JOC The Journal of Organic Chemistry

Note

Ruthenium-Catalyzed 1,6-Aromatic Enamide–Silylalkyne Cycloisomerization: Approach to 2,3-Disubstituted Indoles

Kohei Takamoto, Shohei Ohno, Norimichi Hyogo, Hiromichi Fujioka, and Mitsuhiro Arisawa

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b01288 • Publication Date (Web): 21 Jul 2017

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Note

Ruthenium-Catalyzed 1,6-Aromatic Enamide–Silylalkyne Cycloisomerization: Approach to 2,3-Disubstituted Indoles

Kohei Takamoto, Shohei Ohno, Norimichi Hyogo,

Hiromichi Fujioka, Mitsuhiro Arisawa*

Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamada-oka, Suita, Osaka 565-0871, Japan

e-mail: arisaw@phs.osaka-u.ac.jp

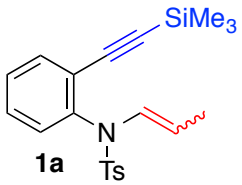
Abstract

Cycloisomerization is an atom economic procedure that converts dienes and enynes into cyclic molecules. To date, cycloisomerization between enamides and silylalkynes has not been explored. We found that *N*-acyl-*N*-vinyl-2-silylalkynylaniline derivatives undergo a cycloisomerization in the presence of a well-defined ruthenium hydride to give a 2,3-disubstitued indole. The vinyl and silylmethyl substituents on the 2- and 3-positions of the indole can be easily converted to other functional groups.

Transition metal-catalyzed cycloisomerization of enynes is a powerful atom economic method for accessing cyclic structures from acyclic precursors with substantially less molecular complexity than that of their products.[1, 2]

Enamides are highly stable and commonly present in natural products and drugs, [3] making these compounds important building blocks in organic chemistry. The majority of synthetic applications of enamides[4] documented in the literature relate to their

asymmetric reductions[5], nucleophilic additions[6], cycloadditions, radical reactions, and oxidation reactions. Transition metal-catalyzed regioselective functionalization of enamides can be used to rapidly construct nitrogen-containing heterocycles.[7] For example, the Mizoroki-Heck reaction has been applied to enamides[8] and enamide-ene ring-closing metathesis[9] for various applications in the total synthesis of natural products. Cyclization between an alkyne and enamide to give piperidine has been catalyzed by a Pt or Au π-electrophilic Lewis acids.[10] In addition, several groups have reported pyrrole synthesis using Rh or Ru catalyzed oxidative annulations of enamides.[11] Fukuyama and Tokuyama reported Cu-catalyzed *N*-arylation of enecarbamates to construct an indole. On the bases of these earlier studies, we envisioned that cycloisomerization between an aromatic enamide and a silylalkyne moiety could give a 2,3-disubstituted indole with synthetically useful vinyl and trimethylsilylmethyl groups at the 2- and 3-positions, respectively. [12] Indole is present in numerous bioactive natural products and pharmaceuticals.[13]



1a

Figure 1. *N*-Toluenesulfonyl-*N*-vinyl-2-trimethylsilylethynylaniline (**1a)**

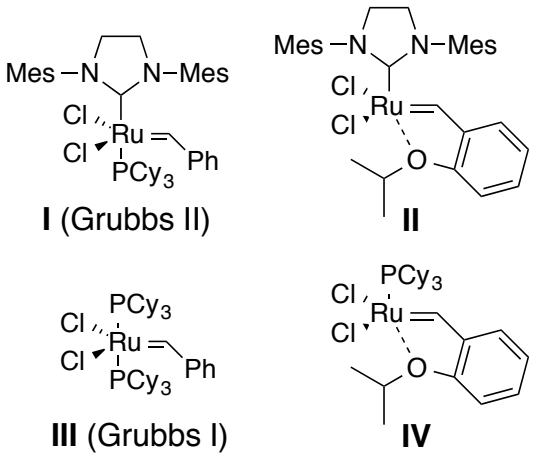
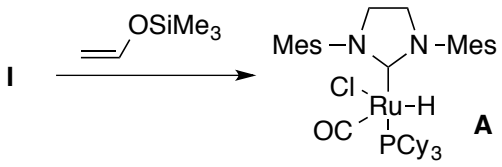


Figure 2. Ruthenium carbene catalysts (**I–IV)**

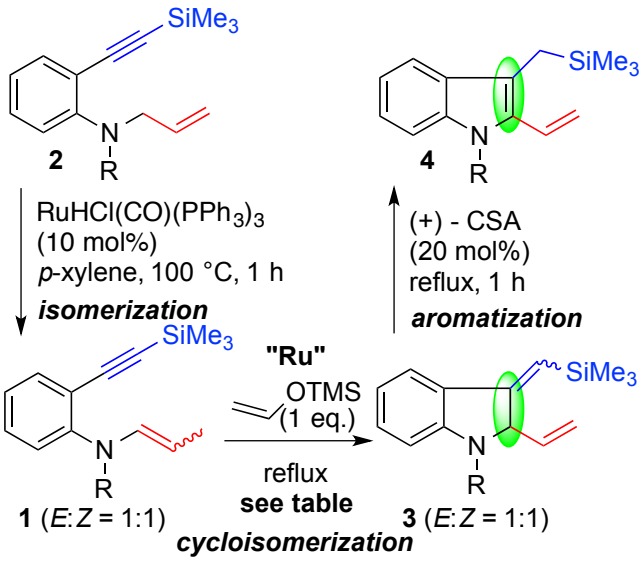


Scheme 1. Ruthenium hydride **A** with a nitrogen-containing heterocyclic carbene ligand.

We prepared *N*-toluenesulfonyl-*N*-vinyl-2-trimethylsilylethynylaniline (**1a**, Figure 1) from **2a** and $RuHCl(CO)(PPh_3)_3$ quantitatively, and attempted cycloisomerization of **1a** under various conditions using a conventional catalyst system, including Pd[12]. However, we obtained only trace amounts of the expected indole. Then, we treated **1a** under various conditions with commercially available ruthenium hydrides, $RuHCl(CO)(PPh_3)_3$ and $RuH_2(CO)(PPh_3)_3$, and ruthenium hydride **A**,[14] which contains a nitrogen-containing heterocyclic carbene ligand (Figure 2, Scheme 1). When **1a** was treated with 10% (mole fraction) of $RuHCl(CO)(PPh_3)_3$ or $RuH_2(CO)(PPh_3)_3$ under reflux in *p*-xylene, the

expected indole **3a** or **4a** was obtained in low yield. The same reaction, with the use of ruthenium hydride **A**, generated from ruthenium carbene catalyst **I** (Scheme 1), followed by aromatization with (+)-10-camphorsulfonic acid, (+)-CSA, yielded the corresponding 3-trimethylsilylmethyl-2-vinylindole **4a** in 41% yield (Table 1, run 1). Compound **4a** could be a useful synthon, because it has functional groups allowing for further chemical transformations at both the 2- and 3-positions of the indole. Before examining these chemical transformations, we optimized the substrate and reaction conditions for this cycloisomerization.

Table 1. Cycloisomerization of **1** to give **3** and **4**.



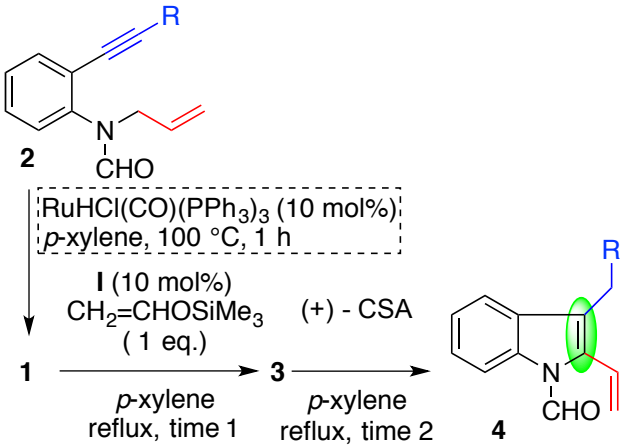
run	substrate		"Ru"	time	isolated yield (%)	
		R =	(mol%)	(h)	**1**	**4**
1	**2a**	Ts	**I** (10)	3	54	41
2	**2a**	Ts	$RuHCl(CO)(PPh_3)_3$ (10)	3	75	trace
3	**2a**	Ts	$RuH_2Cl(CO)(PPh_3)_2$ (10)	3	90	trace
4	**2b**	CHO	**I** (10)	0.5	-	92
5	**2b**	CHO	**I** (5)	2	-	80
6 [a)]	**2b**	CHO	**I** (2)	12	-	83
7	**2b**	CHO	**II** (10)	1	-	80
8	**2b**	CHO	**III** (10)	3	-	61
9	**2b**	CHO	**IV** (10)	3	-	71
10	**2b**	CHO	$RuHCl(CO)(PPh_3)_3$ (10)	3	44	18
11	**2b**	CHO	$RuH_2Cl(CO)(PPh_3)_2$ (10)	3	42	16

a) Performed in a glove box with oxygen and moisture levels less than 1 ppm.

We applied catalyst **A** to the cycloisomerization of **1a** under various reaction conditions, solvents, and temperatures in a conventional heating system. However, the yield of **4a** did not increase. These results suggested that cycloisomerization of **1a** to **3a** requires a

high temperature. Thus, we reduced the size of the substituents on the aromatic amine to promote the cyclization. Formyl derivative **1b** was subjected to the same experimental conditions as those used for run 1. As expected, **1b** was converted to the cyclized compound **4b** in 92% yield (run 4). When the amount of catalyst **I** was reduced, the yield of **4b** decreased, even when the reaction time was increased (runs 5 and 6). In runs 7–9, we respectively used ruthenium carbene catalysts **II**, **III**, and **IV** instead of **I**. Control experiments with commercially available ruthenium hydrides, $RuHClCO(PPh_3)_3$ and $RuH_2CO(PPh_3)_2$, showed no conversion of **1b** to **3b** or **4b**. These results indicate that the presence of a nitrogen-containing heterocyclic carbene ligand might be necessary for this cycloisomerization to proceed quantitatively. We also tried to catalyze the first two steps, i.e., the isomerization/cycloisomerization, with a single catalytic system. Thus, **2b** was treated with Grubbs II (10 mol%) and vinyloxy-trimethylsilane (1 eq.) in refluxing *p*-xylene for 4 hours and we obtained the corresponding **3b** in only 14% yield. Furthermore, control experiments with the use of $Pd(OAc)_2(PPh_3)_2$[15] or $[IrCl(cod)]_2$[16], which has been used in a previous 1,6-enyne cycloisomerization, failed to convert **1b** to **3b** or **4b**.

Table 2. Effect of the alkyne substituent on the reaction yield.

