Tetrahedron 69 (2013) 3403–3409

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of spiro[4.5]cyclohexadienones with an allene motif via a base-promoted intramolecular *ipso*-Friedel–Crafts addition of phenols to propargyl bromides

Tetsuhiro Nemoto, Riliga Wu, Zengduo Zhao, Takuya Yokosaka, Yasumasa Hamada *

Graduate School of Pharmaceutical Sciences, Chiba University, 1-8-1 Inohana, Chuo-ku, Chiba 260-8675, Japan

ARTICLE INFO

Article history:
Received 29 January 2013
Received in revised form 18 February 2013
Accepted 22 February 2013
Available online 26 February 2013

Keywords:
Alkylation
Dearomatization
ipso-Friedel–Crafts addition
Palladium
Spiro compounds

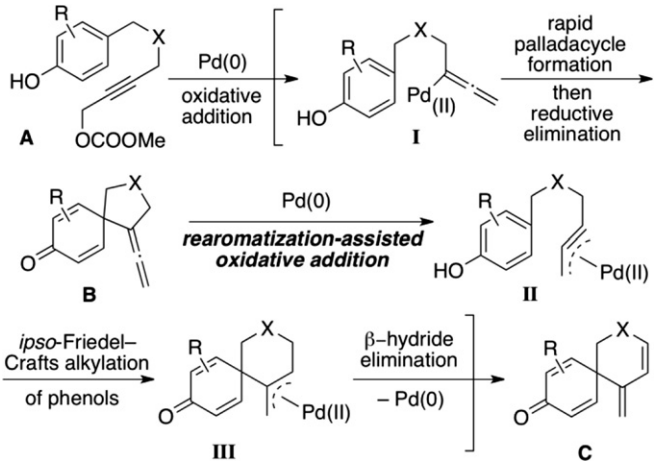
ABSTRACT

We developed a novel synthetic method for allenyl spiro[4.5]cyclohexadienone derivatives based on a base-promoted intramolecular *ipso*-Friedel–Crafts addition of phenols to propargyl bromides. The present spirocyclization proceeded in a CH_2Cl_2–*tert*-BuOH mixed solvent system using potassium *tert*-butoxide as the base, and produced the corresponding spiro[4.5]cyclohexadienone derivatives with an allene motif in up to 99% yield. This-type allenyl spirocycle was also accessible through Pd-catalyzed intramolecular *ipso*-Friedel–Crafts alkylation when a propargyl carbonate derivative with a naphthol unit was used as a substrate. Acid-promoted skeletal rearrangement of the reaction adducts was also examined.

1. Introduction

Efficient construction of spirocyclic frameworks is an important topic in synthetic organic chemistry because of their broad distribution in biologically active natural products and pharmaceuticals, as well as their usefulness in complex molecule syntheses. Among the various spirocycles, spirocyclohexadienones are the most important class of compounds in organic synthesis.[1] Extensive efforts have been focused on the development of an efficient synthetic method based on hypervalent iodine reagents,[2] *ipso*-halocyclization,[3] radical cyclization,[4] arene–Ru complex-mediated dearomatization,[5] Cu-catalyzed oxygenation of α-azido-*N*-arylamides,[6] transition metal-catalyzed *ipso*-Friedel–Crafts allylic alkylation of phenols,[7,8] and Pd-catalyzed arylative dearomatization.[9]

We recently reported a novel synthetic method for spirocyclohexadienone derivatives based on a Pd-catalyzed intramolecular *ipso*-Friedel–Crafts addition of phenols to η^3-propargylpalladium(II) complexes (Scheme 1).[10] When *para*-substituted phenol derivatives with a propargyl carbonate moiety **A** was reacted with a Pd catalyst in a $(CH_2Cl)_2$–MeOH mixed solvent system, spiro[5.5]cyclohexadienone derivatives with a diene motif **C** were obtained in excellent yield. Mechanistic studies revealed that this reaction process involved the rearomatization-assisted oxidative addition of intermediate **B**, the initially produced spirocyclohexadienone derivatives with an allene motif, resulting in characteristic reaction profiles. To investigate the reactivity, we planned to synthesize the allenyl spirocyclohexadienone intermediates **B** as pure compounds. They could not be selectively obtained through this Pd catalysis, however, due to the difficulty in stopping this cascade process along the way. Therefore, an alternative synthetic method was developed. In addition, potential synthetic utilities of **B**-type compounds led us



Scheme 1. Pd-catalyzed intramolecular spirocyclization using propargyl carbonate derivatives.

* Corresponding author. Tel./fax: +81 43 226 2920; e-mail addresses: y-hamada@faculty.chiba-u.jp, hamada@p.chiba-u.ac.jp (Y. Hamada).

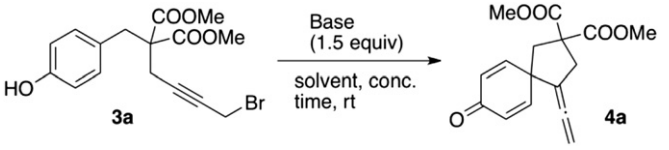
0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.02.082

to begin synthetic work on this class of compounds. Herein, we report a novel synthetic method for spiro[4.5]cyclohexadienones with an allene motif via a base-promoted intramolecular *ipso*-Friedel–Crafts addition of phenols to propargyl bromides.

2. Results and discussions

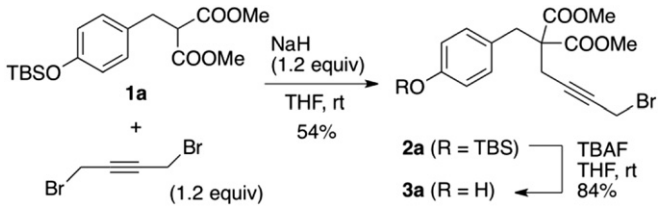
A base-promoted intramolecular *ipso*-nucleophilic addition of phenols to alkyl halides or related electrophiles via a S_N2 mechanism is a classical method for the synthesis of spirocyclohexadienones,[11] and has been recently applied to several natural product syntheses.[12] Thus, we first examined intramolecular *ipso*-Friedel–Crafts addition of phenols via a S_N2' mechanism using propargyl bromide derivative **3a** as a model substrate (Table 1), which could be easily prepared from the corresponding malonate derivative **1a** and 1,4-dibromo-2-butyne (45% yield for two steps) (Scheme 2). We investigated the effect of base in CH_2Cl_2 (0.1 M) and the corresponding product **4a** was obtained in the highest yield (50% yield) when using 1.5 equiv of sodium *tert*-butoxide (entry 5). The yield improved slightly (64% yield) when the reaction was performed in a CH_2Cl_2–*tert*-BuOH (4/1) mixed solvent system under diluted conditions (0.04 M) (entry 7). The yield was significantly affected by the counter cation of *tert*-butoxide, as well as by the solvent ratio. The best result was obtained when the reaction was performed in a CH_2Cl_2–*tert*-BuOH (4/1) mixed solvent system (0.04 M) using potassium *tert*-butoxide as the base (90% yield) (entry 9).

