ₂ (1)	TFA / CH ₂ Cl ₂	rt	0.5	84 (0)

a. Isolated yields.

But-2-ynoic acid 3,5-dimethylphenyl ester (**24**)

a white solid (m.p. 177-178 °C, lit.^{15a} m.p. 175-176 °C) (SiO₂, EtOAc : hexane = 1 : 3).

δ_{H} (CDCl₃, 300 MHz) 2.34 (s, 3H), 2.56 (d, J = 1.1 Hz, 3H), 2.64 (s, 3H), 6.11 (d, J = 0.9 Hz, 1H), 6.85 (s, 1H), 6.97 (s, 1H).

δ_{C} (CDCl₃, 75 MHz)¹⁵ 21.1, 24.2, 25.0, 115.3, 116.1, 116.7, 129.5, 136.4, 141.8, 154.2, 155.1, 160.7.

ν_{max} (NaCl)/cm⁻¹ 1720, 1605, 1455, 1383, 1245, 1037, 854.

LRFABMS m/z 189.05 (M+H)⁺, calcd for C₁₂H₁₃O₂ 189.09.

Entry	Catalyst	Solvent	Temp.	Time	Yields (%) ^a
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	(mol%)		(°C)	(h)	(26a : 26b) : 25
1	PtCl ₄ (5)	ClCH ₂ CH ₂ Cl	70	36	57 (47 : 53) : 0
2	PtCl ₂ (5)	aq. Acetone	60	17	trace : 0 ^b
3	PtCl ₂ (5)	Toluene	80	40	29 (0 : 100) : 44
4	GaCl ₃ (10)	Toluene	80	1	- ^b
5	Pd(OAc) ₂ (2)	TFA / CH ₂ Cl ₂	rt	1	45 (100 : 0) : 0
6	Pd(OAc) ₂ (5)	AcOH	rt	20	8 (trace : ~100) : 0 ^b
7	AuCl ₃ (10)	MeCN	40	33	- ^c

a. Isolated yields. b. Complex mixture was obtained. c. No reaction.

(4H-Furo[3,2-c]pyran-7-ylidene)acetic acid methyl ester (26a, *E*-isomer)

a yellow solid (m.p. 63-64 °C) (SiO₂, EtOAc : hexane = 1 : 5)

δ_{H} (CDCl₃, 400 MHz) 3.71 (s, 3H), 4.67 (s, 2H), 4.99 (d, J = 1.8 Hz, 2H), 6.03 (t, J = 1.5 Hz, 1H), 6.33 (d, J = 1.8 Hz, 1H), 7.41 (d, J = 1.8 Hz, 1H).

δ_{C} (CDCl₃, 100 MHz) 51.3, 63.7, 65.9, 105.3, 108.8, 126.1, 140.9, 144.7, 146.1, 166.9.

ν_{max} (NaCl)/cm⁻¹ 3142, 1705, 1635, 1432, 1358, 1176, 1090, 893, 743.

HRFABMS m/z 195.0665 (M+H)⁺, calcd for C₁₀H₁₁O₄ 195.0657.

(4H-Furo[3,2-c]pyran-7-ylidene)acetic acid methyl ester (26b, *Z*-isomer)

an orange solid (SiO₂, EtOAc : hexane = 1 : 3)

δ_{H} (CDCl₃, 400 MHz) 3.76 (s, 3H), 4.34 (d, J = 1.2 Hz, 2H), 4.71 (s, 2H), 5.47 (s, 1H), 6.32 (d, J = 1.8 Hz, 1H), 7.54 (d, J = 1.8 Hz, 1H).

δ_{C} (CDCl₃, 100 MHz) 51.5, 64.8, 70.8, 107.9, 108.1, 127.2, 135.2, 144.8, 145.2, 166.0.

ν_{max} (NaCl)/cm⁻¹ 1734, 1437, 1249, 1176, 1099, 737.

HRFABMS m/z 195.0656 (M+H)⁺, calcd for C₁₀H₁₁O₄ 195.0657.

The structures of **26a** (*E*-isomer) and **26b** (*Z*-isomer) were confirmed by COSY, NOE, HMQC, and

hydrogenation experiments.

After the hydrogenation with 10 % Pd/C in EtOAc under H₂, **26a** (*E*-isomer) and **26b** (*Z*-isomer) gave **26c** (25-30%) and **26d** (60-65%) respectively. 7-Membered ring compound **26e** was not obtained.