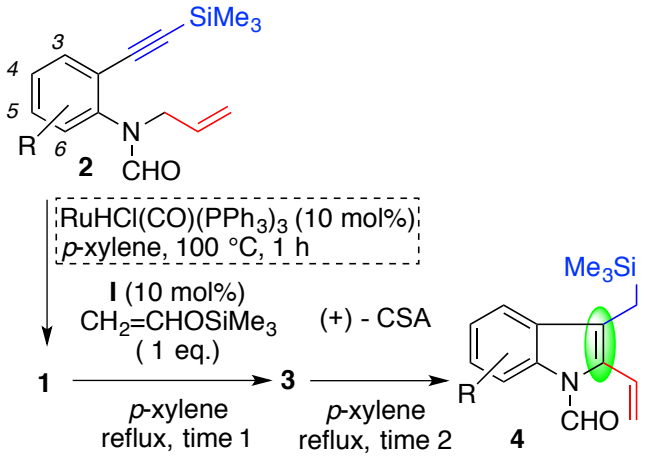


run		R =	time 1 (h)	(+)-CSA (mol%)	time 2 (h)	yield of **4** (%, 3 steps)
1	**2b**	$SiMe_3$	0.5	20	1	**4b** (92)
2	**2c**	$SiMe_2Ph$	0.5	20	1	**4c** (83)
3	**2d**	$SiMe_2Bn$	1	20	1	**4d** (89)
4	**2e**	*t*Bu	1	100	8	**4e** (70)
5	**2f**	CH_2OSi*i*-Pr_3	2	100	2	**4f** (24)
6	**2g**	H	0.5	-	-	**4g** (0)

On the basis of these results, we next examined the effect of alkyne substituents on the yield (Table 2). A one-pot reaction starting from the trialkylsilyl derivatives **2b** ($SiMe_3$), **2c** ($SiMe_2Ph$), and **2d** ($SiMe_2Bn$) gave the corresponding cyclized products **4** in respective yields of 92%, 83%, and 89%, *via* cycloisomerization of **1** to **3** (runs 1–3). The differences among these yields were most likely the result of steric effects. Derivatives with weaker electron donating groups on the alkyne (i.e., *tert*-butyl derivative **1e**, silyloxymethyl derivative **1f**, and proton derivative **1g**) prepared from the corresponding compounds **2** did not participate in this reaction very well. Compound **1g**

gave a complex mixture (run 6), and **1e** and **1f** were converted to **4e** and **4f** in 70% and 24% yields, respectively (runs 4 and 5).

Table 3. Effect of benzene ring substituents on the reaction yield.

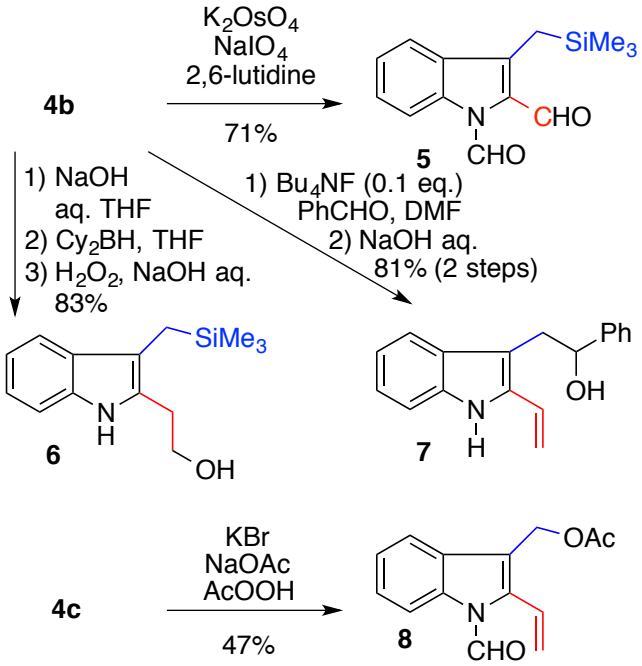


run		R =	time 1 (h)	(+)-CSA (mol%)	time 2 (h)	yield of **4** (%, 3 steps)
1	**2b**	H	0.5	20	1	**4b** (92)
2	**2h**	3-Cl	3	20	12	**4h** (60)
3	**2i**	4-Cl	3	20	6	**4i** (73)
4	**2j**	5-Cl	2.5	20	6	**4j** (85)
5	**2k**	6-Cl	3	40	12	**4k** (62)
6	**2l**	4-Me	3	20	1	**4l** (75)
7	**2m**	5-Me	3	20	1	**4m** (78)
8	**2n**	4-OMe	2.5	20	1	**4n** (84)
9	**2o**	4-CO_2Me	2	20	1	**4o** (64)

The effects of substituents on the benzene ring were used to investigate the scope and mechanism of this cycloisomerization (Table 3). All of the substrates **2h–o** were subjected to the one-pot reaction conditions used in Table 1, entry 2 (Table 3). Compounds **2i–n** were converted to the cycloisomerized product **4** in good to excellent

yields. However, **2h**, with a substituent at the 3-position, and **2o** with a methyl ester substituent at the 4-position, were converted to **4h** (60% yield) and **4o** (64% yield), respectively (Table 3, entries 2 and 9). These results and the structure of product **4** suggest that some ruthenium hydride species reacted with the silylalkyne moiety faster than the vinyl ether moiety on **1** in this cycloisomerization.

Chemical transformations of **4b** were possible (Scheme 2). For example, the vinyl group at the 2-position of indole **4b** was converted to the corresponding formyl derivative **5** via Lemieux–Johnson oxidation or to the hydroxyethyl derivative **6**, by deformylation and hydroboration-oxidation in good yield. The trimethylsilylmethyl group at the 3-position of **4b** reacted with benzaldehyde in the presence of fluoride ions, and the deformydated carbon–carbon bond forming product **7** was obtained in 81% yield. The dimethyl(phenyl)silyl group at the 3-position of **4c** was converted to the corresponding acetoxy derivative **8** in 47% yield.



Scheme 2. Chemical transformations of **4b** and **4c**.

Finally, we used NMR spectroscopy to detarmine the active ruthenium species in this cycloisomerization. We compared the ^{1}H- and ^{31}P-NMR spectra of catalysts (**I** and **A**) in *p*-xylene and the reaction mixture for the cycloisomerization. For catalyst **I**, we observed signals for the benzylidene proton at 19.7 ppm in the ^{1}H-NMR spectrum and tricyclohexylphosphine at 29.8 ppm in the ^{31}P-NMR spectrum. In the spectra of the cycloisomerization reaction mixture, new catalyst **A** peaks appeared within 10 min along with peaks for the cycloisomerized compound **3b**; however, whereas the ruthenium carbene catalyst **I** and substrate **1b** peaks disappeared (Figure 3). Between 141 and 239 min, no peaks from catalyst **A** or peaks indication further generation of **3b** could be observed. These results together with those of our control experiments (Tables 2 and 3) suggest that the cycloisomerization proceeds via ruthenium hydride **A**, and a

plausible reaction mechanism is given in Scheme 3. Ruthenium hydride **A**, generated *in situ* from Grubbs II could selectively coordinate to silylalkyne moiety of **1** to gave cycloisomerized product **3**.

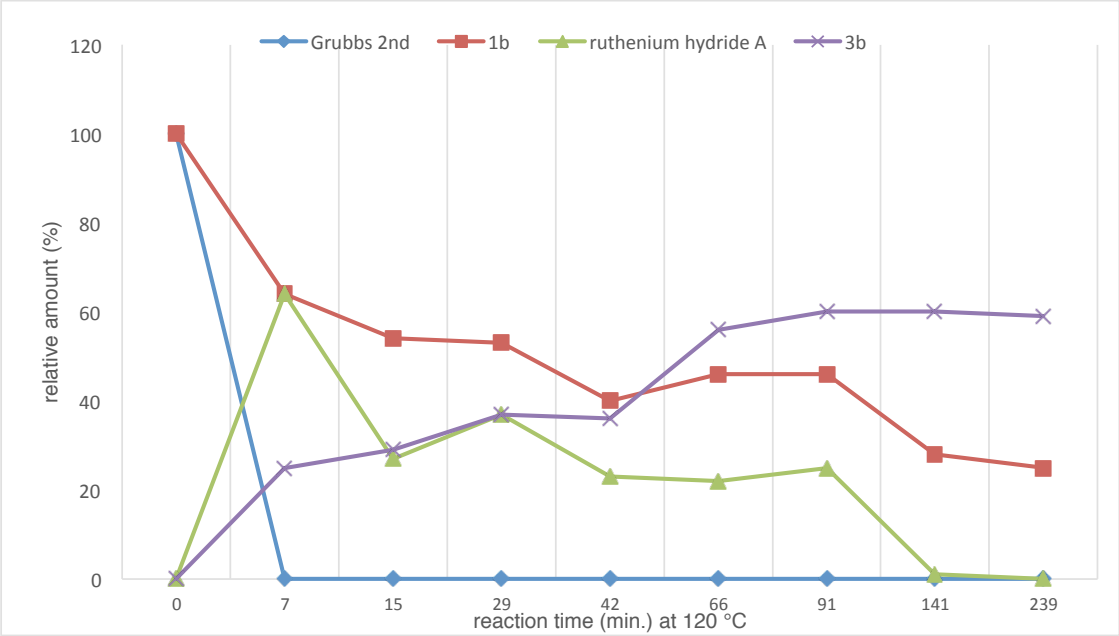
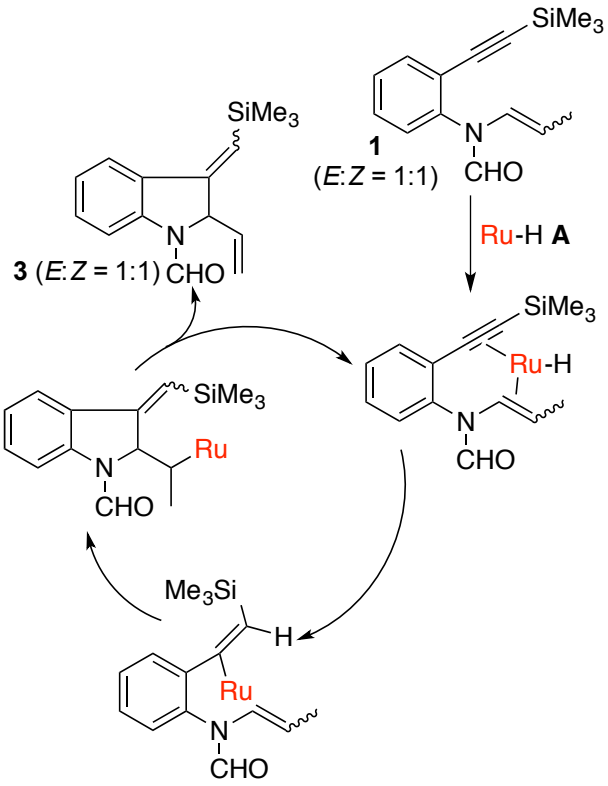


Figure 3. NMR time course experiments.



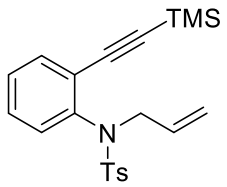
Scheme 3. Proposed reaction mechanism.

In conclusion, our ruthenium hydride-catalyzed cycloisomerization of **1** with trialkylsilylalkyne and enamide moieties, and subsequent aromatization gives a 2,3-disubstituted indole **4**, with vinyl and trimethylsilylmethyl groups at the 2- and 3-positions, respectively. The functional groups of **4** can be efficiently converted to other functional groups. This is an example of a non-metathesis reaction with the use of a ruthenium carbene catalyst[17], which will be of interest owing to the widespread application of these catalysts in functional molecular synthesis.

Experimental Section

Preparation of 2

• Preparation of **2a**



2a

To a stirring solution of 2-iodoaniline (664 mg, 3.03 mmol, 1.0 eq.) in THF (15 ml) and *i*Pr_2NH (15 ml) was added trimethylsilylacetylene (500 µl, 3.63 mmol 1.2 eq.), $PdCl_2(PPh_3)_2$ (53 mg, 0.0758 mmol 2.5 mol%), CuI (14 mg, 0.0758 mmol 2.5 mol%), and the mixture was stirred at 50 °C for 1 h. The mixture was filtered on celite pad and concentrated. The residue was purified by column chromatography to give 2-[(trimethylsilyl)ethynyl]aniline. (*n*-hexane:AcOEt = 12:1) (516 mg, 2.73 mmol, 90%)

To a stirring solution of *2*-[(trimethylsilyl)ethynyl]aniline (516 mg, 2.73 mmol 1.0 eq.) in CH_2Cl_2 (27 ml, 0.1 M), was added pyridine (0.66 ml 8.19 mmol 3.0 eq.) and TsCl (1.04 g, 5.46 mmol, 2.0 eq.). The mixture was stirred for 8 h. at room temperature. The reaction was quenched by the addition of $NaHCO_3$ and the organic compounds were extracted with CH_2Cl_2. The organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The obtained residue was subjected to column chromatography (*n*-hexane:AcOEt = 8:1) to give *N*-tosyl-2-[(trimethylsilyl)ethynyl]aniline (938 mg, 2.73 mmol, quant.).