Table 1
Optimization of the reaction conditions using **3a**



Entry	Base	Solvent	Concn (M)	Time (h)	Yield[a] (%)
1	*i*-Pr_2NEt	CH_2Cl_2	0.1	73	14
2	K_2CO_3	CH_2Cl_2	0.1	46	No reaction
3	Cs_2CO_3	CH_2Cl_2	0.1	46	30
4	NaH	CH_2Cl_2	0.1	47	35
5	NaO–*t*-Bu	CH_2Cl_2	0.1	22	50
6	NaO–*t*-Bu	CH_2Cl_2	0.04	23	62
7	NaO–*t*-Bu	CH_2Cl_2–*t*-BuOH (4/1)	0.04	23	64
8	LiO–*t*-Bu	CH_2Cl_2–*t*-BuOH (4/1)	0.04	18	35
9	KO–*t*-Bu	CH_2Cl_2–*t*-BuOH (4/1)	0.04	8	90
10	KO–*t*-Bu	CH_2Cl_2–*t*-BuOH (9/1)	0.04	8	66
11	KO–*t*-Bu	CH_2Cl_2–*t*-BuOH (1/1)	0.04	8	76
12	KO–*t*-Bu	*t*-BuOH	0.04	8	35

[a] Isolated yield.



Scheme 2. Synthesis of propargyl bromide derivative **3a**.

Having developed efficient conditions, we next examined the scope and limitations of the different substrates (Table 2). In addition to model substrate **3a**, *ortho*-disubstituted phenol derivatives **3b** and **3c**, as well as *meta*-substituted phenol derivatives **3d**–**f** were effective substrates for this reaction system, and products with a spiro[4.5]cyclohexadienone skeleton **4b**–**f** were obtained in 63–97% yield (entries 2–6). Naphthol derivative **3g** was also applicable to this reaction, affording the corresponding naphthoquinone derivative **4g** in 72% yield (entry 7). Moreover, spirocyclization of **3h**, bearing a bulky di(*tert*-butyl)malonate tether, proceeded smoothly to give **4h** in excellent yield (entry 8). In contrast, when phenol derivative **3i**, a substrate bearing a CH_2 unit-longer tether than **3a**, was reacted under the optimized conditions, the desired spiro[5.5]cyclohexadienone was not obtained, and we detected several products that formed through an intermolecular O-alkylation.[13] This finding indicates that the tether length between the phenol and propargyl bromide unit is a crucial factor for this reaction system. Furthermore, *N*-Ts-tethered substrate **3j** was prepared using the synthetic methods shown in Scheme 3. Tosyl amide derivative **5j** was first reacted with propargyl bromide derivative **6** to give **7j** in 89% yield. Deprotection of the TBS group and the acetyl group was performed under basic conditions, affording compound **8j** in 87% yield. Subsequent bromination of the alcohol moiety provided *N*-Ts-tethered substrate **3j** in 59% yield. Spirocyclization of **3j** proceeded under the optimized conditions, producing the corresponding products **4j** in 74% yield.

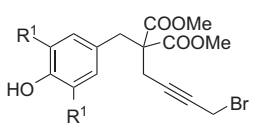
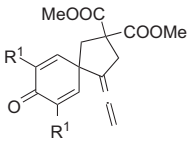
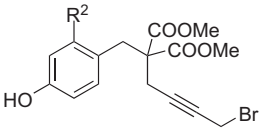
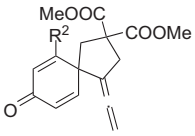
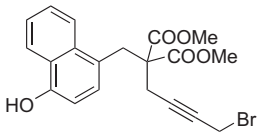
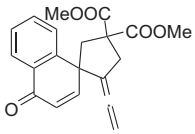
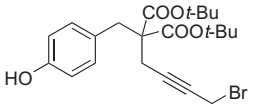
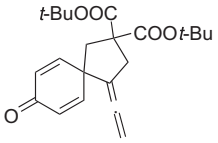
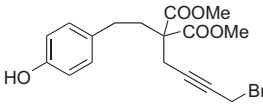
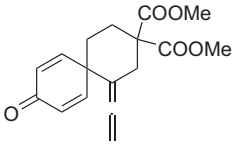
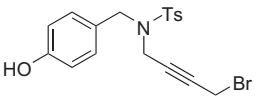
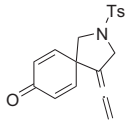
As shown in Scheme 1, allenyl spiro[4.5]cyclohexadienones derived from phenol derivatives were transformed into the corresponding diene-type adducts in the presence of Pd(0) catalyst through the rearomatization-assisted oxidative addition of $C(sp^3)$–$C(sp^2)$ bond. In contrast, a similar oxidative addition process did not occur at 40 °C when naphthoquinone derivative **4g** was used as the substrate.[14] Pd-catalyzed intramolecular *ipso*-Friedel–Crafts alkylation of propargyl carbonate derivative with a naphthol unit **9g** proceeded at 40 °C to provide allenyl spirocycle **4g** in 96% yield (Scheme 4).[15]

Acid-promoted dienone–phenol rearrangement of spirocyclohexadienones is a useful method for synthesizing functionalized phenol derivatives. Treatment of **4a** with several acid promoters, however, did not produce the rearranged phenol derivative. On the other hand, Luche reduction of **3a**, followed by treatment of the obtained alcohol intermediate with *para*-toluenesulfonic acid (TsOH) in CH_3CN, afforded the corresponding bicyclic adduct **10a** in 87% yield in two steps (Scheme 5). Although skeletal rearrangement could be performed using 10 mol % of TsOH, the yield was slightly decreased (79% yield for two steps). When **4d** was utilized as the substrate for this ring expansion process, product **10d** was obtained in 89% yield as the sole product.[16] This result clearly indicated that the allenyl group is selectively rearranged to the less hindered vicinal carbon on the six-membered ring. Halide-substituted spirocycle **4f** and naphthoquinone derivative **4g** were also applicable to this skeletal rearrangement, affording the corresponding multi-cyclic adducts **10f** and **10g** in 62% and 75% yield, respectively.[17]

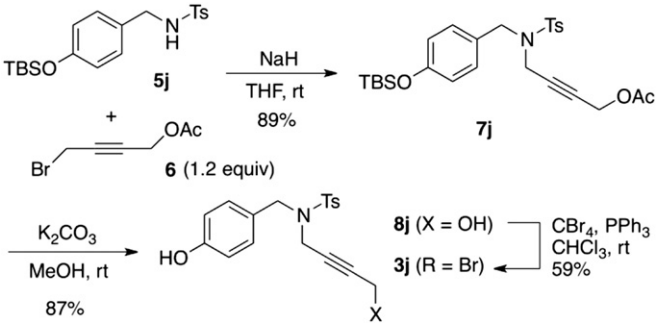
3. Conclusion

We developed a novel synthetic method for obtaining allenyl spiro[4.5]cyclohexadienone derivatives using a base-promoted intramolecular *ipso*-Friedel–Crafts addition of phenols to propargyl bromides. In addition, when using a propargyl carbonate derivative with a naphthol unit as a substrate, Pd-catalyzed intramolecular *ipso*-Friedel–Crafts alkylation proceeded smoothly to afford the corresponding allenyl spirocyclic molecule. Subsequent acid-catalyzed skeletal rearrangements provided the corresponding ring-expanded adducts in excellent yield, demonstrating the potential utility of this synthetic method. Further studies are in progress.

