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Biarylmethane and Fused Heterocyclic Arene Synthesis via in Situ Generated *o*- and/or *p*-Naphthoquinone Methides

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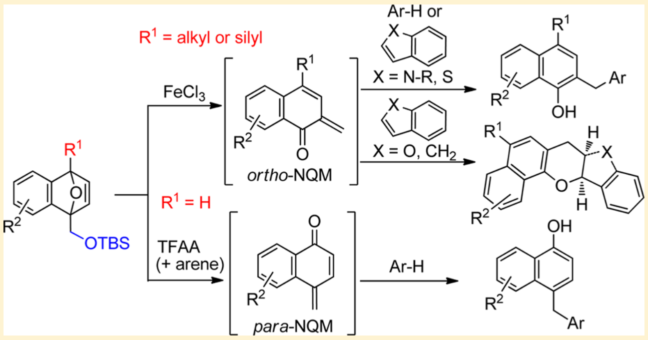
Supporting Information

ABSTRACT: *o*- and/or *p*-naphthoquinone methides (NQMs) can be selectively prepared by the ring opening of 1-(siloxymethyl)-1,4-epoxy-1,4-dihydronaphthalene derivatives based on a substituent effect at the 4 position of the substrates. The 4-alkyl- or silyl-substituted 1-(siloxymethyl)-1,4-epoxy-1,4-dihydronaphthalene was transformed to *o*-NQM (1-naphthoquinone-2-methide), which underwent Friedel−Crafts 1,4-addition of the α,β-unsaturated carbonyl moiety to provide the 2-benzyl-1-naphthol as the biarylmethane and [4 + 2]-cycloaddition with a dienophile to give the fused heterocyclic arene. Meanwhile, the 4-unsubstituted 1-(siloxymethyl)-1,4-epoxy-1,4-dihydronaphthalene could be converted to the corresponding 4-benzyl-1-naphthol by the Friedel−Crafts 1,6-addition of *p*-NQM (1-naphthoquinone-4-methide) generated by the site-selective ring opening of the 1,4-epoxy moiety. Furthermore, the 4-(siloxymethyl)-(1,4-bis(siloxymethyl))-1,4-epoxy-1,4-dihydronaphthalene was transformed into a 2,4-bisbenzyl-1-naphthol or pentacyclic derivative via both the *o*- and *p*-NQM intermediates.



■ INTRODUCTION

Naphthoquinone methides (NQMs) are reactive intermediates possessing a quinone methide (QM) backbone that is composed of a cyclohexadiene core bearing the carbonyl and exomethylene functionalities. These are traditionally prepared from the corresponding phenol derivative possessing an activated benzylic carbon.[1,2] While the reactions utilizing QM intermediates have been widely investigated,[1,2] a limited number of synthetic methods via the NQMs have been reported.[3−6] NQMs are categorized by several subtypes, such as 1-naphthoquinone-2-methide,[3] 2-naphthoquinone-1-methide,[4] and 2-naphthoquinone-3-methide,[5,6] based on the substitution site and pattern of the carbonyl and exomethylene groups and can be prepared from naphthol derivatives. Among them, the *o*-NQM (1-naphthoquinone-2-methide) is regarded as an efficient synthetic precursor to construct a pharmaceutically useful fused heterocyclic arene[7] (e.g., rubioncolin B[7f−h] possessing a potent cytotoxic and antitumor activity) via the [4 + 2]-cycloaddition with an electron-sufficient dienophile and 2-benzyl-1-naphthol as a biarylmethane possessing various bioactivities[8] by the 1,4-addition of the arene nucleophile into the α,β-unsaturated carbonyl moiety of the *o*-NQM (Figure 1, top). Additionally, the *p*-NQM (1-naphthoquinone-4-methide) could also be a good precursor to provide 4-benzyl-1-naphthol derivatives possessing a biarylmethane function[9] via the 1,6-addition by a nucleophilic arene into *p*-NQM (Figure 1, bottom).

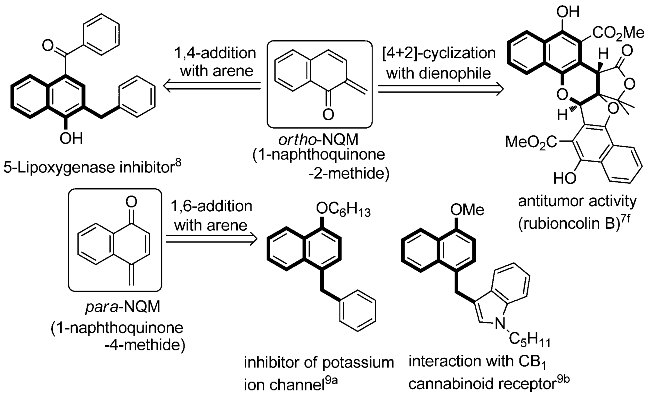


Figure 1. *o*- and *p*-naphthoquinone methide intermediates used to construct a wide variety of backbones of bioactive compounds.