(6,7-Dihydro-4H-furo[3,2-c]pyran-7-yl)acetic acid methyl ester (**26c**)

a pale yellow oil (SiO₂, EtOAc : hexane = 1 : 4)

δ_{H} (CDCl₃, 400 MHz) 2.52 (dd, J = 9.2, 16.2 Hz, 1H), 2.73 (dd, J = 5.0, 16.2 Hz, 1H), 3.30 (m, 1H), 3.70 (s, 3H), 3.75 (dd, J = 4.4, 11.4 Hz, 1H), 3.94 (dd, J = 4.3, 11.4 Hz, 1H), 4.55 (ddd, J = 1.6, 14.0, 19.0 Hz, 2H), 6.16 (d, J = 1.9 Hz, 1H), 7.27 (d, J = 1.9 Hz, 1H).

δ_{C} (CDCl₃, 100 MHz) 32.0, 35.4, 51.9, 64.5, 69.1, 107.0, 116.2, 141.4, 148.9, 172.0.

ν_{max} (NaCl)/cm⁻¹ 1740, 1463, 1261, 1087, 802, 729.

APCI m/z 195.26 (M-H)⁺, calcd for C₁₀H₁₁O₄ 195.20.

(Hexahydrofuro[3,2-c]pyran-7-yl)acetic acid methyl ester (**26d**)

a colorless oil, diastereomer mixture (SiO₂, EtOAc : hexane = 1 : 3)

δ_{H} (CDCl₃, 300 MHz) major diastereomer : 1.45 (ddd, J = 4.0, 8.0, 12.8 Hz, 1H), 1.93 (m, 1H), 2.17-2.51 (m, 4H), 3.05 (t, J = 11.6 Hz, 1H), 3.20 (t, J = 11.2 Hz, 1H), 3.65 (s, 3H), 3.68-3.96 (m, 5H). minor diastereomer : 1.76 (m, 1H), 1.92 (m, 1H), 2.19-2.51 (m, 4H), 3.30 (dd, J = 5.6, 11.6 Hz, 1H), 3.47 (dd, J = 7.2, 11.7 Hz, 1H), 3.67 (s, 3H), 3.67-4.01 (m, 5H).

δ_{C} (CDCl₃, 75 MHz) major diastereomer : 27.7, 33.2, 34.2, 37.1, 51.6, 66.1, 66.6, 67.2, 76.8, 172.7.

minor diastereomer : 27.5, 34.2, 34.7, 36.0, 51.6, 66.2, 67.5, 67.6, 78.5, 172.7.

ν_{max} (NaCl)/cm⁻¹ 1734, 1437, 1269, 1172, 1099.

HRFABMS m/z 201.1132 (M+H)⁺, calcd for C₁₀H₁₇O₄ 201.1127.

Synthesis of Starting Material.

Compounds **1**, **3**, and **11** were prepared via the reaction of the appropriate phenol with the appropriate propargyl bromide (1.5 equiv.) at ambient temperature in DMF in the presence of potassium carbonate (1.2 equiv.). Purification of the crude product was achieved via flash column chromatography.¹⁶

Prop-2-ynyloxybenzene (**1**)

91% (SiO₂, EtOAc : Hexanes = 10 : 1).

But-2-ynyloxybenzene (**3**)

97% (SiO₂, CH₂Cl₂ : Hexanes = 2 : 1)

1-But-2-ynyloxy-3,5-dimethylbenzene (**11**)

99% (SiO₂, CH₂Cl₂ : Hexanes = 3 : 1)

Synthesis of 3-phenylprop-2-ynyloxybenzene (**5**)

3-Phenylprop-2-yn-1-yloxybenzene (**5**)

To a flame dried 150-ml round bottom flask was added phenol (1.11 g, 11.79 mmol), 3-phenyl-2-propyn-1-ol (1.56 g, 11.79 mmol), triphenylphosphine (2.94 g, 11.20 mmol, 0.95 equiv.) and 50 ml of THF. The solution was cooled to 0 °C and diethyl azodicarboxylate (2.6 ml, 16.51 mmol, 1.4 equiv.) was added dropwise via syringe. The ice bath was removed and stirred under argon for 24 hr. Removal of solvent and purification by flash column chromatography (SiO₂, Hexane : CH₂Cl₂ = 3 : 2) yields **5** (1.51 g, 65%) as a white solid.

δ_{H} (CDCl₃, 300 MHz) 4.88 (s, 2H), 6.75-7.04 (m, 3H), 7.26-7.33 (m, 5H), 7.41-7.44 (m, 2H).