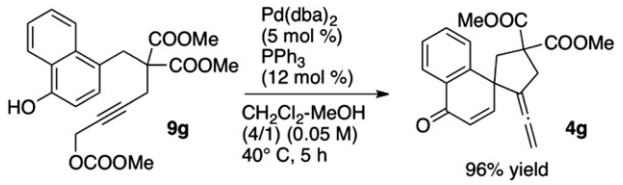
Table 2
Scope and limitations[a]

Entry	Substrates	Products	Time (h)	Yield[b] (%)
1	 **3a** (R^1 = H)	 **4a**	8	90
2	**3b** (R^1 = CH_3)	**4b**	18	97
3	**3c** (R^1 = OCH_3)	**4c**	18	63
4	 **3d** (R^2 = CH_3)	 **4d**	16	92
5	**3e** (R^2 = OCH_3)	**4e**	16	74
6	**3f** (R^2 = Cl)	**4f**	14	66
7	 **3g**	 **4g**	1	72
8	 **3h**	 **4h**	15	99
9	 **3i**	 **4i**	18	0
10	 **3j**	 **4j**	21	74

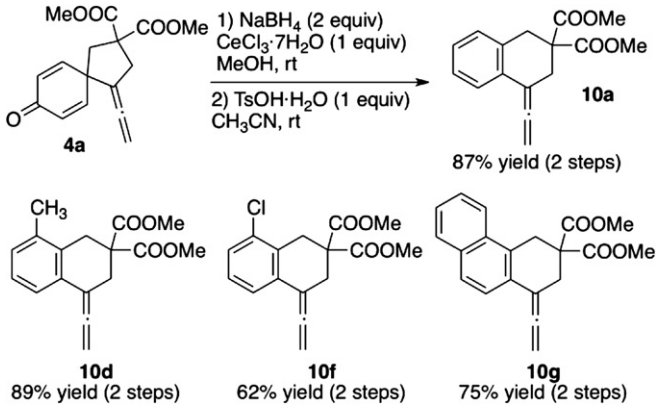
[a] Reaction conditions. KO–*t*-Bu (1.5 equiv), CH_2Cl_2–*t*-BuOH (4/1) (0.04 M), rt.
[b] Isolated yield.



Scheme 3. Synthesis of **3j**.



Scheme 4. Synthesis of **4g** using Pd-catalyzed intramolecular *ipso*-Friedel–Crafts alkylation.



Scheme 5. Derivatization of the reaction adducts using an acid-catalyzed skeletal rearrangement.

4. Experimental

4.1. General

Infrared (IR) spectra were recorded on a JASCO FT/IR 230 Fourier transform infrared spectrophotometer, equipped with ATR (Smiths Detection, DuraSample IR II). NMR spectra were recorded on a JEOL

ecp 400 spectrometer, operating at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR. Chemical shifts in $CDCl_3$ were reported downfield from TMS (=0 ppm) for ^{1}H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to the solvent signal [$CHCl_3$ (77.0 ppm)] as an internal reference. ESI mass spectra were measured on JEOL AccuTOF LC-plus JMS-T100L. Reactions were carried out in dry solvent under argon atmosphere. Other reagents were purified by the usual methods.

4.2. Experimental procedure of the intramolecular *ipso*-Friedel–Crafts addition of phenols to propargyl bromides and compound characterization

4.2.1. Typical experimental procedure for the intramolecular ipso-Friedel–Crafts addition of phenols to propargyl bromides (Table 1, entry 9). Compound **3a** (36.9 mg, 0.10 mmol) and KO–*t*-Bu (16.8 mg, 0.15 mmol) were dissolved in CH_2Cl_2 (2.0 mL) and *t*-BuOH (0.5 mL), and the resulting solution was stirred at room temperature. After 8 h, the reaction was quenched with satd aq NH_4Cl solution, and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over Na_2SO_4, and then concentrated in vacuo. The obtained residue was purified by flash column chromatography (SiO_2, hexane/acetone=7:1) to give dimethyl 8-oxo-4-vinylidenespiro[4.5]deca-6,9-diene-2,2-dicarboxylate **4a** (26.0 mg, 90% yield) as colorless oil. IR (ATR) ν 2954, 1729, 1662, 1624, 1434, 1253, 1201, 1159, 1111, 1080, 853 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.65 (s, 2H), 3.27 (t, J=4.0 Hz, 2H), 3.80 (s, 6H), 4.82 (m, 2H), 6.15 (d, J=9.6 Hz, 2H), 6.80 (d, J=9.6 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 37.9, 43.5, 50.0, 53.3 (2C), 59.6, 80.0, 102.5, 126.8 (2C), 150.9 (2C), 171.2 (2C), 185.8, 202.3; (+)-ESI-HRMS. Calcd for $C_{16}H_{16}NaO_5^+$ (M+Na$^+$): 311.0890. Found: 311.0902.

*4.2.2. Dimethyl 7,9-dimethyl-8-oxo-4-vinylidenespiro[4.5]deca-6,9-diene-2,2-dicarboxylate (**4b**).* Compound **4b** was prepared from **3b** according to the typical procedure shown in Section 4.2.1. Colorless solids. IR (ATR) ν 2954, 1733, 1584, 1461, 1434, 1391, 1275, 1249, 1151, 1074, 907, 867, 839, 781, 763, 728 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.86 (s, 6H), 2.59 (s, 2H), 3.24 (t, J=4.0 Hz, 2H), 3.87 (s, 6H), 4.75 (t, J=4.0 Hz, 2H), 6.55 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 15.9 (2C), 38.0, 43.9, 49.6, 53.2 (2C), 59.5, 79.5, 103.3, 132.8 (2C), 146.3 (2C), 171.5 (2C), 187.0, 202.0; (+)-ESI-HRMS. Calcd for $C_{18}H_{20}NaO_5^+$ (M+Na$^+$): 339.1203. Found: 339.1155.

*4.2.3. Dimethyl 7,9-dimethoxy-8-oxo-4-vinylidenespiro[4.5]deca-6,9-diene-2,2-dicarboxylate (**4c**).* Compound **4c** was prepared from **3c** according to the typical procedure shown in Section 4.2.1. Colorless oil. IR (ATR) ν 3012, 2954, 1730, 1669, 1617, 1434, 1249, 1229, 1202, 1107, 860, 747, 665 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.69 (s, 2H), 3.33 (t, J=4.0 Hz, 2H), 3.65 (s, 6H), 3.81 (s, 6H), 4.79 (t, J=4.0 Hz, 2H), 5.83 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 37.6, 46.0, 48.6, 53.3 (2C), 55.2 (2C), 59.1, 77.2, 79.9, 104.5, 119.2 (2C), 149.6 (2C), 171.7, 176.4, 201.5; (+)-ESI-HRMS. Calcd for $C_{18}H_{20}NaO_7^+$ (M+Na$^+$): 371.1101. Found: 371.1082.

*4.2.4. Dimethyl 6-methyl-8-oxo-4-vinylidenespiro[4.5]deca-6,9-diene-2,2-dicarboxylate (**4d**).* Compound **4d** was prepared from **3d** according to the typical procedure shown in Section 4.2.1. White solids. IR (ATR) ν 2954, 1731, 1663, 1626, 1434, 1259, 1223, 1201, 1162, 1110, 1084, 859, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.00 (s, 3H), 2.61 (d, J=14.8 Hz, 1H), 2.77 (d, J=14.8 Hz, 1H), 3.16–3.23 (m, 1H), 3.37–3.42 (m, 1H), 3.79 (s, 3H), 3.83 (s, 3H), 4.80 (dd, J=4.0, 5.2 Hz, 2H), 6.07 (d, J=2.0 Hz, 1H), 6.10 (s, 1H), 6.81 (d, J=10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 19.8, 39.2, 42.5, 53.1, 53.3, 53.3, 59.7, 79.8, 103.6, 124.6, 127.9, 151.4, 159.5, 170.9, 171.6, 186.3, 201.9; (+)-ESI-HRMS. Calcd for $C_{17}H_{18}NaO_5^+$ (M+Na$^+$): 325.1046. Found: 325.1000.