We have recently revealed that various benzylic C−O bonds could be activated by the safe and inexpensive FeCl$_3$ as a catalyst[10] and the FeCl$_3$-catalyzed ring-opening nucleophilic addition using 1,4-disubstituted 1,4-epoxy-1,4-dihydronaphthalenes, which are easily prepared by the Diels−Alder reaction between benzynes and furans, providing the highly functionalized naphthalene derivatives.[11] Additionally, the 1-(siloxymethyl)-4-alkyl-1,4-epoxy-1,4-dihydronaphthalenes (**1**: R^1 = alkyl) were found to be transformed into *o*-NQM (**A**), which underwent annulation with allylsilanes.[12] We now demonstrate

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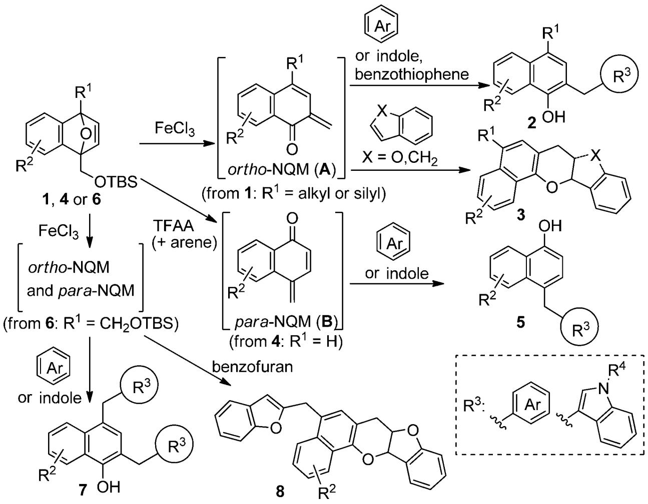
the new $FeCl_3$-catalyzed synthetic methods of biarylmethane (**2**: 2-benzyl-1-naphthol) via the Friedel−Crafts 1,4-addition of arenes to the α,β-unsaturated carbonyl moiety of *o*-NQM (**A**)[13] and the fused heterocyclic arenes (**3**) by the [4 + 2]-cycloaddition of **A** with dienophiles (e.g., benzofuran and indole as heteroarenes) except for the allylsilanes (Scheme 1).

Scheme 1. Synthesis of Biarylmethanes and Fused Heterocyclic Arenes via *o*- and/or *p*-Naphthoquinone Methides

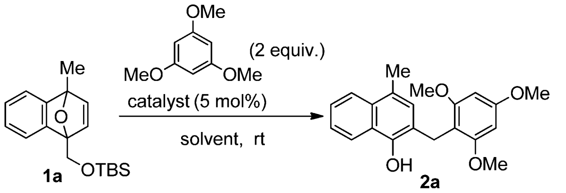


Furthermore, the novel trifluoroacetic anhydride (TFAA)-mediated preparation of *p*-NQM using 4-unsubstituted 1-(siloxymethyl)-1,4-epoxy-1,4-dihydronaphthalenes (**4**: R^1 = H) has also been developed to construct the different types of biarylmethanes (**5**: 4-benzyl-1-naphthols) by the Friedel−Crafts 1,6-addition. Additionally, the 1,4-dibenzylated 1-naphthols[14] (**7**) and the highly functionalized heterocycles (**8**) can be easily prepared by the double functionalization of arenes or heteroarenes via both the *o*- and *p*-NQMs derived from the 1,4-bis(siloxymethyl)-1,4-epoxy-1,4-dihydronaphthalenes (**6**: R^1 = CH_2OTBS).

■ RESULTS AND DISCUSSION

We initially investigated the catalyst (5 mol %) efficiency for the syntheses of 2-benzyl-1-naphthol derivatives via *o*-NQM using 1-[(*tert*-butyldimethylsiloxy)methyl]-4-methyl-1,4-epoxy-1,4-dihydronaphthalene (**1a**)[15] as a substrate and 1,3,5-trimethoxybenzene (2 equiv) as an arene nucleophile in CH_2Cl_2 at room temperature (Table 1). The reaction using catalytic $FeCl_3$ or $AuCl_3$[16] gave the desired product (**2a**) in good yields (78% and 81%, respectively, for entries 1 and 2), while the other Lewis acids, such as $FeBr_3$, $ZnCl_2$, $BF_3{\cdot}Et_2O$, TMSOTf, and $AlCl_3$, were somewhat less effective (entries 3−7). From the viewpoint of the cost performance and general versatility in comparison to $AuCl_3$, the solvent effect was next investigated under the $FeCl_3$-catalyzed conditions. Consequently, $(CH_2Cl)_2$ was the most efficient among the tested solvents including CH_2Cl_2, $CHCl_3$, CH_3CN, CH_3NO_2, and THF (entries 8 vs 1 and 10−13), and the increased amount of 1,3,5-trimethoxybenzene to 4 equiv could improve the reaction efficiency to give **2a** in 88% yield (entry 9).