To a stirring solution of *N*-tosyl-2-[(trimethylsilyl)ethynyl]aniline (938 mg, 2.73 mmol, 1.0 eq.) in MeCN (5.5 ml, 0.50 M), was added K_2CO_3 (755 mg, 5.46 mmol 2.0 eq.) and allyl bromide (1.9 ml 21.8 mmol, 8.0 eq.) and the mixture was refluxed for 9 h. After the mixture was cooled to room temperature, the reaction was quenched by the addition of H_2O and the organic compounds were extracted with Et_2O. The organic layers were washed with brine, dried over Na_2SO_4 and the solvent was removed under reduced pressure. The obtained residue was subjected to column chromatography (*n*-hexane:AcOEt = 10:1) to give **2a** (860 mg, 2.24 mmol, 82%).

2a; Pale yellow oil; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.63 (2H, d, *J* = 8.0 Hz), 7.45 (1H, d, *J* = 7.5 Hz), 7.32-7.24 (5H, m), 5.86 (1H, ddt, *J* = 17.2, 10.3, 6.3 Hz), 5.08 (1H, d, *J* = 17.2 Hz), 5.05 (1H, d, *J* = 10.3 Hz), 4.33 (2H, d, *J* = 6.3 Hz), 2.43 (3H, s), 0.17 (9H, s) ppm; ^{13}C-NMR ($CDCl_3$, 125 MHz): δ: 143.3, 140.3, 137.4, 134.1, 133.5, 132.3, 129.7, 129.2, 128.1, 128.0, 123.8, 118.7, 101.9, 100.0, 53.2, 21.8, -0.1 ppm; HRMS (MALDI-TOF) calcd for $C_{21}H_{25}NO_2NaSiS$ $[M+Na]^+$ 406.1267, found 406.1267.; Anal

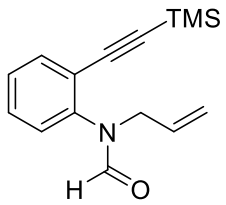
calcd for $C_{21}H_{25}NO_2SiS$: C, 65.76; H, 6.57; N, 3.65, found: C, 65.69; H, 6.68; N, 3.73.

• General procedure A for preparation of **2b**-**2e**, **2h**-**2o**

A solution of formic acid (3.0 eq.) and acetic anhydride (3.6 eq.) was stirred at 60 °C for 3 h. To the resulting mixture was added a 2-iodoaniline derivative (1.0 eq.) in THF (0.1 M) at room temperature and the mixture was stirred for 1 h. Then the solvent was removed in reduced pressure to give the corresponding *N*-formyl-2-iodoaniline derivative.

To a stirred solution of above *N*-formyl-2-iodoaniline compound (1.0 eq.) in THF-*i*Pr_2NH (1:1) was added a suitable acetylene derivative (1.2 eq.), CuI (5 mol%) and $PdCl_2(PPh_3)_2$ (2 mol%). The mixture was stirred at 50 °C for 1 h. The mixture was filtered on celite pad and the mother liquor was concentrated to remove the solvent. The residue was purified by column chromatography to give the corresponding *N*-formyl-2-[(trialkylsilyl)ethynyl]aniline derivative.

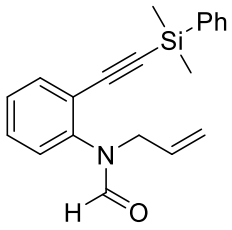
To a stirred solution of *N*-formyl-2-[(trialkylsilyl)ethynyl]aniline (1.0 eq.) in THF were added NaH (1.3 eq.) and allyl bromide (2.0 eq.). The mixture was stirred at 50 °C for 1.5 h. To the mixture, was added of sat. NH_4Cl aq. The organic compounds were extracted with Et_2O, dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to give **2**.



2b

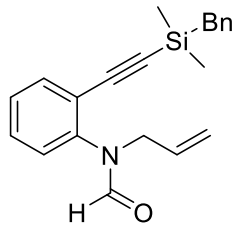
Following the general procedure A , **2b** (1.08 g, 4.18 mmol 46%) was prepared from 2-iodoaniline (2.00 g, 9.10 mmol) and trimethylsilylacetylene (1.5 ml, 10.9 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Colorless oil; ^{1}H-NMR (130 °C, DMSO-d_6, 500 MHz): δ 8.26 (1H, s), 7.53 (1H, d, *J* = 7.4 Hz), 7.46 (1H, dd, *J* = 7.4, 7.4 Hz), 7.34 (2H, m), 5.81 (1H, br m), 5.17 (1H, d, *J* = 17 Hz), 5.08 (1H, d, *J* = 5 Hz), 4,37 (2H, d, *J* = 5.5 Hz), 0.24 (9H, s) ppm; ^{13}C-NMR (70 °C, DMSO-d_6, 125 MHz): δ 161.7, 141.9, 132.63, 132.57, 129.8, 127.3, 127.2, 120.3, 117.2 101.6, 99.5, 47.0, -0.7 ppm; HRMS (MALDI-TOF) calcd for $C_{15}H_{20}NOSi$ $[M+H]^+$ 258.1309, found

258.1307.; Anal calcd for $C_{15}H_{19}NOSi$: C, 69.99; H, 7.44; N, 5.44, found: C, 70.29; H, 7.46; N, 5.44.



2c

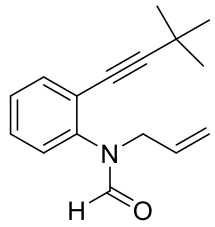
Following the general procedure A, **2c** (176 mg, 0.551 mmol 27%) was prepared from 2-iodoaniline (442 mg, 2.02mmol) and dimethylphenylsilylacethlene (0.43 ml, 2.42 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Pale yellow oil; ^{1}H-NMR (130 °C, DMSO-d_6, 500 MHz) δ: 8.13 (1H, s), 7.50-7.20 (9H, m), 5.62 (1H, br m), 4.99 (1H, d, *J* = 17.2 Hz) 4.90 (1H, d, *J* = 8.6 Hz), 4.21 (2H, br m), 0.32 (6H, s) ppm; ^{13}C-NMR (115 °C, DMSO-d_6, 125 MHz) δ: 162.5, 142.6, 136.4, 133.9, 133.7, 133.3, 130.8, 130.1, 128.4, 128.2, 128.1, 120.9, 118.1, 103.8, 98.2, 47.8, -0.8 ppm; HRMS (MALDI-TOF) calcd for $C_{20}H_{21}NONaSi$ $[M+Na]^+$ 342.1285, found 342.1272.; Anal calcd for $C_{20}H_{21}NOSi$: C, 75.19; H, 6.63; N, 4.38, found: C, 75.45; H, 6.76; N, 4.58.



2d

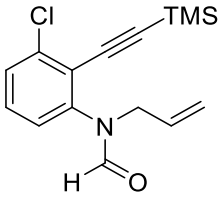
Following the general procedure A, **2d** (1.55 g, 4.64 mmol 70%) was prepared from 2-iodoaniline (1.44 g, 6.59 mmol) and benzyldimethylsilylacetylene[18] (1.38 g, 7.91 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 7:1). Pale yellow oil; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.43 (1H, s), 7.68 (1H, dd, *J* = 8.0, 1.7 Hz), 7.53 (1H, ddd, *J* = 7.7, 7.7, 1.7 Hz), 7.43 (1H, ddd, *J* = 7.7, 7.7, 1.7 Hz) 7.41-7.37 (3H, m), 7.33 (1H, d, *J* = 8.0), 7.25 (2H, d, *J* = 8.0), 5.93 (1H, ddd, *J* = 16.8, 10.3, 6.3 Hz), 5.31 (1H, dd, *J* = 16.8, 1.3 Hz), 5.25 (1H, dd, *J* = 10.3, 1.3 Hz), 4.55 (2H, d, *J* = 6.3 Hz),

2.43 (2H, s), 0.36 (6H, s) ppm; ^{13}C-NMR (70 °C, DMSO-d_6, 125 MHz) δ: 162.6, 142.1, 138.6, 133.7, 132.4, 129.6, 128.3, 128.2, 127.5, 127.5, 124.4, 121.6, 118.2, 102.2, 99.1, 48.2, 25.9, -2.3 ppm; HRMS (MALDI-TOF) calcd for $C_{21}H_{24}NOSi$ $[M+H]^+$ 334.1622, found 334.1621.



2e

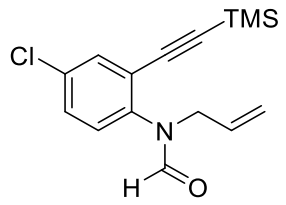
Following the general procedure A, **2e** (460 mg, 1.91 mmol 94%) was prepared from 2-iodoaniline (442 mg, 2.02 mmol) and 3,3-Dimethyl-1-butyne (0.30 ml, 2.42 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Pale yellow oil; ^{1}H-NMR (110 °C, DMSO-d_6, 500 MHz) δ: 8.17 (1H, s), 7.40-7.25 (4H, m), 5.73 (1H, ddt, *J* = 16.6, 10.3, 5.7 Hz), 5.12 (1H, d, *J* = 16.6 Hz), 5.02 (1H, d, *J* = 10.3 Hz), 4.31 (2H, d, *J* = 5.7 Hz), 1.24 (9H, s) ppm; ^{13}C-NMR (110 °C, DMSO-d_6, 125 MHz) δ: 161.4, 141.1, 132.5, 132.0, 128.3, 127.0, 126.9, 121.3, 116.8, 103.2, 75.4, 46.8, 29.9, 27.2 ppm; HRMS (MALDI-TOF) calcd for $C_{16}H_{20}NO$ $[M+H]^+$ 242.1539, found 242.1539.



2h

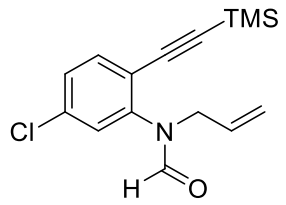
Following the general procedure A, **2h** (483 mg, 1.66 mmol 42%) was prepared from 3-chloro-2-iodoaniline (1.00 g, 3.95 mmol) trimethylsilylacetylene (0.65 ml, 4.74 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Pale yellow oil; ^{1}H-NMR (130 °C, DMSO-d_6, 500 MHz) δ: 8.28 (1H, s), 7.51 (1H, d, *J* = 8.0 Hz), 7.44 (1H, dd, *J* = 8.0, 4.0 Hz), 7.34-7.32 (1H, br m), 5.81-5.79 (1H, br m), 5.19 (1H, d, *J* = 17.2 Hz), 5.10 (1H, d, *J* = 10.3 Hz), 4.36 (2H, d, *J* = 5.7 Hz), 0.26 (9H, s) ppm; ^{13}C-NMR (DMSO-d_6, 125 MHz) δ: 162.3, 143.9, 135.6, 132.6, 130.6, 128.2, 126.3, 120.6, 117.9, 105.6, 98.3, 47.2, -0.5 ppm; HRMS (MALDI-TOF) calcd for

$C_{15}H_{18}ClNONaSi$ $[M+Na]^+$ 314.0738, found 314.0730.; Anal calcd for $C_{15}H_{18}ClNOSi$: C, 61.73; H, 6.22; N, 4.80, found: C, 61.79; H, 6.26; N, 4.80.