*4.2.5. Dimethyl 6-methoxy-8-oxo-4-vinylidenespiro[4.5]deca-6,9-diene-2,2-dicarboxylate (**4e**).* Compound **4e** was prepared from **3e** according to the typical procedure shown in Section 4.2.1. Colorless oil. IR (ATR) ν 2953, 1735, 1660, 1594, 1263, 1224, 853 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.73 (d, J=14.4 Hz, 1H), 2.80 (d, J=14.4 Hz, 1H), 3.09–3.14 (m, 1H), 3.39–3.46 (m, 1H), 3.71 (s, 3H), 3.78 (s, 3H), 3.80 (s, 3H), 4.75–4.87 (m, 2H), 5.50 (d, J=1.2 Hz, 1H), 6.07 (dd, J=1.2, 10.0 Hz, 1H), 6.62 (d, J=10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 39.1, 42.5, 51.8, 53.0, 53.2, 55.8, 60.1, 80.2, 101.1, 104.3, 125.3, 147.2, 170.3, 171.8, 176.5, 188.1, 201.8; (+)-ESI-HRMS. Calcd for $C_{17}H_{18}NaO_6^+$ (M+Na$^+$): 341.0996. Found: 341.0959.

*4.2.6. Dimethyl 6-chloro-8-oxo-4-vinylidenespiro[4.5]deca-6,9-diene-2,2-dicarboxylate (**4f**).* Compound **4f** was prepared from **3f** according to the typical procedure shown in Section 4.2.1. Colorless oil. IR (ATR) ν 2954, 1734, 1659, 1435, 1263, 1216, 975, 869 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.76 (dd, J=1.6, 14.4 Hz, 1H), 2.97 (d, J=14.4 Hz, 1H), 3.22–3.28 (m, 1H), 3.35–3.42 (m, 1H), 3.78 (s, 3H), 3.82 (s, 3H), 4.86–4.90 (m, 2H), 6.13 (dd, J=2.0, 10.0 Hz, 1H), 6.39 (d, J=2.0 Hz, 1H), 6.91 (d, J=10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 39.0, 42.6, 53.3, 53.4, 55.1, 59.8, 80.9, 103.4, 124.3, 128.5, 150.5, 158.1, 170.3, 171.7, 184.7, 202.4; (+)-ESI-HRMS. Calcd for $C_{16}H_{15}ClNaO_5^+$ (M+Na$^+$): 345.0500. Found: 345.0469.

*4.2.7. Dimethyl 4′-oxo-2-vinylidene-4′H-spiro[cyclopentane-1,1′-naphthalene]-4,4-dicarboxylate (**4g**).* Compound **4g** was prepared from **3g** according to the typical procedure shown in Section 4.2.1. Colorless oil. IR (ATR) ν 1725, 1659, 1596, 1432, 1264, 1156, 870, 767 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.95 (d, J=16.8 Hz, 1H), 3.04 (d, J=16.8 Hz, 1H), 3.40–3.53 (m, 2H), 3.81 (s, 3H), 3.84 (s, 3H), 4.56–4.71 (m, 2H), 6.31 (d, J=10.4 Hz, 1H), 6.94 (d, J=10.4 Hz, 1H), 7.35–7.40 (m, 1H), 7.47 (d, J=8.0 Hz, 1H), 7.56–7.60 (m, 1H), 8.11 (dd, J=1.6, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 39.1, 48.2, 50.9, 53.3, 53.3, 59.4, 80.0, 106.9, 125.0, 126.2, 127.0, 127.5, 131.0, 132.9, 147.4, 150.9, 171.3, 171.9, 184.6, 202.9; (+)-ESI-HRMS. Calcd for $C_{20}H_{18}NaO_5^+$ (M+Na$^+$): 361.1046. Found: 361.1023.

*4.2.8. Di-tert-butyl 6-methoxy-8-oxo-4-vinylidenespiro[4.5]deca-6,9-diene-2,2-dicarboxylate (**4h**).* Compound **4h** was prepared from **3h** according to the typical procedure shown in Section 4.2.1. Colorless oil. IR (ATR) ν 2978, 1724, 1666, 1369, 1286, 1168, 1141, 855 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.48 (s, 18H), 2.54 (s, 2H), 3.17 (t, J=4.4 Hz, 2H), 4.79 (t, J=4.4 Hz, 2H), 6.14 (dd, J=1.6, 10.4 Hz, 2H), 6.85 (dd, J=1.6, 10.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 27.8 (6C), 37.7, 43.4, 50.2, 61.1, 79.6, 82.3 (2C), 102.9, 126.7 (2C), 151.4 (2C), 170.6, 186.0, 202.3; (+)-ESI-HRMS. Calcd for $C_{22}H_{28}NaO_5^+$ (M+Na$^+$): 395.1829. Found: 395.1823.

*4.2.9. 2-Tosyl-4-vinylidene-2-azaspiro[4.5]deca-6,9-dien-8-one (**4j**).* Compound **4j** was prepared from **3j** according to the typical procedure shown in Section 4.2.1. White solids. IR (ATR) ν 1665, 1627, 1401, 1348, 1165, 1091, 1033, 856, 817, 665 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.48 (s, 3H), 3.36 (s, 2H), 4.05 (t, J=4.4 Hz, 2H), 4.92 (t, J=4.4 Hz, 2H), 6.22 (d, J=10.0 Hz, 2H), 6.75 (d, J=10.0 Hz, 2H), 7.39 (d, J=8.4 Hz, 2H), 7.73 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 21.6, 48.7, 49.8, 56.3, 82.3, 100.2, 127.9 (2C), 128.6 (2C), 129.8, 129.9 (2C), 132.0 (2C), 144.4, 147.4, 185.4; (+)-ESI-HRMS. Calcd for $C_{18}H_{17}NNaO_5S^+$ (M+Na$^+$): 350.0821. Found: 350.0852.

4.3. Experimental procedure for the preparation of propargyl bromide derivatives and compound characterization

4.3.1. Typical experimental procedure for the preparation of malonate-tethered propargyl bromide derivatives (Scheme 2). To a stirred solution of **1a**[7a] (1.76 g, 5.00 mmol) in THF (20 mL) at 0 °C was added NaH (60% oil, 240 mg, 6.00 mmol), and the resulting mixture was kept stirring at the same temperature. After 30 min, a THF solution of 1,4-dibromo-2-butyne (1.27 g, 6 mmol in 5 mL of THF) was added to the reaction mixture, and the reaction mixture

was stirred for 3 h at room temperature. After dilution with AcOEt, the reaction was quenched with satd aq NH_4Cl solution, washed with brine, dried over Na_2SO_4, and then evaporated in vacuo. The obtained crude residue was purified by flash column chromatography (SiO_2, hexane/AcOEt=20:1) to give **2a** as colorless oil (1.30 g, 54% yield). To a stirred solution of **2a** (1.30 g, 2.70 mmol) in THF (13.5 mL) at 0 °C was added a THF solution of TBAF (1 M solution, 3.2 mL, 3.20 mmol), and the resulting mixture was stirred for 30 min at the same temperature. After dilution with AcOEt, the reaction was quenched with satd aq NH_4Cl solution, washed with brine, dried over Na_2SO_4, and then evaporated in vacuo. The obtained crude residue was purified by flash column chromatography (SiO_2, hexane/acetone=6:1) to give dimethyl 2-(4-bromobut-2-yn-1-yl)-2-(4-hydroxybenzyl)malonate **3a** as white solids (837 mg, 84% yield). IR (ATR) ν 3439, 1718, 1614, 1514, 1436, 1288, 1198, 1106, 1064, 840, 752 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.73 (t, J=1.6 Hz, 2H), 3.31 (s, 2H), 3.76 (s, 6H), 3.93 (t, J=1.6 Hz, 2H), 4.93 (br s, 1H), 6.72 (d, J=8.4 Hz, 2H), 6.99 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 14.8, 22.6, 36.8, 52.8 (2C), 58.4, 79.1, 82.7, 115.4 (2C), 127.3, 130.8 (2C), 154.8, 170.5 (2C); (+)-ESI-HRMS. Calcd for $C_{16}H_{17}BrNaO_5^+$ ($M+Na^+$): 391.0152. Found: 391.0124.