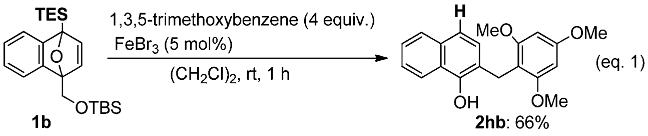
Table 1. Optimization Using 1-(Siloxymethyl)-4-methyl Substrate (1a)



entry	catalyst	solvent	time[a] (h)	yield (%)
1	$FeCl_3$	CH_2Cl_2	0.5	78
2	$AuCl_3$	CH_2Cl_2	0.5	81
3	$FeBr_3$	CH_2Cl_2	0.5	67
4	$ZnCl_2$	CH_2Cl_2	2	60
5	$BF_3{\bullet}Et_2O$	CH_2Cl_2	0.5	69
6	TMSOTf	CH_2Cl_2	0.5	74
7	$AlCl_3$	CH_2Cl_2	0.5	68
8	$FeCl_3$	$(CH_2Cl)_2$	0.5	81
9[b]	$FeCl_3$	$(CH_2Cl)_2$	0.5	88
10	$FeCl_3$	$CHCl_3$	0.25	68
11	$FeCl_3$	CH_3CN	0.25	24
12	$FeCl_3$	CH_3NO_2	0.5	58
13	$FeCl_3$	THF	30	33

[a] The reaction was stopped when **1a** was completely consumed by checking using TLC. [b] 4 equiv of 1.3.5-trimethoxybenzene was used.

The *o*-NQM derivative (**A**) derived from the $FeCl_3$-catalyzed transformation of **1a** efficiently reacted with various arene nucleophiles (1,3-dimethoxybenzene,[17] anisole,[17] 2- or 1-methoxynaphthalene, and *N*-phenylindole[18]) at room temperature to give the corresponding 2-(hetero)arylmethyl-1-naphthols (**2**) in moderate to good yields for 0.5 h (Table 2, entries 1−5). Meanwhile, benzofuran worked as a dienophile in the reaction with *o*-NQM (**A**), and the fused pentacyclic arene derivative including the heterocyclic component (**3a**) was obtained in 74% yield (entry 6). While indene and styrene also underwent the same annulation with *o*-NQM (entries 7 and 8), the reaction of benzothiophene gave 2-[(benzothienyl)methyl]-1-naphthol (**2g**) (entry 9).[19] Furthermore, the 4-silylated substrate (**1b**, 1-[(*tert*-butyldimethylsiloxy)methyl]-4-(triethylsilyl)-1,4-epoxy-1,4-dihydronaphthalene) was also applied to the $FeCl_3$-catalyzed reaction using 1,3,5-trimethoxybenzene as a nucleophile to give the corresponding 2-benzyl-4-silyl-1-naphthol derivative (**2ha**) (entry 10). During the reaction, the TES group was partially cleaved probably by the nucleophilic attack of the chloride anion derived from $FeCl_3$ on the silicon atom, and the 2-benzyl-4-hydro-1-naphthol derivative (**2hb** shown in eq 1) was obtained as a byproduct.



The use of $FeBr_3$ as a stronger Lewis acid could complete the subsequent cleavage of the TES group after the formation of **2ha** to give **2hb** as the sole product (eq 1). The stability of the TES−Ar bond strongly depended on the characteristic feature of the product, and the $FeCl_3$-catalyzed reaction of **1b** in the presence of *N*-phenylindole and the 6,7-bismethoxy-4-silyl substituent (**1c**) with 1,3,5-trimethoxybenzene provided the desilylated products (**2i** and **2j**) (entries 11 and 13), while the TES group remained during the reaction using benzofuran (entry 12).