2i

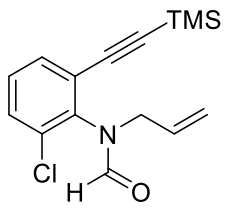
Following the general procedure A, **2l** (112 mg, 0.384 mmol 17%) was prepared from 4-chloro-2-iodoaniline (573 mg, 2.26 mmol) trimethylsilylacetylene (0.38 ml, 2.71 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Colorless oil; ^{1}H-NMR (130 °C, DMSO-d_6, 500 MHz): δ 8.26 (1H, s), 7.54 (1H, s), 7.49 (1H, d, *J* = 8.5 Hz), 7.36 (1H, br m), 5.79 (1H, br m), 5.18 (1H, d, *J* = 17 Hz), 5.10 (1H, d, *J* = 9.5 Hz), 4,35 (2H, d, *J* = 6.0 Hz), 0.25 (9H, s) ppm; ^{13}C-NMR (70 °C DMSO-d_6, 125 MHz): δ 161.6, 140.8, 132.3, 131.8, 131.5, 129.8, 129.0, 122.1, 117.5, 101.1, 100.1, 46.9, -0.9 ppm; HRMS (MALDI-TOF) calcd for $C_{15}H_{19}ClNOSi$ $[M+H]^+$ 292.0919, found 292.0921.; Anal calcd for $C_{15}H_{18}ClNOSi$: C, 61.73; H, 6.22; N, 4.80, found: C, 61.95; H, 6.33; N, 4.78.



2j

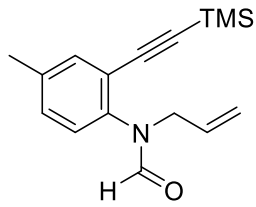
Following the typical procedure A, **2j** (112 mg, 0.384 mmol 17%) was prepared from 5-chloro-2-iodoaniline (573 mg, 2.26 mmol) trimethylsilylacetylene (0.38 ml, 2.71 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Colorless oil; ^{1}H-NMR (130 °C, DMSO-d_6, 500 MHz): δ 9.32 (1H, s), 8.31 (1H, d, *J* = 8.5 Hz), 7.38 (1H, d, *J* = 1.5 Hz), 7.30 (1H, dd, *J* = 8.5, 1.5 Hz), 6.78 (1H, dd, *J* = 18.0, 12.0 Hz), 5.66 (1H, d, *J* = 12.0 Hz), 5.53 (1H, d, *J* = 18.0 Hz), 2.16 (2H, s), 0.05 (9H, s) ppm; ^{13}C-NMR (70 °C, DMSO-d_6, 125 MHz): δ 161.7, 143.2, 133.94, 133.92, 132.4, 127.3, 127.1, 119.1, 117.4, 100.7, 100.6, 46.8, -0.8 ppm; HRMS (MALDI-TOF) calcd for $C_{15}H_{19}ClNOSi$ $[M+H]^+$ 292.0919, found 292.0919.; Anal calcd for $C_{15}H_{18}ClNOSi$: C,

61.73; H, 6.22; N, 4.80, found: C, 61.86; H, 6.27; N, 4.91.



2k

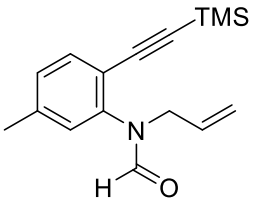
Following the general procedure A, **2k** (377 mg, 1.29 mmol 33%) was prepared from 6-chloro-2-iodoaniline (1.00 g, 3.95 mmol) trimethylsilylacetylene (0.65 ml, 4.74 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Colorless oil; ^{1}H-NMR (DMSO-d_6, 500 MHz) δ: 8.38 (0.3H, s), 8.09 (0.7H, s), 7.65 (0.7H, dd, *J* = 8.0, 1.1 Hz), 7.59 (0.3H, dd, *J* = 8.0, 1.1 Hz), 7.55 (0.7H, dd, *J* = 8.0, 1.1 Hz), 7.50 (0.3H, dd, *J* = 8.0, 1.1 Hz), 7.43 (0.7H, dd, *J* = 8.0, 8.0 Hz), 7.38 (0.3H, dd, *J* = 8.0, 8.0 Hz), 5.94 (0.3H, ddt, *J* = 16.9, 9.7, 6.8 Hz), 5.84-5.76 (0.7H, ddt, *J* = 17.2, 10.3, 6.8 m), 5.18-5.04 (2H,m), 4.44 (0.7H, dd, *J* = 14.9, 6.8 Hz), 4.37 (0.3H, dd, *J* = 15.1, 6.8 Hz), 4.30 (0.3H, dd, *J* = 15.1, 6.8 Hz), 4.164 (0.7H, dd, *J* = 14.9, 6.8 Hz), 0.24 (3H, s), 0.23 (6H, s) ppm; ^{13}C-NMR (DMSO-d_6, 125 MHz) δ: 161.9 161.5, 138.7, 138.3, 133.1, 132.9, 132.8, 132.0, 131.3, 131.2, 130.6, 130.2, 129.6, 129.1, 124.8, 124.2, 118.6, 118.5, 100.90, 100.87, 100.5, 99.9, 51.1, 47.0, -0.8, -0.9 ppm; HRMS (MALDI-TOF) calcd for $C_{15}H_{19}ClNOSi$ $[M+H]^+$ 292.0919, found 292.0918.; Anal calcd for $C_{15}H_{18}ClNOSi$: C, 61.73; H, 6.22; N, 4.80, found: C, 62.03; H, 6.39; N, 4.83.



2l

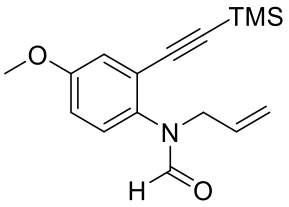
Following the general procedure A, **2l** (611 mg, 2.25 mmol 55%) was prepared from 4-methyl-2-iodoaniline (1.00 g, 4.29 mmol) trimethylsilylacetylene (0.71 ml, 5.15 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Pale yellow oil ; ^{1}H-NMR (110 °C, DMSO-d_6, 500 MHz) δ: 8.20 (1H, s), 7.35 (1H, s), 7.24 (2H, m), 5.77 (1H, br m), 5.16 (1H, d, *J* = 17.2 Hz), 5.06 (1H, d, *J* = 9.7 Hz), 4.33 (2H, d, *J* = 5.2 Hz), 2.31 (3H, s), 0.23 (9H, s) ppm; ^{13}C-NMR (110 °C, DMSO-d_6, 125 MHz) δ: 161.4,

139.2, 136.7, 132.7, 132.5, 130.1, 127.0, 120.2, 116.9, 101.5, 98.9, 46.8, 19.5, -1.0 ppm; HRMS (MALDI-TOF) calcd for $C_{16}H_{22}NOSi$ $[M+H]^+$ 272.1465 found 272.1464.



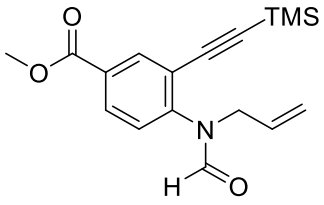
2m

Following the general procedure A, **2m** (421 mg, 1.55 mmol 36%) was prepared 4-methyl-2-iodoaniline (1.00 g, 4.29 mmol) trimethylsilylacetylene (0.71 ml, 5.15 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Pale yellow oil ; ^{1}H-NMR (110 °C, DMSO-d_6, 500 MHz) δ: 8.23 (1H, s), 7.41 (1H, d, *J* = 8.2 Hz), 7.16 (2H, m), 5.78 (1H, br m), 5.18 (1H, d, *J* = 17.2 Hz), 5.07 (1H, d, *J* = 10.3 Hz), 4.36 (2H, d, *J* = 5.2 Hz), 2.35 (3H, s), 0.22 (9H, s) ppm; ^{13}C-NMR (110 °C, DMSO-d_6, 125 MHz) δ: 161.3, 141.6, 139.8, 132.5, 132.2, 127.6, 127.5, 117.3, 116.8, 101.6, 98.5, 46.8, 20.2, -1.0 ppm; HRMS (MALDI-TOF) calcd for $C_{16}H_{22}NOSi$ $[M+H]^+$ 272.1465 found 272.1465.



2n

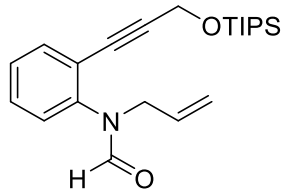
Following the general procedure A, **2n** (251 mg, 0.872 mmol 30%) was prepared from 2-iodo-4-methoxyaniline (735 mg, 2.95 mmol) trimethylsilylacetylene (0.49 ml, 3.54 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Pale yellow oil; ^{1}H-NMR (130 °C, DMSO-d_6, 500 MHz): δ: 8.15 (1H, s), 7.25 (1H, d, *J* = 8.0 Hz), 7.04-7.01 (2H, br m), 5.79 (1H, br m), 5.16 (1H, d, *J* = 17.2 Hz), 5.08 (1H, d, *J* = 9.7 Hz), 4.29 (2H, d, *J* = 5.7 Hz), 3.81 (3H, s), 0.24 (9H, s) ppm; ^{13}C-NMR (120 °C, DMSO-d_6, 125 MHz) δ: 161.9, 157.9, 134.9, 132.7, 129.0, 121.8, 117.3, 116.6, 116.2, 101.5, 99.3, 55.4, 47.2, -0.7 ppm; HRMS (MALDI-TOF) calcd for $C_{16}H_{22}NO_2Si$ $[M+H]^+$ 288.1414, found 288.1415.; Anal calcd for $C_{16}H_{21}NO_2Si$: C, 66.86; H, 7.36; N, 4.87, found: C, 66.85; H, 7.49; N, 4.85.



2o

Following the general procedure A, **2o** (90 mg, 0.285 mmol 17%) was prepared from Methyl 4-amino-3-iodobenzoate (460 mg, 1.66 mmol) trimethylsilylacetylene (0.28 ml, 1.99 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 8:1). Colorless plates; m.p.: 56-58 °C (from *n*-hexane); ^{1}H-NMR (65 °C, DMSO-d_6, 500 MHz) δ: 8.37 (1H, s), 8.02 (1H, s), 7.98 (1H, d, *J* = 8.6 Hz), 7.55 (1H, d, *J* = 8.6 Hz) 5.75 (1H, ddt, *J* = 16.9, 10.6, 5.2 Hz), 5.18 (1H, d, *J* = 16.9 Hz), 5.08 (1H, d, *J* = 10.6 Hz), 4.43 (2H, d, *J* = 5.2 Hz), 3.88 (3H, s), 0.23 (9H, s) ppm; ^{13}C-NMR (65 °C, DMSO-d_6, 125 MHz) δ: 164.0, 161.2, 145.2, 133.0, 131.8, 129.7, 127.7, 126.5, 119.4, 116.9, 100.14, 100.07, 51.6, 46.2, -1.3 ppm; HRMS (MALDI-TOF) calcd for $C_{17}H_{22}NO_3Si$ $[M+H]^+$316.1363 found 316.1363.

• Preparation of **2f**



2f

A solution of formic acid (0.23 ml, 6.06 mmol, 3.0 eq.) and acetic anhydride (0.69 ml, 7.27 mmol, 3.6 eq.) was stirred at 60 °C for 3 h. To the resulting mixture was added 2-iodoaniline (442 mg, 2.02 mmol, 1.0 eq.) in THF (20 ml, 0.1 M) at room temperature and the mixture was stirred for 1 h. Then the solvent was removed in reduced pressure to give *N*-formyl-2-iodoaniline (500 mg, 2.02 mmol, quant.)

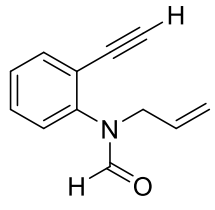
To a stirred solution of above *N*-formyl-2-iodoaniline (500 mg, 2.02 mmol 1.0 eq.) in THF-*i*Pr_2NH (1:1) (20 ml, 0.1 M) were added 3-propyn-1-ol (0.14 ml, 2.43 mmol, 1.2 eq.), CuI (19 mg, 0.101 mmol, 5 mol%) and $PdCl_2(PPh_3)_2$ (28 mg, 0.0404 mmol, 2 mol%). The mixture was stirred at 50 °C for 1 h. The mixture was filtered on celite pad and concentrated to remove the solvent.