δ_{C} (CDCl₃, 75 MHz) 56.6, 84.0, 115.0, 121.4, 122.3, 128.2, 128.6, 129.4, 131.8, 157.8.

ν_{max} (NaCl)/cm⁻¹ 2235, 1598, 1491, 1214, 1034.

HRFABMS m/z 208.0894 (M)⁺, calcd for C₁₅H₁₂O 208.0888

Synthesis of 4-phenoxy-but-2-ynoic acid methyl ester (**7**) and 4-(3,5-dimethyl-phenoxy)-but-2-ynoic acid methyl ester (**21**)

4-Phenoxy-but-2-ynoic acid methyl ester (**7**)

To a solution of **1** (730 mg, 5.52 mmol) in THF (20 ml) was added *n*-BuLi (3.62 ml, 1.6 M solution in hexanes, 5.80 mmol, 1.05 equiv.) dropwise at -78 °C. After being stirred at -78 °C for 30 min,

ClCO₂Me (725 μ l, 9.38 mmol) was added and the reaction mixture was allowed to warm to rt and stirred for 12 hr. After removing most of the solvent, ether was added and washed with water. The aqueous layer was extracted with ether and the combined organic layers were dried over MgSO₄, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:10) to give **7** (839 mg; 80%) as colorless oil.

δ_{H} (CDCl₃, 300 MHz) 3.73 (s, 2H), 4.76 (s, 2H), 6.92-7.02 (m, 3H), 7.29-7.32 (t, J =7.4 Hz, 2H).

δ_{C} (CDCl₃, 75 MHz) 52.7, 55.2, 114.7, 121.6, 129.5, 153.1, 157.1.

ν_{max} (NaCl)/cm⁻¹ 2241, 1716, 1598, 1495, 1434, 1258, 1073.

HRFABMS m/z 190.0616 (M)⁺, calcd for C₁₁H₁₀O₃ 190.0630.

4-(3,5-Dimethyl-phenoxy)-but-2-ynoic acid methyl ester (**21**)

yield 88 %, pale yellow oil (SiO₂, hexanes : EtOAc = 12 : 1)

δ_{H} (CDCl₃, 300 MHz) 2.29 (s, 6H), 3.76 (s, 3H), 4.75 (s, 2H), 6.56 (s, 2H), 6.66 (s, 1H).

δ_{C} (CDCl₃, 75 MHz) 21.4, 52.7, 55.3, 78.0, 82.5, 112.5, 123.7, 139.4, 153.3, 157.3.

ν_{max} (NaCl)/cm⁻¹ 2245, 1719, 1595, 1436, 1259.

HRFABMS m/z 218.0932 (M)⁺, calcd for C₁₃H₁₄O₃ 218.0943.

Synthesis of (1-Methylbut-2-ynoxy)benzene (**19**)

(1-Methylprop-2-ynoxy)benzene (**III**)

To a flame dried 50-ml round bottom flask was added (S)-(-)-3-butyn-2-ol (360 mg, 5.06 mmol), phenol (500 mg, 5.31 mmol, 1.05 equiv.), triphenylphosphine (1.32g, 5.06 mmol) and 25 ml of THF. The solution was cooled to 0 °C and diethyl azodicarboxylate (955 μ L, 6.07 mmol, 1.2 equiv.) was

added dropwise via syringe. The ice bath was removed and stirred under argon for 18 hr. Removal of solvent and purification by flash column chromatography (hexanes : EtOAc = 5 : 1) yields (1-Methylprop-2-ynyloxy)benzene (525 mg; 71%) as a colorless oil in 89% ee as determined by HPLC analysis (Chiraicel OD, 5% *i*-POH in Hexanes, 225nm) t_r = 4.6 (minor), t_r = 6.8 (major).

δ_H (CDCl₃, 300 MHz) 1.66 (d, J = 6.9 Hz, 3 H), 2.46 (d, J = 2 Hz, 1 H), 4.86 (qd, J = 6.6 Hz, 1H), 6.94-7.01 (m, 3 H), 7.24-7.30 (m, 2 H).

δ_C (CDCl₃, 75 MHz) 22.1, 66.3, 73.8, 82.9, 115.7, 121.4, 129.3, 157.2.

$\nu_{\max}$ (NaCl)/cm⁻¹ 3293, 1598, 1495, 1235, 1092.