While the reaction of the 4-alkyl- or silyl-1-(siloxymethyl) substrates (**1**) and nucleophilic arenes gave the 2-benzyl-1-naphthol derivatives (**2**) (Tables 1 and 2), the 4-benzyl-1-naphthol

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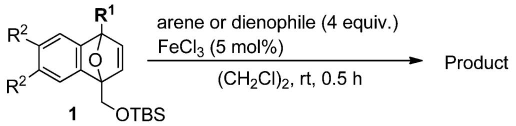
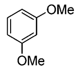
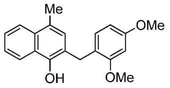
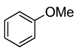
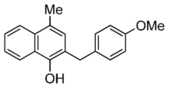
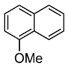
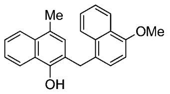
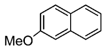
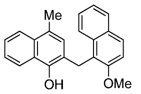
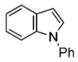
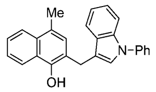
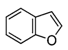
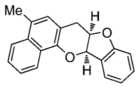
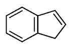
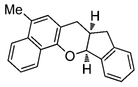
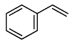
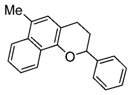
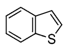
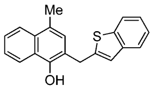
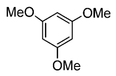
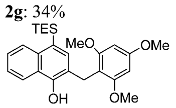
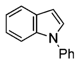
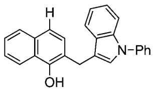
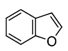
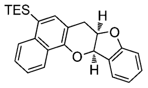
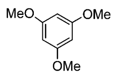
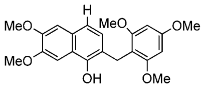
Table 2. 2-(Arylmethyl)-1-naphthol Syntheses

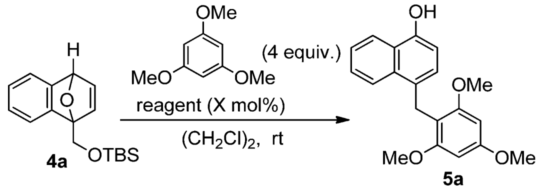


entry	substrate		arene or dienophile	product
	R^1	R^2		
1	Me	H (**1a**)		 **2b**: 71%
2	Me	H (**1a**)		 **2c**: 55%
3[a]	Me	H (**1a**)		 **2d**: 83%
4[a]	Me	H (**1a**)		 **2e**: 47%
5	Me	H (**1a**)		 **2f**: 64%
6	Me	H (**1a**)		 **3a**: 74%
7	Me	H (**1a**)		 **3b**: 90%
8[b]	Me	H (**1a**)		 **3c**: 77%
9[a]	Me	H (**1a**)		 **2g**: 34%
10	TES	H (**1b**)		 **2ha**: 75%
11	TES	H (**1b**)		 **2i**: 72%
12[b]	TES	H (**1b**)		 **3d**: 14%
13	TES	MeO (**1c**)		 **2j**: 63%

[a] 2 equiv of arene was used. [b] For 2 h.

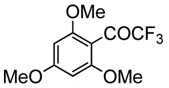
derivative (**5a**) was obtained by the use of 1-[(*tert*-butyldimethylsiloxy)methyl]-1,4-epoxy-1,4-dihydronaphthalene (**4a**) as a 4-unsubstituted substrate with 1,3,5-trimethoxybenzene (Table 3). BF$_3$·Et$_2$O was an effective Lewis acid catalyst in comparison to FeCl$_3$ and AuCl$_3$ (entries 3 vs 1 and 2).

Table 3. Reaction Using 1-(Siloxymethyl) Substrate 1b



entry	reagent	*X*	time (h)	yield (%)
1	FeCl$_3$	5	0.5	37
2	AuCl$_3$	5	0.5	61
3	BF$_3$•Et$_2$O	5	0.5	80
4	TFA	5	24	trace
5	TFA	100	2	78
6	TFAA	100	2	quant[a]
7	TFA	40	24	71[b]
8	TFAA	40	24	65[c]
9	Ac$_2$O	100	24	no reaction

[a] 37% of 1-(trifluoroacetyl)-2,4,6-trimethoxybenzene (**9**, Scheme 2) was obtained as a byproduct. [b] 29% of **4a** was recovered. [c] 15% of **4a** was recovered.; TFAA: trifluoroacetic anhydride, TFA: trifluoroacetic acid.