*4.3.2. Dimethyl 2-(4-bromobut-2-yn-1-yl)-2-(4-hydroxy-3,5-dimethylbenzyl)malonate (**3b**).* Compound**3b** was prepared from the corresponding malonate derivative[10] and 1,4-dibromo-2-butyne according to the typical procedure shown in Section 4.3.1. White solids. IR (ATR) ν 3420, 2917, 1752, 1725, 1489, 1432, 1270, 1248, 1202, 1147, 1062 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.17 (s, 6H), 2.74 (t, J=2.0 Hz, 2H), 3.24 (s, 2H), 3.75 (s, 6H), 3.94 (t, J=2.0 Hz, 2H), 4.78 (br s, 1H), 6.72 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 14.8, 15.9 (2C), 22.6, 36.8, 52.6 (2C), 58.4, 77.2, 78.9, 82.9, 122.9, 126.5, 129.9 (2C), 151.4, 170.4 (2C); (+)-ESI-HRMS. Calcd for $C_{18}H_{21}BrNaO_5^+$ ($M+Na^+$): 419.0465. Found: 419.0449.

*4.3.3. Dimethyl 2-(4-bromobut-2-yn-1-yl)-2-(4-hydroxy-3,5-dimethoxylbenzyl)malonate (**3c**).* Compound **3c** was prepared from the corresponding malonate derivative[10] and 1,4-dibromo-2-butyne according to the typical procedure shown in Section 4.3.1. Colorless oil. IR (ATR) ν 1732, 1613, 1517, 1458, 1428, 1338, 1292, 1246, 1204, 1108 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.76 (t, J=2.4 Hz, 2H), 3.33 (s, 2H), 3.77 (s, 6H), 3.86 (s, 6H), 3.95 (t, J=2.4 Hz, 2H), 5.44 (br s, 1H), 6.40 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 14.8, 22.7, 37.8, 52.8 (2C), 56.3 (2C), 58.4, 79.2, 82.8, 106.5 (2C), 126.1, 133.9, 146.8 (2C), 170.2 (2C); (+)-ESI-HRMS. Calcd for $C_{18}H_{21}BrNaO_7^+$ ($M+Na^+$): 451.0363. Found: 451.0357.

*4.3.4. Dimethyl 2-(4-bromobut-2-yn-1-yl)-2-(4-hydroxy-2-methylbenzyl)malonate (**3d**).* Compound **3d** was prepared from the corresponding malonate derivative[7a] and 1,4-dibromo-2-butyne according to the typical procedure shown in Section 4.3.1. Colorless oil. IR (ATR) ν 3451, 2952, 1729, 1608, 1205, 1435, 1293, 1269, 1206, 1063 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.26 (s, 3H), 2.76 (t, J=2.0 Hz, 2H), 3.36 (s, 2H), 3.74 (s, 6H), 3.91 (t, J=2.0 Hz, 2H), 4.67 (br s, 1H), 6.56 (dd, J=2.8, 8.4 Hz, 1H), 6.62 (d, J=2.8 Hz, 1H), 6.95 (d, J=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 14.7, 19.8, 22.9, 33.4, 52.8 (2C), 58.4, 78.8, 83.1, 112.8, 117.3, 125.9, 131.6, 139.1, 154.4, 170.5 (2C); (+)-ESI-HRMS. Calcd for $C_{17}H_{19}BrNaO_5^+$ ($M+Na^+$): 405.0308. Found: 405.0306.

*4.3.5. Dimethyl 2-(4-bromobut-2-yn-1-yl)-2-(4-hydroxy-2-methoxylbenzyl)malonate (**3e**).* Compound **3e** was prepared from the corresponding malonate derivative[10] and 1,4-dibromo-2-butyne according to the typical procedure shown in Section 4.3.1. Colorless oil. IR (ATR) ν 3444, 2952, 1732, 1616, 1510, 1434, 1295, 1208, 1158, 1125 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.70 (t, J=2.4 Hz, 2H), 3.34 (s, 2H), 3.72 (s, 3H), 3.74 (s, 6H), 3.93 (t, J=2.4 Hz, 2H), 4.91 (br s, 1H), 6.31–6.34 (m, 2H), 7.04 (d, J=8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 15.0, 23.1, 31.6, 52.6 (2C), 55.2, 57.7, 78.2, 83.4, 98.7, 106.8, 115.8, 132.5, 156.2, 159.1, 170.6 (2C); (+)-ESI-HRMS. Calcd for $C_{17}H_{19}BrNaO_6^+$ ($M+Na^+$): 422.0257. Found: 422.0244.

*4.3.6. Dimethyl 2-(4-bromobut-2-yn-1-yl)-2-(2-chloro-4-hydroxybenzyl)malonate (**3f**).* Compound **3f** was prepared from the corresponding malonate derivative[7a] and 1,4-dibromo-2-butyne according to the typical procedure shown in Section 4.2.1. Colorless oil. IR (ATR) ν 3418, 2952, 1734, 1609, 1500, 1437, 1211, 1051, 772 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.79 (t, J=2.4 Hz, 2H), 3.49 (s, 2H), 3.76 (s, 6H), 3.92 (t, J=2.4 Hz, 2H), 5.10 (br s, 1H), 6.68 (dd, J=2.8, 8.4 Hz, 1H), 6.82 (d, J=2.8 Hz, 1H), 7.21 (d, J=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 14.7, 23.3, 33.9, 53.1 (2C), 57.7, 79.2, 82.7, 114.2, 116.6, 124.7, 132.8, 135.2, 155.7, 170.5 (2C); (+)-ESI-HRMS. Calcd for $C_{16}H_{16}BrClNaO_5^+$ ($M+Na^+$): 424.9762. Found: 424.9777.

*4.3.7. Dimethyl 2-(4-bromobut-2-yn-1-yl)-2-((4-hydroxynaphthalen-1-yl)methyl)malonate (**3g**).* Compound **3g** was prepared from the corresponding malonate derivative[7a] and 1,4-dibromo-2-butyne according to the typical procedure shown in Section 4.2.1. White solids. IR (ATR) ν 3432, 1742, 1708, 1281, 1210, 1064, 834, 753 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.77 (t, J=2.4 Hz, 2H), 3.67 (s, 6H), 3.81 (s, 2H), 3.97 (t, J=2.4 Hz, 2H), 5.79 (s, 1H), 6.67 (d, J=8.0 Hz, 1H), 7.20 (d, J=8.4 Hz, 1H), 7.43–7.43 (m, 2H), 8.05 (d, J=8.4 Hz, 1H), 8.20 (dd, J=2.0, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 14.7, 23.3, 32.7, 52.8 (2C), 58.6, 79.1, 83.2, 107.9, 122.4, 123.6, 123.7, 124.7, 124.8, 126.4, 128.3, 133.7, 151.2, 170.5 (2C); (+)-ESI-HRMS. Calcd for $C_{20}H_{19}BrNaO_5^+$ ($M+Na^+$): 441.0308. Found: 441.0324.