Synthesis of (1-Methylbut-2-ynyloxy)benzene (9)

To a solution of **III** (350 mg, 2.39 mmol) in THF (25 ml) was added *n*-BuLi (1.64, 1.6 M solution in hexanes, 2.63 mmol, 1.1 equiv.) dropwise at ice / EtOH temperature. After stirring for 20 minutes, iodomethane (180 μ L, 2.87 mmol, 1.2 equiv.) was added. The reaction was monitored by ¹H NMR based on the disappearance of the alkyneyl proton resonance. After completion of reaction, 1 ml of EtOH was added to the reaction. Removal of solvent and purification by flash column chromatography (hexanes : CH₂Cl₂ = 10 : 1) yields **9** (375 mg; 98%) as a pale yellow oil.

δ_H (CDCl₃, 300 MHz) 1.61 (d, J = 6.5 Hz, 3 H), 1.81 (d, J = 2 Hz, 3 H), 4.82 (m, 1 H), 6.92-6.99 (m, 3H), 7.24-7.29 (m, 2H).

δ_C (CDCl₃, 75 MHz) 3.6, 22.5, 63.8, 78.5, 81.8, 115.6, 121.0, 129.3, 157.5.

$\nu_{\max}$ (NaCl)/cm⁻¹ 2250, 1599, 1494, 1236, 1237, 1065.

HRFABMS m/z 160.0877 (M)⁺, calcd for C₁₁H₁₂O 160.0888.

Syntheses of O-(2-butynyl)-N-Boc-3-aminophenol (13) and 3-amino-O-(2-butynyl)-phenol (15)

N-Boc-3-aminophenol (**IV**)

To a solution of 3-aminophenol (3 g, 26.94 mmol) in THF (50 ml) was added (Boc)₂O (6.5 g, 29.63 mmol) in THF (10 ml). After being stirred at reflux for 24 h, the reaction mixture was dissolved in EtOAc, washed with 1% HCl, H₂O, sat. NaHCO₃, and brine successively, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:3) to give *N*-Boc-3-aminophenol (5.64 g, quant.) as a yellow solid (m.p. 124-128 °C).

δ_{H} (CDCl₃, 300 MHz) 1.51 (s, 9H), 5.57 (br s, 1H), 6.49 (s, 1H), 6.51 (ddd, J = 0.8, 2.4, 8.1 Hz, 1H), 6.70 (ddd, J = 0.7, 2.0, 8.1 Hz, 1H), 7.09 (br s, 1H), 7.10 (t, J = 8.1 Hz, 1H).

O-(2-butynyl)-*N*-Boc-3-aminophenol (**13**)

To a solution of *N*-Boc-3-aminophenol (2.7 g, 12.86 mmol), K₂CO₃ (2.2 g, 15.44 mmol), and KI (213.6 mg, 1.29 mmol) in DMF (24 ml) was added 1-bromo-2-butyne (1.25 ml, 14.15 mmol) at rt, and the reaction mixture was heated to 70 °C. After 48 h, H₂O was added and the crude product was extracted with ether, washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:8) to give **13** (1.34 g, 40%) as a yellow solid (m.p. 70-73 °C).

δ_{H} (CDCl₃, 300 MHz) 1.50 (s, 9H), 1.85 (t, J = 2.3 Hz, 3H), 4.61 (q, J = 2.3 Hz, 2H), 6.48 (br s, 1H), 6.62 (ddd, J = 0.7, 2.4, 8.2 Hz, 1H), 6.92 (dd, J = 1.2, 7.9 Hz, 1H), 7.0 (t, J = 2.2 Hz, 1H), 7.15 (t, J = 8.1 Hz, 1H).

δ_{C} (CDCl₃, 75 MHz) 3.6, 28.3, 56.5, 74.0, 80.5, 83.6, 105.2, 109.6, 111.3, 129.6, 139.6, 152.6, 158.4.

ν_{max} (NaCl)/cm⁻¹ 3341, 2305, 2231, 1732, 1701, 1606, 1540, 1236, 1158, 1020.

HRFABMS m/z 261.1375 (M)⁺, calcd for C₁₅H₁₉NO₃ 261.1365.

3-amino-O-(2-butynyl)-phenol (**15**)

A solution of **13** (0.97 g, 3.71 mmol) in TFA (3 ml) and CH₂Cl₂ (12 ml) was stirred for 30 min. at rt. The solvent was blown off with Ar, the residue was diluted with CH₂Cl₂, basified with sat. NaHCO₃, extracted with CH₂Cl₂, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:3) to give **15** (446 mg, 74%) as a yellow oil.