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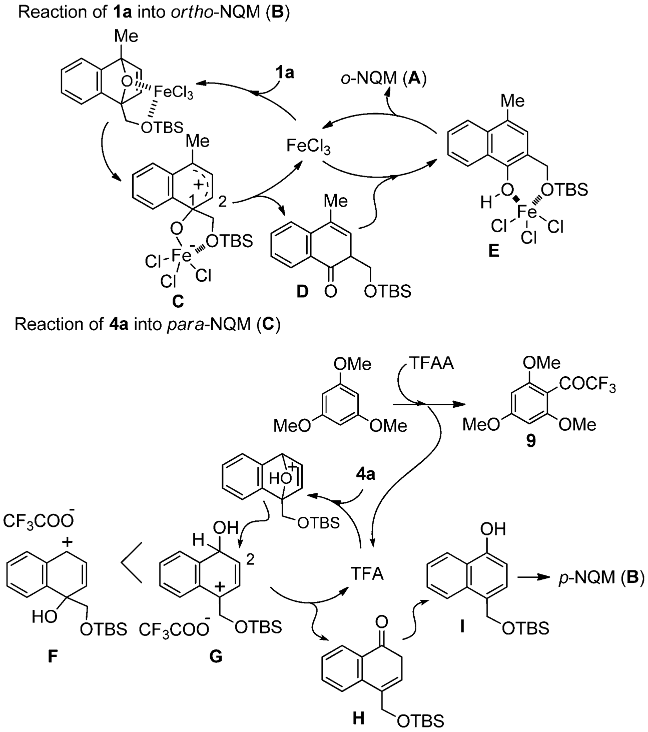
Although the catalytic use (5 mol %) of trifluoroacetic acid (TFA) as a Brønsted acid was less effective (entry 4), the stoichiometric amount (1 equiv) of TFA efficiently facilitated the desired reaction to give **5a** in 78% yield (entry 5). Intriguingly, the reaction using trifluoroacetic anhydride (TFAA, 1 equiv) as a neutral additive also effectively provided **5a** in quantitative yield accompanied by the formation of 2-[(trifluoromethyl)carbonyl]-1,3,5-trimethoxybenzene (**9**, 37% yield) (entry 6), which indicated that TFA (ca. 40 mol %) was gradually generated as a consequence of the trifluoroacetylation and moderately facilitated the desired reaction in the presence of an excessive amount of 1,3,5-trimethoxybenzene (see Scheme 2). Furthermore, the reaction efficiency became significantly diminished with decreasing amounts of TFA or TFAA, and the substrate was never completely consumed even after 24 h (entries 7 and 8). Meanwhile, the equivalent use of acetic anhydride (Ac$_2$O) instead of TFAA was not effective (entry 9).

The reactions of various 4-unsubstituted 1-(siloxymethyl) substrates **4** and arenes were applicable under the TFAA-mediated reaction conditions (Table 4). 1-Methoxynaphthalene, 2-methoxynaphthalene, and *N*-phenylindole were reacted with **4a** to give the corresponding 4-[(hetero)arylmethyl]-1-naphthol derivatives **5b**−**d** (entries 1−3), and the substrate possessing bromines at the 6 and 7 positions (**4b**) was also applied to provide the 6,7-dibromo-1-naphthol derivative (**5e**) (entry 4). Meanwhile, benzofuran and benzothiophene as the nucleophiles were insufficient for the reactions using **4a** to give the complex mixtures.

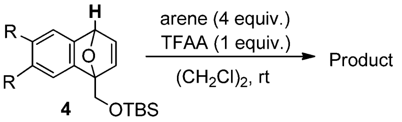
The TFAA-mediated system could be adapted for the reaction of the 4-alkyl or silyl 1-(siloxymethyl) substrates (**1**), and the comparative studies for the reaction efficiency using catalytic FeCl$_3$ are described by eqs 2−5. The reaction efficiency with the addition of TFAA was strongly affected by the property and combination of the substrate **1** and arene/dienophile. While the yields of the products (**2a** and **2f**) derived

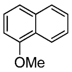
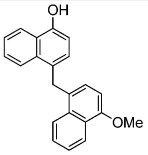
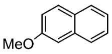
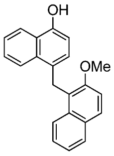
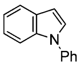
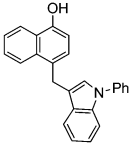
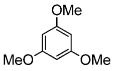
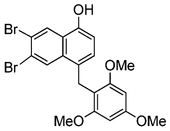
Scheme 2. Proposed Reaction Mechanism for the Formation of *o*- and *p*-Naphthoquinone Methides[a]



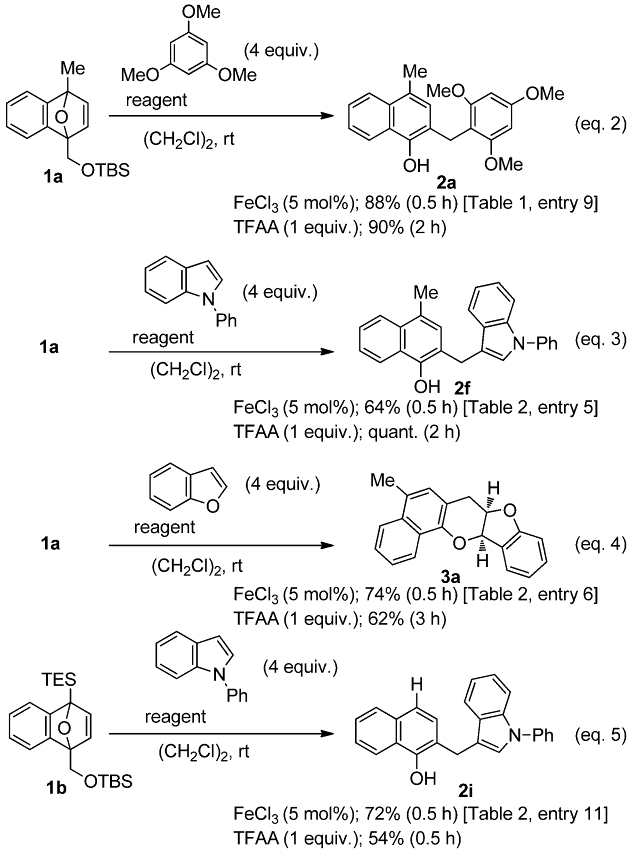
[a]Key: TFAA, trifluoroacetic anhydride; TFA, trifluoroacetic acid; NQM, naphthoquinone methide.