*4.3.8. Di-tert-butyl 2-(4-bromobut-2-yn-1-yl)-2-(4-hydroxybenzyl) malonate (**3h**).* Compound **3h** was prepared from the corresponding malonate derivative[10] and 1,4-dibromo-2-butyne according to the typical procedure shown in Section 4.2.1. Colorless oil. IR (ATR) ν 3430, 2978, 1712, 1516, 1368, 1294, 1218, 1139, 1105, 841, 755 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.47 (s, 18H), 2.64 (t, J=2.0 Hz, 2H), 3.21 (s, 2H), 3.94 (t, J=2.0 Hz, 2H), 5.10 (br s, 1H), 6.71 (d, J=8.4 Hz, 2H), 7.06 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 14.9, 22.7, 27.9 (6C), 36.3, 59.0, 78.6, 82.1 (2C), 83.4, 115.1 (2C), 127.8, 131.3 (2C), 154.7, 169.0 (2C); (+)-ESI-HRMS. Calcd for $C_{22}H_{29}BrNaO_5^+$ ($M+Na^+$): 475.1091. Found: 475.1095.

*4.3.9. Dimethyl 2-(4-bromobut-2-yn-1-yl)-2-(4-hydroxyphenethyl) malonate (**3i**).* Compound **3i** was prepared from the corresponding malonate derivative[7a] and 1,4-dibromo-2-butyne according to the typical procedure shown in Section 4.2.1. Colorless oil. IR (ATR) ν 3454, 2953, 1725, 1514, 1436, 1201, 1061, 822, 754 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.29–2.33 (m, 2H), 2.44–2.48 (m, 2H), 2.96 (t, J=2.4 Hz, 2H), 3.74 (s, 6H), 3.88 (t, J=2.4 Hz, 2H), 4.64 (s, 1H), 6.75 (d, J=8.4 Hz, 2H), 7.07 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 14.7, 23.5, 29.5, 34.3, 52.9 (2C), 56.8, 78.5, 82.0, 115.2 (2C), 129.5 (2C), 132.8, 154.0, 170.6 (2C); (+)-ESI-HRMS. Calcd for $C_{17}H_{19}BrNaO_5^+$ ($M+Na^+$): 405.0308. Found: 405.0299.

*4.3.10. Synthesis of compound **7j**.* To a stirred solution of **5j**[7a] (3.86 g, 9.86 mmol) in THF (30 mL) at 0 °C was added NaH (60% oil. 473 mg, 11.8 mmol). After being stirred for 30 min at room temperature, a solution of freshly prepared alkynyl bromide **6** (2.83 g, 14.8 mmol) in THF (19 mL) was added to the mixture. After being stirred for 12 h at room temperature, the reaction was quenched with water, and the mixture was extracted with AcOEt. The combined organic layers were washed with water and brine, dried over $NaSO_4$, and then concentrated in vacuo. The obtained residue was purified by flash column chromatography (SiO_2, hexane/AcOEt=10:1) to give 4-(*N*-(4-((*tert*-butyldimethylsilyl)oxy)benzyl)-4-methylphenylsulfonamido) but-2-yn-1-yl acetate **7j** (4.44 g, 90% yield) as white solids. IR (ATR) ν 2929, 2857, 1748, 1509, 1348, 1254, 1221, 1159, 1091, 903, 752, 657 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.19 (s, 6H), 0.98 (s, 9H), 2.07 (s, 3H),

2.45 (s, 3H), 3.95 (s, 2H), 4.24 (s, 2H), 4.38 (s, 2H), 6.80 (d, *J*=8.0 Hz, 2H), 7.19 (d, *J*=8.0 Hz, 2H), 7.32 (d, *J*=8.0 Hz, 2H), 7.78 (d, *J*=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ −4.5 (2C), 18.2, 20.6, 21.5, 25.6 (3C), 35.6, 49.5, 51.8, 79.4, 79.8, 120.2 (2C), 127.3, 127.9 (2C), 129.4 (2C), 130.0 (2C), 136.0, 143.5, 155.6, 169.9; (+)-ESI-HRMS. Calcd for $C_{26}H_{35}NNaO_5SSi^+$ ($M+Na^+$): 524.1897. Found: 524.1907.

*4.3.11. Synthesis of compound **8j**.* To a stirred solution of **7j** (100 mg, 0.2 mmol) in MeOH (2 mL) was added K_2CO_3 (82.8 mg, 0.6 mmol). After being stirred for 12 h at room temperature, the reaction was quenched with satd aq NH_4Cl solution, and the mixture was extracted with AcOEt. The combined organic layers were washed with water and brine, dried over Na_2SO_4, and then concentrated in vacuo. The obtained residue was purified by flash column chromatography (SiO_2, hexane/AcOEt=2:1) to give *N*-(4-hydroxybenzyl)-*N*-(4-hydroxybut-2-yn-1-yl)-4-methylbenzenesulfonamide **8j** (60 mg, 87% yield) as white solids. IR (ATR) ν 3353, 2920, 1509, 1349, 1155, 1090, 988, 899, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.41 (s, 3H), 3.79 (s, 2H), 3.85 (s, 2H), 4.14 (s, 2H), 6.73 (d, *J*=8.4 Hz, 2H), 7.08 (d, *J*=8.4 Hz, 2H), 7.42 (d, *J*=8.4 Hz, 2H), 7.75 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (DMSO-d_6): δ 21.0, 35.7, 48.7, 49.1, 76.3, 85.7, 115.3 (2C), 125.1, 127.5 (2C), 129.6 (2C), 129.8 (2C), 135.6, 143.4, 157.1; (+)-ESI-HRMS. Calcd for $C_{18}H_{29}NNaO_4S^+$ ($M+Na^+$): 368.0927. Found: 368.0918.

*4.3.12. N-(4-Bromobut-2-yn-1-yl)-N-(4-hydroxybenzyl)-4-methylbenzenesulfonamide (**3j**).* To a stirred solution of **8j** (60.0 mg, 0.17 mmol) in CH_2Cl_2 (0.58 mL) at 0 °C was added PPh_3 (57.7 mg, 0.22 mmol) and CBr_4 (73.0 mg, 0.22 mmol). After being stirred for 2 h at room temperature, the reaction mixture was concentrated in vacuo, and then passed through a short pad of silica to remove triphenylphosphine oxide. The filtrate was concentrated and the obtained residue was purified by flash column chromatography (SiO_2, hexane/AcOEt=5:1) to give **3j** (41.7 mg, 59% yield) as colorless oil. IR (ATR) ν 3430, 1613, 1596, 1514, 1324, 1208, 1152, 1089, 900, 813, 746, 657 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.46 (s, 3H), 3.60 (t, *J*=2.0 Hz, 2H), 3.95 (t, *J*=2.0 Hz, 2H), 4.25 (s, 2H), 5.07 (s, 1H), 6.80 (d, *J*=8.4 Hz, 2H), 7.21 (d, *J*=8.4 Hz, 2H), 7.35 (d, *J*=8.4 Hz, 2H), 7.78 (d, *J*=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 13.6, 21.6, 35.7, 49.5, 79.6, 80.9, 115.6 (2C), 126.7, 127.8 (2C), 129.6 (2C), 130.4 (2C), 135.8, 143.7, 155.6; (+)-ESI-HRMS. Calcd for $C_{18}H_{18}BrNNaO_3S^+$ ($M+Na^+$): 430.0083. Found: 430.0091.