δ_{H} (CDCl₃, 300 MHz) 1.86 (t, J = 2.3 Hz, 3H), 3.59 (br s, 1H), 4.58 (q, J = 2.3 Hz, 2H), 6.27-6.38 (m, 3H), 7.04 (t, J = 8.1 Hz, 1H).

δ_{C} (CDCl₃, 75 MHz) 3.6, 56.1, 74.2, 83.4, 101.9, 104.7, 108.4, 130.0, 147.7, 159.0.

ν_{max} (NaCl)/cm⁻¹ 3454, 3373, 3220, 2301, 2228, 1623, 1601, 1495, 1290, 1181, 1158, 1022.

HRFABMS m/z 161.0844 (M)⁺, calcd for C₁₀H₁₁NO 161.0841.

Synthesis of O-(2-butynyl)-3-bromophenol (**17**)

2-Butynyl methanesulfonate

To a solution of 2-butyne-1-ol (1 ml, 13.10 mmol) in CH₂Cl₂ (15 ml) was added NEt₃ (2.0 ml, 14.41 mmol) and MsCl (1.1 ml, 14.41 mmol) at 0 °C. After being stirred for 2 h at rt, the reaction mixture was washed with H₂O, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:5) to give 2-butynyl methanesulfonate quantitatively (1.9 g) as a colorless oil.

δ_{H} (CDCl₃, 300 MHz) 1.87 (t, J = 2.4 Hz, 3H), 3.08 (s, 3H), 4.79 (q, J = 2.4 Hz, 2H).

O-(2-butynyl)-3-bromophenol (17)

To a solution of 3-bromophenol (565.8 mg, 3.21 mmol) in DMF (8 ml) was added NaH (153.8 mg, 3.85 mmol) and 2-butynyl methanesulfonate (521.8 mg, 3.53 mmol) in DMF (1 ml) at 0 °C. After 2 h, water was added and the crude product was extracted with EtOAc (10 ml x 3), washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:20) to give **17** (710.8 mg, 99%) as a colorless oil.

δ_{H} (CDCl₃, 300 MHz) 1.86 (t, J = 2.3 Hz, 3H), 4.62 (q, J = 2.3 Hz, 2H), 6.86-6.90 (m, 1H), 7.07-7.16 (m, 3H).

δ_{C} (CDCl₃, 75 MHz) 3.6, 56.6, 73.5, 84.2, 113.8, 118.2, 122.7, 124.3, 130.4, 158.5.

ν_{max} (NaCl)/cm⁻¹ 2306, 2232, 1591, 1575, 1476, 1219, 1012, 770, 679.

HREIMS m/z 223.9837 (M)⁺, calcd for C₁₀H₉⁷⁹BrO 223.9837.

Synthesis of N-(2-butynyl)-N-(methoxycarbonyl)-3-amino-1-methoxybenzene (19)

N-(methoxycarbonyl)-3-amino-1-methoxybenzene (V)

To a solution of *m*-anisidine (3 ml, 26.70 mmol) in EtOAc (20 ml) and H₂O (10 ml) was added NaHCO₃ (4.5 g, 53.39 mmol) and ClCO₂Me (2.3 ml, 29.37 mmol) at 0 °C. After 1 h, the reaction mixture was extracted with EtOAc (20 ml x 3), washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:4) to give (3-Methoxyphenyl)carbamic acid methyl ester (4.49 g, 93%).

δ_{H} (CDCl₃, 300 MHz) 3.73 (s, 3H), 3.74 (s, 3H), 6.58 (ddd, J = 0.8, 2.5, 8.3 Hz, 1H), 6.88 (dd, J =

1.2, 8.0 Hz, 1H), 7.12, (b, 2H), 7.15, (t, $J = 8.2$ Hz, 1H).

N-(2-butynyl)-N-(methoxycarbonyl)-3-amino-1-methoxybenzene (**19**)

To a solution of **V** (250.2 mg, 1.38 mmol) in DMF (4 ml) was added NaH (83 mg, 2.07 mmol) and 2-butynyl methanesulfonate (225 mg, 1.52 mmol) in DMF (1 ml) at 0 °C. After 2 h, water was added and the crude product was extracted with EtOAc (10 ml x 3), washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:5) to give **19** (322 mg, quant.) as a pale yellow oil.