Table 4. 4-(Arylmethyl)-1-naphthol Syntheses



entry	R	arene	product
1	H (**4a**)		 **5b**: 74% (2 h)
2	H (**4a**)		 **5c**: 36% (2 h) [30% (2.5 h)][a]
3	H (**4a**)		 **5d**: quant. (3 h)
4	Br (**4b**)		 **5e**: 52% (3 h)

[a]$BF_3 \cdot Et_2O$ (5 mol %) was used instead of TFAA.

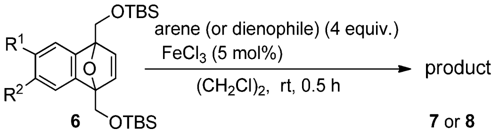


from **1a** and 1,3,5-trimethoxybenzene or *N*-phenylindole were improved (eqs 2 and 3) using a stoichiometric amount of TFAA, the reaction efficiency between **1a** and benzofuran or **1b** and *N*-phenylindole slightly decreased (eqs 4 and 5).

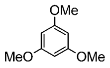
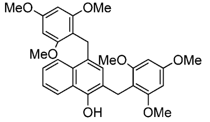
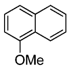
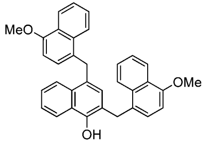
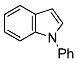
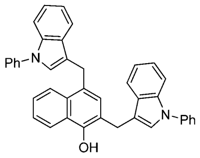
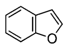
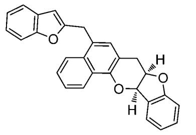
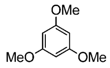
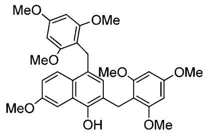
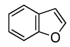
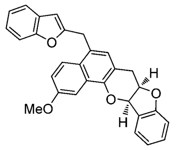
The reactions using the 4-substituted and unsubstituted substrates can proceed via the different carbocation intermediates (Scheme 2). The 1,4-epoxy moiety of the 4-methylated substrate (**1a**) is site-selectively cleaved via a five-membered transition state by the coordination between two oxygen atoms of the 1,4-epoxy moiety and the siloxy group to give the carbocation intermediate **C**. The subsequent rearrangement of the siloxymethyl group to the 2-position (**C** → **D**) and the aromatization provides a 2-(siloxymethyl)-1-naphthol intermediate (**E**).[20] The further $FeCl_3$-catalyzed elimination of the siloxy group[21] gives *o*-NQM (**A**), which reacts with an arene by nucleophilic attack or a dienophile via the [4 + 2]-cycloaddition into the corresponding 2-benzyl-1-naphthol or the condensed heterocyclic arene derivative, respectively. Among the coupling partners bearing olefin moieties connected to the benzene nucleus, benzofuran, indene and styrene preferentially act as dienophiles toward *o*-NQM, while the indole derivatives possessing the relatively high nucleophilicity promote the 1,4-addition of the α,β-unsaturated carbonyl moiety of *o*-NQM. Furthermore, HCl derived from $FeCl_3$ can also catalyze the present reactions. On the other hand, TFA generated by the reaction of TFAA and an arene facilitates the ring opening of the 1-unsubstituted substrate (**4a**) to give two different carbocation intermediates (**F** and **G**). The favorable *tert*-carbocation (**G**) was formed and underwent a hydride shift to the neighboring 2-position. The following aromatization gives the 4-(siloxymethyl)-1-naphthol intermediate (**I**).[20] The *p*-NQM can be generated by the subsequent acid-catalyzed elimination of the siloxy group[21] and reacts with an arene to give the corresponding 4-benzyl-1-naphthol derivative.

It is noteworthy that the $FeCl_3$-catalyzed double functionalizations via both the *o*- and *p*-NQMs derived from the 1,4-bis(siloxymethyl) 1,4-epoxy-1,4-dihydronaphthalenes (**6**) gave the corresponding bifunctionalized products (**7** and **8**) (Table 5).