To a stirred solution of above residue (2.02 mmol, 1.0 eq.) in CH_2Cl_2 were added Et_3N (0.42 ml, 3.03 mmol, 1.5 eq.) and triisopropylsilyl chloride (0.52 ml, 2.43 mmol, 1.2 eq.). The mixture was refluxed for 6 h. To the resulting mixture was added additional Et_3N (0.42 ml, 3.03 mmol, 1.5 eq.) and triisopropylsilyl chloride (0.52 ml, 2.43 mmol, 1.2 eq.). The mixture was refluxed for 12 h. To the mixture, was added of sat. $NaHCO_3$ aq. The organic compounds were extracted with CH_2Cl_2. The organic layers were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane/AcOEt = 1:2) to give *N*-formyl-2-[(trialkylsilyl)ethynyl]aniline (329 mg, 0.99 mmol, 49% (2 steps)).

To a stirred solution of *N*-formyl-2-[(trialkylsilyl)ethynyl]aniline (329 mg, 0.99 mmol, 1.0 eq.) in THF (10 ml, 0.1 M) were added NaH (52 mg, 1.29 mmol, 1.3 eq.) and allyl bromide (0.17 ml, 1.98 mmol, 2.0 eq.). The mixture was stirred at 50 °C for 1.5 h. To the mixture, was added sat. NH_4Cl aq. The organic compounds were extracted with Et_2O. The organic layers were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane/AcOEt = 4:1) to give **2f** (315 mg, 0.846 mmol 42%).

2f; Pale yellow oil; ^{1}H-NMR (115 °C, DMSO-d_6, 500 MHz) δ: 8.24 (1H, s), 7.55-7.30 (4H, m) 5.77 (1H, br m), 5.14 (1H, d, *J* = 17.2 Hz), 5.06 (1H, d, *J* = 9.7 Hz), 4.64 (2H, s), 4.38 (2H, br m), 1.11-1.06 (21H, m) ppm; ^{13}C-NMR (115 °C, DMSO-d_6, 125 MHz) δ: 161.2, 141.1, 132.6, 132.4, 129.1, 127.3, 127.0, 120.2 116.9, 92.9, 80.4, 51.5, 46.7, 17.1, 11.1 ppm; HRMS (MALDI-TOF) calcd for $C_{22}H_{33}NO_2NaSi$ $[M+Na]^+$ 394.2173, found 394.2172.

• Preparation of **2g**



2g

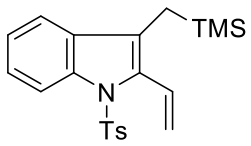
To a stirred solution of **2b** (91 mg, 0.354 mmol) in THF (3.5 mL) was added *n*-Bu_4NF (0.42 ml, 0.420 mmol, 1.0 M in THF). The mixture was stirred at 0 °C for 0.5 h. To the mixture, was added of sat. NH_4Cl aq. The organic compounds were extracted with Et_2O.

The organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane/AcOEt = 4:1) to give **2g** (315 mg, 0.846 mmol 42%).

2g; Pale yellow oil; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 8.31 (1H, s), 7.59 (1H, dd, *J* = 7.4, 1.7 Hz), 7.40 (1H, ddd *J* = 7.7, 7.4, 1.7 Hz), 7.31 (1H, ddd, *J* = 7.4, 7.4, 1.1 Hz), 7.21 (1H, dd, *J* = 7.7, 1.1 Hz), 5.86-5.79 (1H, ddt, *J* = 16.9, 10.3, 3.9Hz), 5.15 (1H, dd, *J* = 16.9, 1.4 Hz), 5.10 (1H, dd, *J* = 10.3, 1.4 Hz), 4.43 (2H, d, *J* = 3.9 Hz), 3.30 (1H, s) ppm; ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: 162.6, 142.2, 134.0, 132.3, 129.8, 127.6, 127.6, 120.7, 118.3, 82.8, 79.8, 48.2 ppm; HRMS (MALDI-TOF) calcd for $C_{12}H_{12}NO$ $[M+H]^+$ 186.0913, found 186.0914.

General procedure B: One-pot isomerization/cycloisomerization/aromatization from 2 to 4

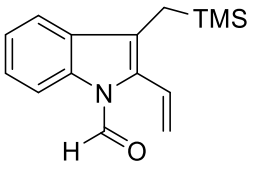
To a stirred solution of **2** (1.0 eq.) in degassed *p*-xylene (0.0125 M) was added $RuHCl(CO)(PPh_3)_3$ (10 mol%) under an Ar atmosphere and the mixture was stirred at 100 °C for 1 h. To the reaction mixture, was added vinyloxytrimethylsilane (1.0 eq.) and Grubbs II (10 mol%) at room temperature. The mixture was refluxed until TLC showed complete consumption of the isomerization product. Then to the reaction mixture was added (+)-CSA (20 mol%) and the mixture was refluxed until TLC showed complete consumption of the cycloisomerization product. The reaction mixture was concentrated in vacuo to remove the solvent, and the obtained residue was purified by flash column chromatography on silica gel to give **4**.



4a

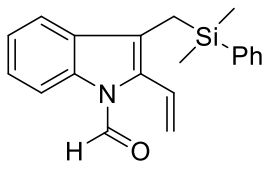
Following the general procedure B, **4a** (7 mg, 0.0193 mmol 41%) was obtained from *N*-allyl-*N*-formyl-2-((trimethylsilyl)ethynyl)aniline (18 mg 0.0474 mmol), $RuHCl(CO)(PPh_3)_3$ (5 mg, 0.00474 mmol), Grubbs 2nd catalyst (4 mg, 0.00474 mmol), trimethyl(vinyloxy)silane (7 μl, 0.0474 mmol) and (+)-10-canphorsulfonic acid (3 mg,

0.0948 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 20:1). Reaction time in cyclization and aromatization are 3 h. and 1 h., respectively. Colorless needles; m.p.:77-81 °C (from *n*-hexane); ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 8.20 (1H, d, *J* = 8.6 Hz), 7.51(2H, d, *J* = 8.1 Hz), 7.32-7.06 (6H, m), 5.53 (1H, dd, *J* = 11.5, 1.8 Hz), 5.37 (1H, dd, *J* = 17.8, 1.8 Hz), 2.27 (3H, s), 2.17 (2H, s), -0.13 (9H, s) ppm; ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 144.3, 136.9, 134.6, 132.2, 132.0, 129.2 128.6, 126.7, 125.1, 123.6, 123.4, 119.7, 117.8, 115.9, 21.4, 14.5, -0.8 ppm; HRMS (MALDI-TOF) calcd for $C_{21}H_{25}NO_2NaSiS$ $[M+Na]^+$ 406.1267, found 406.1253.



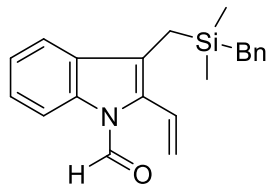
4b

Following the general procedure B, **4b** (14 mg, 0.0554 mmol 92%) was obtained from **2b** (16 mg 0.0602 mmol), $RuHCl(CO)(PPh_3)_3$ (6 mg, 0.00602 mmol), Grubbs 2nd catalyst (5 mg, 0.00602 mmol), trimethyl(vinyloxy)silane (9 μl, 0.0602 mmol) and (+)-10-canphorsulfonic acid (3 mg, 0.0120 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 25:1). Reaction time in cyclization and aromatization are 0.5 h. and 1 h., respectively. Pale yellow oil; ^{1}H-NMR (55 °C, $CDCl_3$, 500 MHz): δ 9.37 (1H, s), 8.37 (1H, d, *J* = 8.0 Hz), 7.43 (1H, d, *J* = 7.5 Hz), 7.35 (1H, dd, *J* = 8.0, 7.5 Hz), 7.29 (1H, dd, *J* = 8.0, 7.5 Hz), 6.82 (1H, dd, *J* = 17.5, 11.5 Hz), 5.62 (1H, d, *J* = 11.5 Hz), 5.51 (1H, d, *J* = 17.5 Hz), 2.22 (2H, s), 0.05 (9H, s) ppm; ^{13}C-NMR (55 °C, $CDCl_3$, 125 MHz): δ 159.4, 135.4, 131.0, 130.2, 125.6, 125.5, 124.1, 121.7, 120.2, 119.6, 115.7, 14.3, -0.6 ppm; HRMS (MALDI-TOF) calcd for $C_{15}H_{20}NOSi$ $[M+H]^+$ 258.1309, found 258.1307.; Anal calcd for $C_{15}H_{19}NOSi$: C, 69.99; H, 7.44; N, 5.44, found: C, 70.31; H, 7.55; N, 5.40.



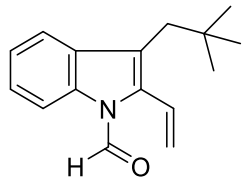
4c

Following the general procedure B, **4c** (171 mg, 0.535 mmol 83%) was obtained from **2c** (206 mg 0.646 mmol), $RuHCl(CO)(PPh_3)_3$ (62 mg, 0.0646 mmol), Grubbs 2nd catalyst (55 mg, 0.0646 mmol), trimethyl(vinyloxy)silane (96 μl, 0.646 mmol) and (+)-10-canphorsulfonic acid (30 mg, 0.129 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 25:1). Reaction time in cyclization and aromatization are 0.5 h. and 1 h, respectively. Pale yellow oil; ^{1}H-NMR (55 °C, $CDCl_3$, 400 MHz) δ: 9.25 (1H, s), 8.31 (1H, d, *J* = 8.2 Hz), 7.40-7.14 (8H, m), 6.54 (1H, dd, *J* = 17.9, 11.9 Hz), 5.43 (1H, d, *J* = 11.9 Hz), 5.29 (1H, d, *J* = 17.9 Hz), 2.35 (2H, s), 0.25 (6H, s) ppm; ^{13}C-NMR (55 °C, $CDCl_3$, 100 MHz) δ: 159.3, 138.3, 135.3, 133.6, 130.9, 130.6, 129.3, 127.9, 125.5, 125.2, 124.0, 120.7, 120.4, 119.7, 115.6, 14.0, -2.4 ppm; HRMS (MALDI-TOF) calcd for $C_{20}H_{21}NONaSi$ $[M+Na]^+$ 342.1285, found 342.1289.; Anal calcd for $C_{20}H_{21}NOSi$: C, 75.19; H, 6.63; N, 4.38, found: C, 75.24; H, 6.59; N, 4.49.



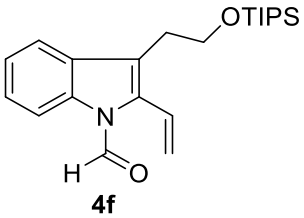
4d

Following the general procedure B, **4d** (29 mg, 0.0845 mmol 89%) was obtained from **2d** (32 mg 0.965 mmol), $RuHCl(CO)(PPh_3)_3$ (9 mg, 0.00965 mmol), Grubbs 2nd catalyst (8 mg, 0.00965 mmol), trimethyl(vinyloxy)silane (14 μl, 0.0965 mmol) and (+)-10-canphorsulfonic acid (5 mg, 0.0193 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 25:1). Reaction time in cyclization and aromatization are 3 h. and 1 h, respectively. Pale yellow oil; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 9.37 (1H, s), 8.41 (1H, d, *J* = 7.2 Hz), 7.40-7.01 (8H, m), 6.76 (1H, dd, *J* = 17.8, 11.8 Hz), 5.60 (1H, dd, *J* = 11.8, 1.0 Hz), 5.45 (1H, dd, *J* = 17.8, 1.0 Hz), 2.26 (2H, s), 2.20 (2H, s), 0.00 (6H, s) ppm; ^{13}C-NMR (70 °C, DMSO-d_6, 125 MHz) δ: 159.5, 139.4, 139.3, 135.1, 130.8, 130.2, 128.3, 128.1, 125.6, 125.0, 124.2, 124.1, 121.0, 120.5, 119.4, 26.1, 12.4, -2.7 ppm; HRMS (MALDI-TOF) calcd for $C_{21}H_{24}NOSi$ $[M+H]^+$ 334.1622, found 334.1622.