4.4. Pd-catalyzed *ipso*-Friedel–Crafts alkylation using 9g

Compound **9g** (82.8 mg, 0.20 mmol), $Pd(dba)_2$ (5.8 mg, 0.01 mmol), and PPh_3 (6.3 mg, 0.024 mmol) were dissolved in CH_2Cl_2 (3.2 mL) and MeOH (0.8 mL), and the resulting solution was stirred at 40 °C. After 5 h, the reaction was concentrated in vacuo, and the obtained residue was purified by flash column chromatography (SiO_2, hexane/AcOEt=4:1) to give **4g** (64.8 mg, 96% yield) as colorless oil. Compound **9g**: White solids. IR (ATR) ν 3430, 1734, 1438, 1376, 1267, 1208, 1062, 950, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.70 (t, *J*=2.0 Hz, 2H), 3.34 (s, 2H), 3.70 (s, 3H), 3.72 (s, 6H), 3.93 (t, *J*=2.0 Hz, 2H), 4.82 (br s, 1H), 6.32–6.34 (m, 2H), 7.05 (d, *J*=8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 23.1, 32.9, 52.8 (2C), 55.2, 55.9, 58.5, 77.4, 83.6, 107.9, 122.4, 123.6, 123.7, 124.7, 124.8, 126.3, 128.4, 133.7, 151.3, 155.3, 170.5 (2C); (+)-ESI-HRMS. Calcd for $C_{22}H_{22}NaO_8^+$ ($M+Na^+$): 437.1207. Found: 437.1186.

4.5. Experimental procedure for the skeletal rearrangement of the spirocyclic adducts and compound characterization

4.5.1. Typical experimental procedure for the skeletal rearrangement of the spirocyclic adducts. To a stirred solution of **4a** (34.6 mg, 0.12 mmol) in MeOH (2.4 mL) at 0 °C was added $CeCl_3\cdot 7H_2O$ (48.0 mg, 0.12 mmol), and the resulting suspension was stirred for 10 min. $NaBH_4$ (9.0 mg, 0.24 mmol) was added to the reaction, and the reaction was stirred for 1 h, and then quenched with water. After a half of solvent was evaporated in vacuo, the mixture was diluted with AcOEt, washed with brine, and then dried over Na_2SO_4. After concentration in vacuo, the obtained alcohol adduct was directly utilized for the next reaction. To a stirred solution of the crude product in CH_3CN (2.4 mL) at room temperature was added $TsOH\cdot H_2O$ (23.0 mg, 0.12 mmol). After being stirred for 1 h at room temperature, the reaction mixture was quenched with satd aq $NaHCO_3$ solution. Aqueous layer was extracted with AcOEt, and the combined organic layers were washed with brine. After concentration in vacuo, the obtained residue was purified by flash column chromatography (SiO_2, hexane/acetone=30:1) to give dimethyl 4-vinylidene-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate **10a** (28.5 mg, 87% yield) as colorless solids. IR (ATR) ν 2953, 1735, 1435, 1272, 1238, 1075, 763 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.08 (t, *J*=3.2 Hz, 2H), 3.31 (s, 2H), 3.71 (s, 6H), 5.13 (t, *J*=3.2 Hz, 2H), 7.12–7.18 (m, 3H), 7.40–7.43 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 33.4, 35.3, 52.8 (2C), 53.5, 78.9, 97.9, 126.4, 126.6, 127.1, 129.0, 129.6, 132.4, 171.0 (2C), 207.3; (+)-ESI-HRMS. Calcd for $C_{16}H_{16}NaO_4^+$ ($M+Na^+$): 295.0941. Found: 295.0911.

*4.5.2. Dimethyl 8-methyl-4-vinylidene-3,4-dihydronaphthalene-2,2(1H)-dicarboxylate (**10d**).* Compound **10d** was prepared from **4d** according to the typical experimental procedure shown in Section 4.5.1. Colorless solids. IR (ATR) ν 2924, 1732, 1434, 1313, 1254, 1191, 1175, 1065, 862, 785 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.28 (s, 3H), 3.04 (t, *J*=3.2 Hz, 2H), 3.18 (s, 2H), 3.72 (s, 6H), 5.10 (t, *J*=3.2 Hz, 2H), 6.98–7.07 (m, 2H), 7.28 (d, *J*=7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 19.7, 32.4, 33.1, 52.8 (2C), 53.7, 78.4, 98.2, 124.3, 126.0, 128.6, 129.6, 131.1, 136.3, 171.1 (2C), 207.5; (+)-ESI-HRMS. Calcd for $C_{17}H_{18}NaO_4^+$ ($M+Na^+$): 309.1097. Found: 309.1067.

*4.5.3. Dimethyl 8-chloro-4-vinylidene-3,4-dihydronaphthalene-2,2(1H)-dicarboxylate (**10f**).* Compound **10f** was prepared from **4f** according to the typical experimental procedure shown in Section 4.5.1. Colorless solids. IR (ATR) ν 2924, 1737, 1446, 1254, 1197, 1057, 787 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.04 (t, *J*=3.2 Hz, 2H), 3.34 (s, 2H), 3.74 (s, 6H), 5.14 (t, *J*=3.2 Hz, 2H), 7.08 (dd, *J*=8.0, 8.0 Hz, 1H), 7.21 (d, *J*=8.0 Hz, 1H), 7.34 (d, *J*=8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 32.8, 33.1, 52.9 (2C), 53.4, 79.0, 97.7, 125.0, 127.0, 127.7, 130.5, 132.2, 134.3, 170.8 (2C), 207.6; (+)-ESI-HRMS. Calcd for $C_{16}H_{15}ClNaO_4^+$ ($M+Na^+$): 329.0551. Found: 329.0533.

*4.5.4. Dimethyl 1-vinylidene-1,2-dihydrophenanthrene-3,3(4H)-dicarboxylate (**10g**).* Compound **10g** was prepared from **4g** according to the typical experimental procedure shown in Section 4.5.1. White solids. IR (ATR) ν 2952, 1732, 1434, 1257, 1196, 858, 817, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.14 (t, *J*=2.4 Hz, 2H), 3.69 (s, 2H), 3.72 (s, 6H), 5.20 (t, *J*=2.4 Hz, 2H), 7.42–7.54 (m, 3H), 7.61 (d, *J*=7.6 Hz, 1H), 7.77 (d, *J*=8.0 Hz, 1H), 8.01 (d, *J*=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 31.4, 33.1, 52.9 (2C), 53.6, 79.0, 98.8, 123.0, 124.4, 125.6, 126.4, 126.8, 127.0, 127.6, 128.5, 132.0, 132.7, 171.1 (2C), 208.2; (+)-ESI-HRMS. Calcd for $C_{20}H_{18}NaO_4^+$ ($M+Na^+$): 345.1097. Found: 345.1082.

Acknowledgements

This work was supported by a Grant-in Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology, Japan, the Research Foundation For Pharmaceutical Sciences, Chiba University, and the Inohana Foundation (Chiba University).

References and notes

1. For reviews, see: (a) Sannigrahi, M. *Tetrahedron* **1999**, *55*, 9007; (b) Kotha, S.; Deb, A. C.; Lahiri, K.; Manivannan, E. *Synthesis* **2009**, 165; (c) Roche, S. T.; Porco, J. A., Jr. *Angew. Chem., Int. Ed.* **2011**, *50*, 4068; (d) Zhuo, C.-X.; Zhang, W.; You, S.-L. *Angew. Chem., Int. Ed.* **2012**, *51*, 12662.