Table 5. Double Functionalization of 1,4-Bis(siloxymethyl) Substrate



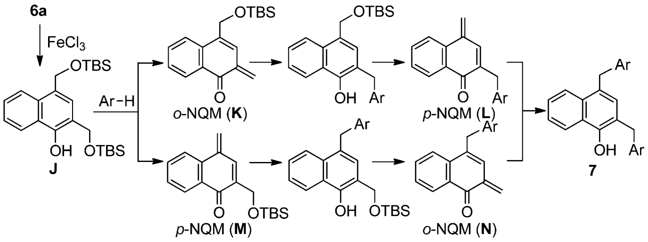
6 **7** or **8**

entry	substrate	arene	product
1	R^1, R^2 = H (**6a**)		 **7a**: 65% (77%)[a]
2	R^1, R^2 = H (**6a**)		 **7b**: 84%
3	R^1, R^2 = H (**6a**)		 **7c**: 68%
4	R^1, R^2 = H (**6a**)		 **8a**: 54%
5	R^1 = H R^2 = MeO (**6b**)		 **7d**: 72%
6	R^1 = H R^2 = MeO (**6b**)		 **8b**: 21%

[a] TFAA (1 equiv) for 2 h was used instead of $FeCl_3$.

The simple substrate **6a** could be transformed into the 1,4-bis(arylmethyl)-1-naphthol derivative **7a–c** in the presence of 1,3,5-trimethoxybenzene, 1-methoxynaphthalene, or *N*-phenylindole as an arene nucleophile (entries 1–3). The reaction of **6a** and benzofuran provided a highly functionalized heterocycle (**8a**) by the nucleophilic attack on the *p*-NQM and the [4 + 2]-cycloaddition to the *o*-NQM (entry 4). The unsymmetrical substrate (**6b**) bearing a methoxy group on the aromatic nucleus could also be site-selectively converted to the corresponding 1,4-bis(arylmethyl)-1-naphthol derivative (**7d**) or fused heterocyclic product (**8b**) in the presence of 1,3,5-trimethoxybenzene or benzofuran, respectively (entries 5 and 6).[22]

Scheme 3. Proposed Reaction Mechanisms of the Double Functionalization



Two possible reaction mechanisms are considered (Scheme 3). First, the $FeCl_3$-catalyzed ring-opening reaction of the 1,4-epoxy moiety of the substrate (**6a**) and the subsequent rearrangement and aromatization produced the 1,4-bis(siloxymethyl)-1-naphthol (**J**) intermediate as shown in Scheme 2. *o*-NQM (**K**) is then initially generated to provide a 2-benzyl-1-naphthol, which is transformed into *p*-NQM (**L**). Alternatively, the reaction via the initial generation of *p*-NQM (**M**) is also plausible.

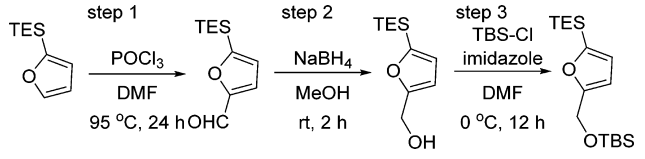
In conclusion, we have developed a selective preparation method of the reactive *o*- and *p*-NQM intermediates by the substitution effect at the 4-position of the 1-(*tert*-butyldimethylsiloxy)methyl]-1,4-epoxy-1,4-dihydronaphthalenes as substrates. The selective transformation to *o*-NQM could be achieved by the introduction of an alkyl or silyl substituent at the 4-position, while the 4-unsubstituted substrate was converted to *p*-NQM. The combination of the nucleophilic attack of arenes on the *o*- and/or *p*-NQMs and [4 + 2]-cycloaddition of dienophiles with *o*-NQM could construct various types of pharmaceutically useful biarylmethanes (2-benzyl-1-naphthol, 4-benzyl-1-naphthol, and 2,4-bisbenzyl-1-naphthol derivatives) and highly functionalized fused heteroaromatic arenes, respectively.

■ EXPERIMENTAL SECTION

1. General Information. All reactions were performed in oven-dried glassware under argon. Anhydrous $(CH_2Cl)_2$ as a solvent was purchased from a commercial source and used without further purification. Flash column chromatography was performed with silica gel. ^1H and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ or CD_3OD as a solvent and internal standard (^1H NMR δ = 7.26; ^{13}C NMR δ = 77.0 for $CDCl_3$; ^1H NMR δ = 3.4, 4.8; ^{13}C NMR δ = 49.3 for CD_3OD) with tetramethylsilane as an internal standard. ESI high-resolution mass spectra (HRMS) were measured by IT-TOF.