4e

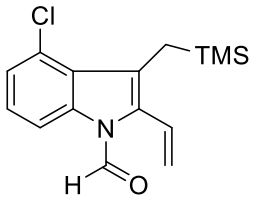
Following the general procedure B, **4e** (38 mg, 0.157 mmol 70%) was obtained from **2e** (54 mg 0.223 mmol), $RuHCl(CO)(PPh_3)_3$ (21 mg, 0.0223 mmol), Grubbs 2nd catalyst (19 mg, 0.0223 mmol), trimethyl(vinyloxy)silane (33 μl, 0.223 mmol) and (+)-10-canphorsulfonic acid (50 mg, 0.0223 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 25:1). Reaction time in cyclization and aromatization are 3 h. and 1 h, respectively. Pale yellow oil; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 9.39 (1H, s), 8.44 (1H, d, *J* = 7.7 Hz), 7.55 (1H, dd, *J* = 7.7 Hz, 1.1Hz), 7.33 (1H, ddd, *J* = 7.7, 7.4, 1.1 Hz), 7.31 (1H, ddd, *J* = 7.7, 7.4, 1.1 Hz) 6.84 (1H, dd, *J* = 17.6, 12.2 Hz), 5.70 (1H, d, *J* = 12.2 Hz), 5.49 (1H, d, *J* = 17.6 Hz), 2.67 (2H, s), 0.99 (9H, s) ppm; ^{13}C-NMR (55 °C, $CDCl_3$, 125 MHz) δ: 160.2, 135.1, 133.8, 131.6, 125.9, 125.2, 124.1, 122.2, 120.9, 120.3, 115.8, 37.1, 34.1, 30.3 ppm; HRMS (MALDI-TOF) calcd for $C_{16}H_{20}NO$ $[M+H]^+$ 242.1539, found 242.1530.



4f

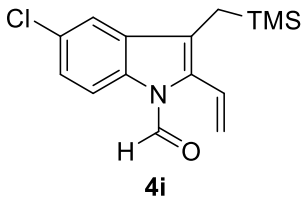
Following the general procedure B, **4f** (16 mg, 0.0431 mmol 24%) was obtained from **2f** (66 mg 0.180 mmol), $RuHCl(CO)(PPh_3)_3$ (17 mg, 0.0180 mmol), Grubbs 2nd catalyst (15 mg, 0.0180 mmol), trimethyl(vinyloxy)silane (27 μl, 0.180 mmol) and (+)-10-canphorsulfonic acid (42 mg, 0.180 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 20:1). Reaction time in cyclization and aromatization are 2 h. and 4 h., respectively. Colorless oil; ^{1}H-NMR (40 °C, $CDCl_3$, 500 MHz) δ: 9.33 (1H, s), 8.34 (1H, d, *J* = 7 Hz), 7.55 (1H, d, *J* = 7 Hz), 7.34 (1H, t, *J* = 7 Hz), 7.30 (1H, t, *J* = 7 Hz), 6.85 (1H, dd, *J* = 17, 12 Hz), 5.68 (1H, d, *J* = 12 Hz), 5.67 (1H, d, *J* = 17 Hz), 3.95 (2H, t, *J* = 7 Hz), 3.02 (2H, t, *J* = 7 Hz)., 1.09-0.98 (21H, m); ^{13}C-NMR (75 °C, DMSO-d_6, 125 MHz) δ: 159.7, 134.0, 133.6, 130.1, 124.8, 124.6, 123.6, 121.4, 119.0,

118.1, 114.3, 62.3, 27.3, 17.3, 11.1.; HRMS (MALDI-TOF) calcd for $C_{22}H_{33}NO_2Si$ $[M]^+$ 371.2275, found 371.2274.



4h

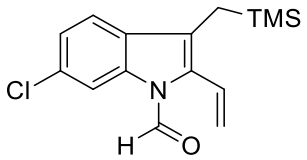
Following the general procedure B, **4h** (35 mg, 0.119 mmol 60%) was obtained from **2h** (58 mg 0.199 mmol), $RuHCl(CO)(PPh_3)_3$ (19 mg, 0.0199 mmol), Grubbs 2nd catalyst (17 mg, 0.0199 mmol), trimethyl(vinyloxy)silane (30 μl, 0.199 mmol) and (+)-10-canphorsulfonic acid (9 mg, 0.0398 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 25:1). Reaction time in cyclization and aromatization are 3 h. and 12 h., respectively. Colorless plates; m.p.:52-54 °C (from *n*-hexane); ^{1}H-NMR (55 °C, $CDCl_3$, 500 MHz) δ: 9.37 (1H, s), 8.41 (1H, d, *J* = 6.9 Hz), 7.28-7.24 (2H, m), 6.79 (1H, dd, *J* = 17.8, 12.0 Hz), 5.73 (1H, d, *J* = 12.0 Hz), 5.54 (1H, d, *J* = 17.8 Hz), 2.62 (2H, s), 0.07 (9H, s) ppm; ^{13}C-NMR (55 °C, $CDCl_3$, 125 MHz) δ: 159.6, 136.9, 131.2, 127.3, 126.9, 126.1, 125.9, 125.3, 121.9, 121.6, 114.6, 14.9, -0.7 ppm; HRMS (MALDI-TOF) calcd for $C_{15}H_{19}ClNOSi$ $[M+H]^+$ 292.0919, found 292.0917.; Anal calcd for $C_{15}H_{18}ClNOSi$: C, 61.73; H, 6.22; N, 4.80, found: C, 61.75; H, 6.41; N, 4.90.



4i

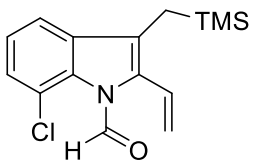
Following the general procedure B, **4i** (40 mg, 0.137 mmol 73%) was obtained from **2i** (55 mg 0.187 mmol), $RuHCl(CO)(PPh_3)_3$ (18 mg, 0.0187 mmol), Grubbs 2nd catalyst (16 mg, 0.0187 mmol), trimethyl(vinyloxy)silane (28 μl, 0.187 mmol) and (+)-10-canphorsulfonic acid (9 mg, 0.0374 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 40:1). Reaction time in cyclization and aromatization are 3 h. and 6 h, respectively. Colorless needles; m.p.:75-76 °C (from *n*-hexane); ^{1}H-NMR (55 °C, $CDCl_3$, 500 MHz): δ 9.32 (1H, s), 8.31 (1H, d, *J* = 8.5 Hz), 7.38 (1H, d, *J* = 1.5 Hz), 7.30 (1H, dd, *J* = 8.5, 1.5 Hz), 6.78 (1H, dd, *J* = 18.0, 12.0 Hz), 5.66 (1H, d, *J* =

12.0 Hz), 5.53 (1H, d, *J* = 18.0 Hz), 2.16 (2H, s), 0.05 (9H, s) ppm; ^{13}C-NMR (55 °C, $CDCl_3$, 125 MHz): δ 159.3, 133.7, 132.6, 131.6, 130.0, 125.8, 125.2, 121.4, 121.0, 119.5, 117.0, 14.4, -0.5 ppm; HRMS (MALDI-TOF) calcd for $C_{15}H_{19}ClNOSi$ $[M+H]^+$ 292.0919, found 292.0916.; Anal calcd for $C_{15}H_{18}ClNOSi$: C, 61.73; H, 6.22; N, 4.80, found: C, 62.08; H, 6.43; N, 4.65.



4j

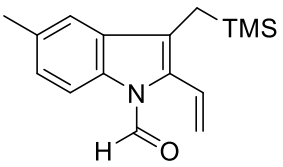
Following the general procedure B, **4j** (34 mg, 0.116 mmol 85%) was obtained from **2j** (40 mg 0.136 mmol), $RuHCl(CO)(PPh_3)_3$ (13 mg, 0.0136 mmol), Grubbs 2nd catalyst (12 mg, 0.0136 mmol), trimethyl(vinyloxy)silane (22 μl, 0.136 mmol) and (+)-10-canphorsulfonic acid (6 mg, 0.0272 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 40:1). Reaction time in cyclization and aromatization are 2.5 h. and 6 h, respectively. Colorless needles; m.p.:65-67 °C (from *n*-hexane); ^{1}H-NMR (55 °C, $CDCl_3$, 500 MHz): δ 9.32 (1H, s), 8.48 (1H, s), 7.32 (1H, d, *J* = 8.3 Hz), 7.27 (1H, dd, *J* = 8.3, 2.0 Hz), 6.77 (1H, dd, *J* = 17.5, 11.8 Hz), 5.64 (1H, d, *J* = 11.8 Hz), 5.51 (1H, d, *J* = 17.5 Hz), 2.18 (2H, s), 0.04 (9H, s) ppm; ^{13}C-NMR (55 °C, $CDCl_3$, 125 MHz): δ 159.4, 135.7, 131.7, 130.9, 129.7, 125.3, 124.8, 121.4, 120.9, 120.4, 116.3, 14.5, -0.5 ppm; HRMS (MALDI-TOF) calcd for $C_{15}H_{19}ClNOSi$ $[M+H]^+$ 292.0919, found 292.0917.; Anal calcd for $C_{15}H_{18}ClNOSi$: C, 61.73; H, 6.22; N, 4.80, found: C, 61.92; H, 6.49; N, 4.73.



4k

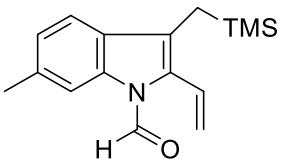
Following the general procedure B, **4k** (23 mg, 0.0781 mmol 62%) was obtained from **2k** (37 mg 0.125 mmol), $RuHCl(CO)(PPh_3)_3$ (12 mg, 0.0125 mmol), Grubbs 2nd catalyst (11 mg, 0.0125 mmol), trimethyl(vinyloxy)silane (19 μl, 0.125 mmol) and (+)-10-canphorsulfonic acid (12 mg, 0.050 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 25:1). Reaction time in cyclization and aromatization are

3 h. and 12 h., respectively. Colorless plates; m.p.:56-57 °C (from *n*-hexane); ^{1}H-NMR (55 °C, $CDCl_3$, 500 MHz): 10.44 (1H, s), 7.37 (1H, d, *J* = 8.0 Hz), 7.32 (1H, d, *J* = 8.0 Hz), 7.19 (1H, dd, *J* = 8.0, 8.0 Hz), 7.15 (1H, dd, *J* = 17.8, 11.2 Hz), 5.52 (1H, d, *J* = 11.2 Hz), 5.49 (1H, d, *J* = 17.8 Hz), 2.27 (2H, s), 0.03 (9H, s) ppm; ^{13}C-NMR (55 °C, $CDCl_3$, 125 MHz) δ: 159.9, 134.5, 133.0, 131.6, 129.0, 127.1, 124.0, 121.6, 119.2, 118.1, 117.9, 14.1 , -0.3 ppm; HRMS (MALDI-TOF) calcd for $C_{15}H_{19}ClNOSi$ $[M+H]^+$ 292.0919, found 292.0918.; Anal calcd for $C_{15}H_{18}ClNOSi$: C, 61.73; H, 6.22; N, 4.80, found: C, 61.85; H, 6.44; N, 4.74.