δ_{H} (CDCl₃, 300 MHz) 1.78 (t, $J = 2.3$ Hz, 3H), 3.71 (s, 3H), 3.79 (s, 3H), 4.32 (q, $J = 2.3$ Hz, 2H), 6.78-6.91 (m, 3H), 7.25 (t, $J = 7.7$ Hz, 1H).

δ_{C} (CDCl₃, 75 MHz) 3.4, 40.4, 52.9, 55.1, 74.6, 79.7, 112.1, 112.5, 118.7, 129.3, 142.6, 155.4, 159.7.

ν_{max} (NaCl)/cm⁻¹ 2300, 2227, 1711, 1606, 1450, 1246, 1032.

HRFABMS m/z 234.1127 (M+H)⁺, calcd for C₁₃H₁₆NO₃ 234.1130.

Synthesis of but-2-ynoic acid 3,5-dimethylphenyl ester (**23**)

But-2-ynoic acid 3,5-dimethylphenyl ester (**23**)

To a solution of 3,5-dimethylphenol (500 mg, 4.05 mmol) in CH₂Cl₂ (7 ml) was added 2-butynoic acid (347.6 mg, 4.05 mmol), DMAP (50.0 mg, 0.405 mmol), and the solution of DCC (844.4 mg, 4.05 mmol) in CH₂Cl₂ (1 ml) at 0 °C. After 2 h, the precipitate was filtered off and the filtrate was washed with H₂O, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:8) to give **23** (729.6 mg, 96%) as

a white solid (m.p. 39-41 °C).

δ_{H} (CDCl₃, 300 MHz) 2.04 (s, 3H), 2.32 (s, 6H), 6.73 (s, 2H), 6.87 (s, 1H).

δ_{C} (CDCl₃, 75 MHz) 3.8, 21.1, 72.1, 87.6, 118.8, 127.9, 139.3, 149.9, 152.0.

ν_{max} (NaCl)/cm⁻¹ 1726, 1618, 1589, 1469, 1233, 1135, 1054.

HRFABMS m/z 189.0934 (M+H)⁺, calcd for C₁₂H₁₃O₂ 189.0916.

Synthesis of 4-(Furan-3-ylmethoxy)-but-2-ynoic acid methyl ester (25)

3-Furymethyl propargyl ether (VI)

3-Furymethanol (1.5 ml, 17.24 mmol) was added dropwise at to a stirred suspension of NaH (758.6 mg, 18.97 mmol) in THF (15 ml). After 10 min., propargyl bromide (2.1 ml, 18.97 mmol) was added and the mixture was stirred for 16 h at rt. Water was added and the crude product was extracted with EtOAc (30 ml x 3) and dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:8) to give 3-Furymethyl propargyl ether (1.7 g, 72%) as a colorless oil.²

δ_{H} (CDCl₃, 300 MHz) 2.44 (t, J = 2.4 Hz, 1H), 4.13 (d, J = 2.4, 2H), 4.47 (s, 2H), 6.41 (br s, 1H), 7.39 (d, J = 1.6 Hz, 1H), 7.43 (s, 1H).

δ_{C} (CDCl₃, 75 MHz) 56.68, 62.5, 74.6, 79.5, 110.4, 121.2, 141.2, 143.4.

4-(Furan-3-ylmethoxy)-but-2-ynoic acid methyl ester (25)

To a solution of 3-Furymethyl propargyl ether (944.4 mg, 6.94 mmol) in THF (14 ml) was added *n*-BuLi (4.8 ml, 1.6 M solution in hexanes, 7.63 mmol) dropwise at -78 °C. After 1 h, ClCO₂Me (650 μ l, 8.32 mmol) was added to the reaction mixture and the mixture was stirred for 3 h. Water

was added and the crude product was extracted with EtOAc (10 ml x 3) and dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel by eluting EtOAc-hexane (1:5) to give **25** (1.15 g, 85%) as a colorless oil.

δ_{H} (CDCl₃, 300 MHz) 3.77 (s, 3H), 4.24 (s, 2H), 4.47 (s, 2H), 6.40 (br s, 1H), 7.39 (d, J = 1.6 Hz, 1H), 7.42 (s, 1H).

δ_{C} (CDCl₃, 75 MHz) 52.8, 56.2, 63.0, 77.9, 83.4, 110.3, 120.8, 141.3, 143, 6, 153.5.

ν_{max} (NaCl)/cm⁻¹ 2240, 1716, 1436, 1261, 1059, 751.

HREIMS m/z 193.0500 (M-H)⁺, calcd for C₁₀H₉O₄ 193.0501.

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