2. For recent representative examples, see: (a) Canesi, S.; Bouchu, D.; Ciufolini, M. A. *Angew. Chem., Int. Ed.* **2004**, *43*, 4336; (b) Dohi, T.; Maruyama, A.; Yoshimura, M.; Morimoto, K.; Tohma, H.; Kita, Y. *Angew. Chem., Int. Ed.* **2005**, *44*, 6193; (c) Dohi, T.; Maruyama, A.; Minamitsuji, Y.; Takenaga, N.; Kita, Y. *Chem. Commun.* **2007**, 1224; (d) Dohi, Y.; Minamitsuji, Y.; Maruyama, A.; Hirose, S.; Kita, Y. *Org. Lett.* **2008**, *10*, 3559; (e) Liang, J.; Chen, J.; Du, F.; Zeng, X.; Li, L.; Zhang, H. *Org. Lett.* **2009**, *11*, 2820; (f) Mendelsohn, B. A.; Ciufolini, M. A. *Org. Lett.* **2009**, *11*, 4739; (g) Traoré, M.; Maynadier, M.; Souard, F.; Choisnard, L.; Vial, H.; Wong, Y.-S. *J. Org. Chem.* **2011**, *76*, 1409 Reviews; (h) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299; (i) Dohi, T. *Chem. Pharm. Bull.* **2010**, *58*, 135.
3. (a) Appel, T. R.; Yehia, N. A. M.; Baumeister, U.; Hartung, H.; Kluge, R.; Ströhl, D.; Fanghänel, E. *Eur. J. Org. Chem.* **2003**, 47; (b) Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2005**, *127*, 12230; (c) Tang, B.-X.; Yin, Q.; Tang, R.-Y.; Li, J.-H. *J. Org. Chem.* **2008**, *73*, 9008; (d) Yin, Q.; You, S.-L. *Org. Lett.* **2012**, *14*, 3526.
4. (a) González-López de Turiso, F.; Curran, D. P. *Org. Lett.* **2005**, *7*, 151; (b) Lanza, T.; Leardini, R.; Minozzi, M.; Nanni, D.; Spagnolo, P.; Zanardi, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 9439.
5. (a) Pigge, F. C.; Coniglio, J. J.; Rath, N. P. *Org. Lett.* **2003**, *5*, 2011; (b) Pigge, F. C.; Dhanya, R.; Hoefgen, E. R. *Angew. Chem., Int. Ed.* **2007**, *46*, 2887.
6. Chiba, S.; Zhang, L.; Lee, J.-Y. *J. Am. Chem. Soc.* **2010**, *132*, 7266.
7. (a) Nemoto, T.; Ishige, Y.; Yoshida, M.; Kohno, Y.; Kanematsu, M.; Hamada, Y. *Org. Lett.* **2010**, *12*, 5020; (b) Wu, Q.-F.; Liu, W.-B.; Zhuo, C.-X.; Rong, Z.-Q.; Ye, K.-Y.; You, S.-L. *Angew. Chem., Int. Ed.* **2011**, *50*, 4455; (c) Yoshida, M.; Nemoto, T.; Zhao, Z.; Ishige, Y.; Hamada, Y. *Tetrahedron: Asymmetry* **2012**, *23*, 859 Similar catalytic dearomatization processes using indoles and pyrroles as nucleophiles, see: (d) Wu, Q.-F.; He, H.; Liu, W.-B.; You, S.-L. *J. Am. Chem. Soc.* **2010**, *132*, 11418; (e) Zhuo, C.-X.; Liu, W.-B.; Wu, Q.-F.; You, S.-L. *Chem. Sci.* **2012**, *3*, 205; (f) Wu, Q.-F.; Zheng, C.; You, S.-L. *Angew. Chem., Int. Ed.* **2012**, *51*, 1680.
8. For examples of transition metal-catalyzed Friedel–Crafts allylic alkylation of phenols, see: (a) Malkov, A. V.; Davis, S. L.; Baxendale, I. R.; Mitchell, W. L.; Kocovsky, P. *J. Org. Chem.* **1999**, *64*, 2751; (b) Fernández, I.; Hermatschweiler, R.; Breher, F.; Pregosin, P. S.; Veiros, L. F.; Calhorda, M. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 6386; (c) Suzuki, Y.; Nemoto, T.; Kakugawa, K.; Hamajima, A.; Hamada, Y. *Org. Lett.* **2012**, *14*, 2350; (d) Xu, Q.-L.; Dai, L.-X.; You, S.-L. *Org. Lett.* **2012**, *14*, 2579.
9. (a) Rousseaux, S.; García-Fortanet, J.; Del Aguila Sanchez, M. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2011**, *133*, 9282 See also; (b) Wu, K.-J.; Dai, L.-X.; You, S.-L. *Org. Lett.* **2012**, *14*, 3772.
10. Nemoto, T.; Zhao, Z.; Yokosaka, T.; Suzuki, Y.; Wu, R.; Hamada, Y. *Angew. Chem., Int. Ed.* **2013**, *52*, 2217.
11. (a) Winstein, S.; Baird, R. *J. Am. Chem. Soc.* **1957**, *79*, 756; (b) Masamune, S. *J. Am. Chem. Soc.* **1961**, *83*, 1009; (c) Baird, R.; Winstein, S. *J. Am. Chem. Soc.* **1962**, *84*, 788.
12. (a) Lalic, G.; Corey, E. J. *Org. Lett.* **2007**, *9*, 4921; (b) Dai, M.; Danishefsky, S. J. *Tetrahedron Lett.* **2008**, *49*, 6610; (c) Magnus, P.; Sane, N.; Fauber, B. P.; Lynch, V. *J. Am. Chem. Soc.* **2009**, *131*, 16045; (d) Eey, S. T.-C.; Lear, M. J. *Org. Lett.* **2010**, *12*, 5510.
13. Cyclic dimer was produced as the major by-product.
14. When **4g** was treated with Pd catalyst in $(CH_2Cl)_2$–MeOH mixed solvent at a refluxed temperature, the corresponding diene-type adduct was gradually produced, accompanied by the formation of several by-products.
15. Synthesis of allene derivatives via a similar Pd-catalyzed reaction process, see: (a) Kimura, M.; Wakamiya, Y.; Horino, Y.; Tamaru, Y. *Tetrahedron Lett.* **1997**, *38*, 3963; (b) Kozawa, Y.; Mori, M. *Tetrahedron Lett.* **2001**, *42*, 4869; (c) Kozawa, Y.; Mori, M. *J. Org. Chem.* **2003**, *68*, 8068; (d) Bi, H.-P.; Liu, X.-Y.; Gou, F.-R.; Guo, L.-N.; Duan, X.-H.; Shu, X.-Z.; Liang, Y.-M. *Angew. Chem., Int. Ed.* **2007**, *46*, 7068; (e) Bi, H.-P.; Liu, X.-Y.; Gou, F.-R.; Guo, L.-N.; Duan, X.-H.; Liang, Y.-M. *Org. Lett.* **2007**, *9*, 3527; (f) Shi, Y.; Huang, J.; Yang, Y.-F.; Wu, L.-Y.; Niu, Y.-N.; Huo, P.-F.; Liu, X.-Y.; Liang, Y.-M. *Adv. Synth. Catal.* **2009**, *351*, 141.
16. The product structure was determined by NOE experiments.
17. For other derivatizations of **4a**, see Ref. 10.