4l

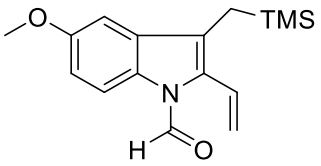
Following the general procedure B, **4l** (50 mg, 0.181 mmol 75%) was obtained from **2l** (66 mg 0.240 mmol), $RuHCl(CO)(PPh_3)_3$ (23 mg, 0.0240 mmol), Grubbs 2nd catalyst (20 mg, 0.0240 mmol), trimethyl(vinyloxy)silane (36 μl, 0.240 mmol) and (+)-10-canphorsulfonic acid (11 mg, 0.0480 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 25:1). Reaction time in cyclization and aromatization are 3 h. and 1 h, respectively. Colorless needles; m.p.: 63-65 °C (from *n*-hexane); ^{1}H-NMR (55 °C, $CDCl_3$, 500 MHz) δ: 9.33 (1H, s), 8.24 (1H, d, *J* = 8.0 Hz), 7.21 (1H, s), 7.16 (1H, d, *J* = 8.0 Hz), 6.80 (1H, dd, *J* = 17.8, 11.8 Hz), 5.59 (1H, d, *J* = 11.8 Hz), 5.49 (1H, d, *J* = 17.8 Hz), 2.46 (3H, s), 2.19 (2H, s), 0.06 (9H, s) ppm; ^{13}C-NMR (55 °C, $CDCl_3$, 125 MHz) δ: 159.1, 133.6, 133.5, 131.2, 130.3, 126.7, 125.5, 121.5, 119.8, 119.6, 115.3, 21.5, 14.3, -0.7 ppm; HRMS (MALDI-TOF) calcd for $C_{16}H_{22}NOSi$ $[M+H]^+$ 272.1465 found 272.1464.



4m

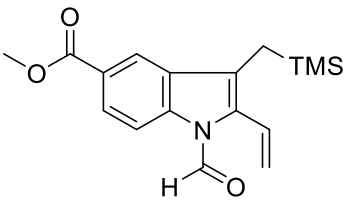
Following the general procedure B, **4m** (53 mg, 0.194 mmol 78%) was obtained from **2m** (68 mg 0.249 mmol), $RuHCl(CO)(PPh_3)_3$ (24 mg, 0.0249 mmol), Grubbs 2nd catalyst (21 mg, 0.0249 mmol), trimethyl(vinyloxy)silane (37 μl, 0.249 mmol) and

(+)-10-canphorsulfonic acid (12 mg, 0.0498 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 25:1). Reaction time in cyclization and aromatization are 3 h. and 1 h., respectively. Pale yellow oil; ^{1}H-NMR (55 °C, $CDCl_3$, 500 MHz): δ: 9.35 (1H, s), 8.22 (1H, s), 7.30 (1H, d, *J* = 8.0 Hz), 7.12 (1H, d, *J* = 8.0 Hz), 6.80 (1H, dd, *J* = 17.8, 12.0 Hz), 5.58 (1H, d, *J* = 12.0 Hz), 5.47 (1H, d, *J* = 17.8 Hz), 2.49 (3H, s), 2.19 (2H, s), 0.05 (9H, s) ppm; ^{13}C-NMR (55 °C, $CDCl_3$, 125 MHz) δ: 159.4, 135.8, 135.7, 129.6, 128.8, 125.5, 125.4, 121.7, 119.4, 119.2, 116.0, 21.8, 14.4, -0.7 ppm; HRMS (MALDI-TOF) calcd for $C_{16}H_{22}NOSi$ $[M+H]^+$ 272.1465 found 272.1460.



4n

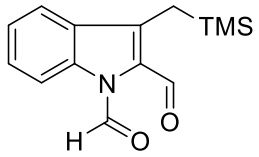
Following the general procedure B, **4n** (37 mg, 0.128 mmol 81%) was obtained from **2n** (45 mg 0.158 mmol), $RuHCl(CO)(PPh_3)_3$ (15 mg, 0.0158 mmol), Grubbs 2nd catalyst (13 mg, 0.0158 mmol), trimethyl(vinyloxy)silane (24 μl, 0.158 mmol) and (+)-10-canphorsulfonic acid (7 mg, 0.0316 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 25:1). Reaction time in cyclization and aromatization are 2.5 h. and 1 h., respectively. Colorless needles; m.p.:50-52 °C (from *n*-hexane); ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 9.31 (1H, s), 8.33 (1H, br s), 6.97 (1H, dd, *J* = 8.9, 2.3 Hz), 6.89 (1H, d, *J* = 2.3 Hz), 6.80 (1H, br m), 5.64 (1H, d, *J* = 11.5 Hz), 5.51 (1H, d, *J* = 17.8 Hz), 3.89 (3H, s), 2.19 (2H, s), 0.07 (9H, s) ppm; ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: 159.5, 157.0, 132.2, 131.1, 130.0, 125.3, 125.3, 121.7, 120.6, 113.5, 103.2, 55.9, 14.5, -0.4 ppm; HRMS (MALDI-TOF) calcd for $C_{16}H_{22}NO_2Si$ $[M+H]^+$ 288.1414, found 288.1413.; Anal calcd for $C_{16}H_{21}NO_2Si$: C, 66.86; H, 7.36; N, 4.87, found: C, 67.06; H, 7.57; N, 4.80.



4o

Following the general procedure B, **4o** (8 mg, 0.0263 mmol 64%) was obtained from **2o**

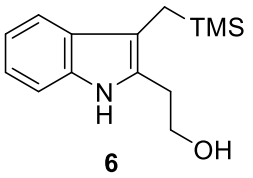
(13 mg 0.0412 mmol), $RuHCl(CO)(PPh_3)_3$ (4 mg, 0.00412 mmol), Grubbs 2nd catalyst (4 mg, 0.00412 mmol), trimethyl(vinyloxy)silane (6 μl, 0.0412 mmol) and (+)-10-canphorsulfonic acid (2 mg 0.00824 mmol) after column chromatography on silica gel (*n*-hexane/AcOEt = 25:1). Reaction time in cyclization and aromatization are 3 h. and 1 h., respectively. Pale yellow oil; ^{1}H-NMR (50 °C, $CDCl_3$, 400 MHz)δ: 9.37 (1H, s), 8.40 (1H, d, *J* = 8.4 Hz), 8.16 (1H, s), 8.04 (1H, dd, *J* = 8.4, 1.1 Hz), 6.81 (1H, dd, *J* = 17.9, 11.7 Hz), 5.67 (1H, d, *J* = 11.7 Hz), 5.55 (1H, d, *J* = 17.9 Hz), 3.96 (3H, s), 2.25 (2H, s), 0.05 (9H, s) ppm; ^{13}C-NMR (50 °C, $CDCl_3$, 100 MHz) δ: 167.5, 159.7, 138.2, 131.6, 131.2, 127.2, 1265, 125.4, 122.13, 122.05, 121.4, 115.6, 52.4, 14.6, -0.4 ppm; HRMS (MALDI-TOF) calcd for $C_{17}H_{22}NO_3Si$ $[M+H]^+$316.1363 found 316.1363.



5

To a solution of **4b** (16 mg, 0.0633 mmol) and 2,6-lutidine (14 mg, 0.126 mmol) in H_2O/1,4-dioxane = 1:3 (1.2 mL) was added potassium osmate(VI) dihydrate (1 mg, 0.00317 mmol) and sodium periodate (54 mg, 0.252 mmol) at 0 °C. The mixture was stirred at 0 °C for 1 h. The mixture was diluted with EtOAc and the organic layer was washed with sat. $Na_2S_2O_3$ aq. and brine, dried over Na_2SO_4, filtered, and concentrated. The obtained residue was purified by column chromatography on silica gel *n*-hexane/AcOEt = 8:1) to give **5** (12 mg, 0.0447 mmol, 71%).

5; Colorless plates; m.p. 102-103 °C (from CH_2Cl_2/*n*-hexane); ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 10.26 (1H, s), 10.05 (1H, s), 8.53 (1H, d, *J* = 7.9 Hz), 7.62 (1H, d, *J* = 7.9 Hz), 7.57 (1H, ddd, *J* = 7.9, 7.9, 1.1 Hz), 7.37 (1H, ddd, *J* = 7.9, 7.9, 1.1, Hz), 2.60 (2H, s), 0.08 (9H, s) ppm; ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: 180.4, 161.8, 141.1, 137.2, 131.1, 129.1, 128.8, 124.8, 121.9, 117.7, 15.7, -1.1 ppm; HRMS (MALDI-TOF) calcd for $C_{14}H_{17}NO_2NaSi$ $[M+Na]^+$ 282.0921, found 282.0920.; Anal calcd for $C_{14}H_{17}NO_2Si$: C, 64.83; H, 6.61; N, 5.40, found: C, 64.62; H, 6.86; N, 5.27.

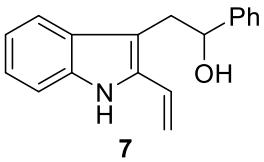


6

To a stirred solution of **4b** (28 mg, 0.107 mmol) in THF-H_2O (1:1) (1.1 mL, 0.1 M) was added dropwisely a solution of 1*N* NaOH aq. (0.16 mL, 0.160 mmol,) at 0 °C. The mixture was stirred at an ambient temperature for 2 h, and then sat. NH_4Cl aq. was added. The mixture was diluted with AcOEt and washed with water and brine. The combined organic layers were dried over Na_2SO_4, filtered, and concentratedto give 2-vinyl-3-[(trimethylsilyl)methyl]indole.

To a stirred solution of above 2-vinyl-3-[(trimethylsilyl)methyl]indole in anhydrous THF (1.1 ml, 0.1 M) was added Cy_2BH. (48 mg, 0.268 mmol, 2.5 eq.) at room temperature. The mixture stirred at 50 °C for 2 h. After cooling, H_2O (1.1 ml), 1*N* NaOH (1.1 ml), 30% H_2O_2 (1.1 ml) was added at 0 °C. After stirred at room temperature for 0.5 h., to the mixture was added sat. $Na_2S_2O_3$ aq. The mixture was diluted with AcOEt and washed with water and brine. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The obtained residue was purified by column chromatography on silica gel *n*-hexane/AcOEt = 2:1) to give **6** (22 mg, 0.0893 mmol, 83%).

6; Colorless oil ; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 8.40 (1H, br), 7.41 (1H, d, *J* = 8.0 Hz), 7.27 (1H, d, *J* = 8.0 Hz), 7.10 (1H, dd, *J* = 8.0, 8.0 Hz), 7.04 (1H, dd, *J* = 8.0, 8.0 Hz), 3.96 (2H, t, *J* = 5.7 Hz), 2.93 (2H, t, *J* = 5.7 Hz), 2.07 (2H, s), 0.00 (9H, s) ppm; ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 135.5, 131.0, 128.5, 120.9, 118.9, 118.5, 110.2, 109.7, 62.5, 28.9, 13.4, -1.0 ppm; HRMS (MALDI-TOF) calcd for $C_{14}H_{21}NOSi$ $[M+H]^+$ 247.1387, found 247.1387.

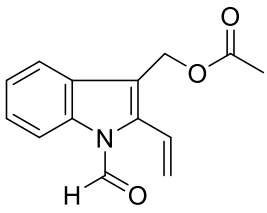


7

To a stirred solution of **4b** (27 mg, 0.106 mmol) in anhydrous DMF (0.43 mL) was added MS 4A (55 mg 200 w%), benzaldehyde (34 mg, 0.319 mmol) and *n*-Bu_4NF (11μl, 0.0106 mmol, 1.0 M in THF). The resulting mixture was stirred at 80 °C for 6 h, and then 1*N* NaOH (0.16 mL) was added at room temperature. After stirred for 0.5 h, the

mixture was added sat. NH_4Cl aq. The organic compounds were extracted with Et_2O. The organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane/AcOEt = 4:1) to give **7** (23 mg, 0.0859 mmol 81%).

7; Pale yellow oil; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 8.13 (1H, br s), 7.57 (1H, d, *J* = 9.8 Hz), 7.43-7.27 (6H, m), 7.20(1H, ddd, *J* = 10.3, 8.6, 1.2 Hz), 7.10 (1H, ddd, *J* = 10.3, 8.6, 1.2 Hz), 6.76 (1H, dd, *J* = 17.8, 11.5, Hz), 5.48 (1H, d, *J* = 17.8 Hz), 5.24 (1H, d, *J* = 11.5 Hz) 4.96 (1H, dd, *J* = 8.6, 4.6 Hz) 3.17 (2H, ddd, 14.3, 8.6, 4.6) ppm; ^{13}C-NMR ($CDCl_3$, 125 MHz) δ: 143.9, 136.2, 133.8, 128.9, 128.4, 127.5, 125.7, 125.3, 123.3, 119.8, 119.1, 111.7, 111.6, 110.7, 74.4, 34.9 ppm; HRMS (MALDI-TOF) calcd for $C_{18}H_{17}NONa$ $[M+Na]^+$ 286.1202, found 286.1201.



8

To a stirred solution of **4c** (12 mg, 0.0388 mmol) in AcOH (0.4 ml, 0.1 M) was added KBr (6 mg 0.0466 mmol, 1.2 eq.), NaOAc (10 mg, 0.116 mmol), and 1*N* AcOOH (0.24 ml, 0.240 mmol 6 eq.) at 16 °C. The mixture was stirred at an ambient temperature for 3 h, and then was added sat. $Na_2S_2O_3$ aq.. The mixture was diluted with Et_2O and washed with water and brine. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The obtained residue was purified by column chromatography on silica gel *n*-hexane/AcOEt = 6:1) to give **8** (4 mg, 0.0181 mmol, 47%).

8; Colorless needles; m.p.: 81-84 °C (from *n*-hexane); ^{1}H-NMR (40 °C, DMSO-d_6, 400 MHz) δ: 9.44 (1H, s), 8.27 (1H, d, *J* = 7.8 Hz), 7.71 (1H, d, *J* = 7.3 Hz), 7.41-7.33 (2H, m), 7.13 (1H, dd, *J* = 17.6, 11.6 Hz), 5.79 (1H, dd, *J* = 11.6, 1.3 Hz), 5.72 (1H, dd, *J* = 17.6, 1.3 Hz), 5.25 (2H, s), 2.04 (3H, s) ppm; ^{13}C-NMR (40 °C, DMSO-d_6, 100 MHz) δ: 170.1, 160.4, 136.7, 133.9, 129.1, 125.4, 124.2, 124.1, 123.9, 119.5, 115.0, 114.6, 56.4, 20.5 ppm; HRMS (MALDI-TOF) calcd for $C_{14}H_{13}NO_3$ $[M]^+$ 243.0890, found 243.0890.

Acknowledgements

This work was partially supported by a Grant-in-Aid from JSPS KAKENHI (Grant No. JP A16H010260) for Precisely Designed Catalysts with Customized Scaffolding, A262880510, T15K149760 and T15KT00630; the Platform Project for Supporting Drug Discovery and Life Science Research (Platform for Drug Discovery, Informatics and Structural Life Science) from the Ministry of Education, Culture, Sports, Science, and Technology, Japan (MEXT), JST ACT-C Grant Number JPMJCR12YM, Japan

Supporting information available: 1H and 13C NMR charts of compounds **2**, **4**, **5**, **6**, **7** and **8**.

References

(1) For selected recent reviews of the transition-metal-catalyzed cycloisomerization, see: (a) Fang, G.; Bi, X. *Chem. Soc. Rev.* **2015**, *44*, 8124-8173. (b) Neff, R. K.; Frantz, D. E. *Tetrahedron* **2015**, *71*, 7-18. (c) Michelet, V. In Comprehensive Organic Synthesis II; Knochel, P., Molander, G. A., Eds.; Elsevier: 2014; Vol. 5, p 1483. (d) Fürstner, A. *Acc. Chem. Res.* **2014**, *47*, 925-938. (e) Yamamoto, Y. *Chem. Rev.* **2012**, *112*, 4736-4769. (f) Fehr, C. *Synlett* **2012**, *23*, 990-1006. (g) Aubert, C.; Fensterbank, L.; Garcia, P.; Malacria, M.; Simonneau, A. *Chem. Rev.* **2011**, *111*, 1954-1993.

(2) For reviews of the transition-metal-catalyzed intramolecular heterocyclization of enyne, see: (a) Harris, R. J.; Widenhoefer, R. A. *Chem. Soc. Rev.* **2016**, *45*, 4533-4551. (b) Dorel, R.; Echavarren, A. M. *J. Org. Chem.* **2015**, *80*, 7321-7332. (c) Fuerstner, A. *Acc. Chem. Res.* **2014**, *47*, 925-938. (d) Obradors, C.; Echavarren, A. M. *Acc. Chem. Res.* **2014**, *47*, 902-912. (e) Olszewski, T. K.; Bieniek, M.; Skowerski, K.; Grela, K. *Synlett* **2013**, *24*, 903-919. (f) Braun, I.; Asiri, A. M.; Hashmi, A. S. K. *ACS Catal.* **2013**, *3*, 1902-1907. (g) Zhang, D. H.; Zhang, Z.; Shi, M. *Chem. Comm.* **2012**, *48*, 10271-10279.

(3) Selected examples, see: (a) Okamoto, K.; Sakagami, M.; Feng, F.; Togame, H.;

Takemoto, H.; Ichikawa, S.; Matsuda, A. *Org. Lett.* **2011**, *13,* 5240-5243. (b) Villa, M. V. J.; Targett, S. M.; Barnes, J. C.; Whittingham, W. G.; Marquez, R. *Org. Lett.* **2007**, *9,* 1631-1633. (c) Mathieson, J. E.; Crawford, J. J.; Schmidtmann, M.; Marquez, R. *Org. Biomol. Chem.* **2009**, *7,* 2170-2175. (d) Wang, X.; Porco, J. A. *J. Am. Chem. Soc.* **2003**, *125,* 6040-6041. (e) Kuranaga, T.; Sesoko, Y.; Sakata, K.; Maeda, N.; Hayata, A.; Inoue, M. *J. Am. Chem. Soc.* **2013**, *135,* 5467-5474, and reference cited.

(4) Courant, T.; Dagousset, G.; Masson, G. *Synthesis* **2015**, *47*, 1799–1826.

(5) Gopalaiah, K.; Kagan, H. B. *Chem. Rev.* **2011**, *111*, 4599-4657.

(6) reviews, Wang, M. X. *Chem. Commun.* **2015**, *51,* 6039-6049. Dake, G. R. *Synlett* **2012**, *23*, 814–824

(7) Gigant, N.; Chausset-Boissarie, N.; Gillaizeau, I. *Chem. Eur. J.* **2014**, *20*, 7548-7564.

(8) For reviews see:(a) Dounay, A. B.; Overman, L. E.; *Chem. Rev.* **2003,** *103*, 2945-2964. (b) Zhou, F.; Liu, Y.-L.; Zhou, J. *Adv. Synth. Catal.* **2010**, *352*, 1381-1407. (c) Steven, A.; Overman, L. E. *Angew. Chem. Int. Ed.* **2007**, *46*, 5488-5508. (d) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442-4489. (e) Kawagishi, F.; Toma, T.; Inui, T.; Yokoshima, S.; Fukuyama, T. *J. Am. Chem. Soc.* **2013**, *135*, 13684-13687. (f) Tsukano, C.; Zhao, L.; Takemoto, Y.; Hirama, M. *Eur. J. Org. Chem.* **2010**, 4198-4200. (g) Ding, R.; Sung, B.-F; Lin, G.-Q *Org. Lett.* **2012**, *14*, 4446-4449.

(9) (a) Kinderman, S. S.; van Maarseveen, J. H.; Schoemaker, H. E.; Hiemstra, H.; Rutjes, F. P. J. T. *Org. Lett.* **2001**, *3*, 2045-2048, (b) Arisawa, M.; Terada, Y.; Nakagawa, M.; Nishida, A. *Angew. Chem. Int. Ed.* **2002**, *41*, 4732-4734. (c) Benasar, M. L.; Roca, T.; Monerris, M.; Garcia-Diaz, D. *J. Org. Chem.* **2006**, *71*, 7028-7034. (d) Toumi, M.; Couty, F.; Evano, G. *J. Org. Chem.* **2008**, *73*, 1270-1281.

(10) (a) Deng, H.; Yang, X.; Tong, Z.; Li, Z.; Zhai, H. *Org. Lett.* **2008,** *10,* 1791-1793. (b) Cheng, B.; Wu, F.; Yang, X.; Zhou, Y.; Wan, X.; Zhai, H. *Chem. Eur. J.* **2011,** *17,* 12569-12572.

(11) (a) Rakshit, S.; Patureau, F. W.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 9585-9587. (b) Wang, L.; Ackermann, L. *Org. Lett.* **2013**, *15*, 176–179. (c) Li, B.; Wang, N.; Liang, Y.; Xu, S.; Wang, B. *Org. Lett.* **2013**, *15*, 136–139. (d) Murugan, K.; Liu, S.-T. *Tetrahedron Lett.* **2013**, *54*, 2608–2611. (e) Zhao, M.-N.; Ren, Z.-H.; Wang, Y.-Y.; Guan, Z.-H. *Chem. Eur. J.* **2014**, *20*, 1839–1842. (f) Zhao, M.-N.; Ren, Z.-H.;

Wang, Y.-Y.; Guan, Z.-H. *Org. Lett.* **2014**, *16*, 608–611. (g) Loh, T. P.; Xu, Y.-X.; He, T.; Zhang, Q.-C. *Chem. Commun.* **2014**, *50*, 3033-3035.

(12) Although there is one report of cycloisomerization between aromatic enamide and alkyne, the substrate scope was limited to alkynes with carbon-based sunstituents. Trost, B. M.; Pedregal, C. *J. Am. Chem. Soc.* **1992**, *114*, 7292-7294.

(13) Saxton, J. E. (ed.) *Chemistry of Heterocyclic Compounds: Indoles, Part Four, The Monoterpenoid Indole Alkaloids* (Wiley, 1983).

(14) (a) Arisawa, M.; Terada, Y.; Nakagawa M.; Nishida, A. *Angew. Chem. Int. Ed.* **2002**, *41*, 4732-4734. (b) Terada, Y.; Arisawa, M.; Nishida, A. *Angew. Chem. Int. Ed.* **2004**, *43*, 4063-4067. (c) Arisawa, M.; Terada, Y.; Takahashi, K.; Nakagawa, M.; Nishida, A. *J. Org. Chem.* **2006**, *71*, 4255-4261.

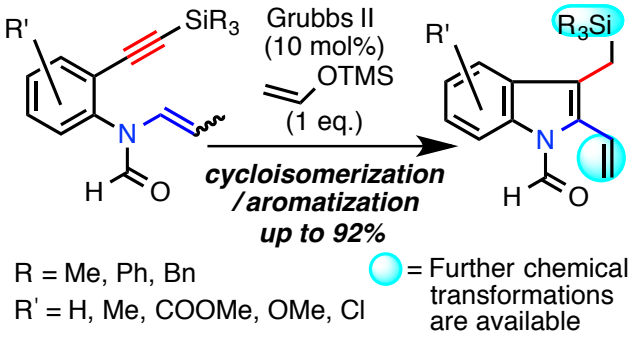
(15) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 714-715

(16) Chatani, N.; Inoue, H.; Morimoto, T.; Muto, T.; Murai, S. *J. Org. Chem*, **2001**, *66*, 4433-4436.

(17) For reviews, see: (a) Alcaide, B.; Almendros, P. *Chem. Eur. J.* **2003**, *9*, 1258-1262. (b) Schmidt, B. *Eur. J. Org. Chem.* **2004**, *9*, 1865-1880. (c) Arisawa, M.; Terada, Y.; Takahashi, K.; Nakagawa, M.; Nishida, A. *Chem. Rec.* **2007**, *7*, 238-253. (d) Alcaide, B.; Almendros, P.; Luna, A. *Chem. Rev.* **2009**, *109*, 3817-3858.

(18) Trost, B. M.; Frederiksen, M. U.; Papillon, J. P. N.; Harrington, P. E.; Shin, S.; Shireman, B. T. *J. Am. Chem. Soc.*, **2005**, 127, 3666-3667.

TOC


R'
SiR3
Grubbs II
(10 mol%)
OTMS
(1 eq.)
N
H
O
cycloisomerization
/aromatization
up to 92%
R3Si
R = Me, Ph, Bn
R' = H, Me, COOMe, OMe, Cl
= Further chemical
transformations
are available