2. Procedures To Prepare the Substrates and Their Spectroscopic Data. Substrates **1a** and **6a** were prepared according to ref 12.

2.1. Synthetic Procedure of 5-[(tert-Butyldimethylsiloxy)methyl]-2-(triethylsilyl)furan.



Step 1: To a solution of the 2-(triethylsilyl)furan (1.82 g, 10.0 mmol) in anhydrous DMF (30 mL) was added $POCl_3$ (1.0 mL, 10.8 mmol) at 0 °C. The reaction mixture was subsequently heated at 95 °C. After being stirred for 5 h, the reaction mixture was cooled to room temperature, and 4 N NaOH aq. (25 mL) was added for the hydrolysis. After dilution with AcOEt, the organic layer was washed with water, dried with Na_2SO_4, and filtered. The filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography using hexane–AcOEt (10/1) as eluent to give 5-formyl-2-triethylsilylfuran (1.25 g, 5.92 mmol) in 59% yield.

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5-Formyl-2-(triethylsilyl)furan: colorless oil; IR (ATR) (cm^{-1}) 2956, 2877, 1683, 1560, 1461, 1106, 1019, 805, 760; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 7.22 (d, J = 3.6 Hz, 1H), 6.76 (d, J = 3.6 Hz, 1H), 1.00 (t, J = 7.2 Hz, 9H), 0.83 (q, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ178.0, 167.1, 156.4, 122.5, 120.5, 7.2, 2.9; ESI-HRMS m/z 233.0963 ([M + Na]$^+$), calcd for $C_{11}H_{18}O_2SiNa$ 233.0968.

Step 2: To a solution of 5-formyl-2-triethylsilylfuran (1.21 g, 5.75 mmol) in MeOH (5 mL) was added sodium borohydride (262 mg, 6.91 mmol) at 0 °C. The reaction mixture was subsequently stirred at room temperature for 12 h. The reaction was quenched with water. After MeOH was removed in vacuo, the residue was diluted with AcOEt, dried with Na_2SO_4, and filtrated. The filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography using hexane−AcOEt (10/1) as a eluent to give 5-(hydroxymethyl)-2-(triethylsilyl)furan (1.13 g, 5.32 mmol) in 93% yield.

5-(Hydroxymethyl)-2-(triethylsilyl)furan: colorless oil; IR (ATR) (cm^{-1}) 3310, 2954, 2876, 1459, 1415, 1238, 1180, 1012, 792, 723; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (d, J = 3.6 Hz, 1H), 6.27 (d, J = 3.6 Hz, 1H), 4.63 (d, J = 5.6 Hz, 2H), 1.72 (t, J = 5.6 Hz, 1H), 0.98 (t, J = 8.0 Hz, 9H), 0.76 (q, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 158.1, 121.5, 107.5, 57.8, 7.3, 3.2; ESI-HRMS m/z 211.1163 ([M − H]$^-$), calcd for $C_{11}H_{19}O_2Si$ 211.1160.

Step 3: To a solution of the 5-(hydroxymethyl)-2-(triethylsilyl)-furan (1.14 g, 5.36 mmol) in anhydrous DMF (10 mL) was added imidazole (552 mg, 8.10 mmol in 5 mL of anhydrous DMF) at 0 °C. The reaction mixture was stirred at room temperature for 0.5 h. TBSCl (1.22 g, 8.09 mmol in 5 mL of anhydrous DMF) was subsequently added at 0 °C. The reaction mixture was stirred at room temperature for 19 h. The reaction mixture was quenched with satd $NaHCO_3$ and extracted with diethyl ether. The obtained organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography using hexane−AcOEt (45/1) as a eluent to give 5-[(*tert*-butyldimethylsiloxy)methyl]-2-(triethylsilyl)-furan (1.57 g, 4.81 mmol) in 90% yield.

5-[(tert-Butyldimethylsiloxy)methyl]-2-(triethylsilyl)furan: colorless oil; IR (ATR) (cm^{-1}) 2954, 1462, 1254, 1080, 834, 720; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (d, J = 3.2 Hz, 1H), 6.21 (d, J = 3.2 Hz, 1H), 4.67 (s, 2H), 0.98 (t, J = 8.4 Hz, 9H), 0.90 (s, 9H), 0.78−0.72 (m, 6H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 157.8, 121.3, 107.1, 58.4, 25.8, 18.4, 7.3, 3.2, −5.2; ESI-HRMS m/z 349.1981 ([M + Na]$^+$), calcd for $C_{17}H_{34}O_2Si_2Na$ 349.1990.

*2.2. Synthetic Procedure of **1b**.* To a solution of the 5-[(*tert*-butyldimethylsiloxy)methyl]-2-(triethylsilyl)furan (170 mg, 0.52 mmol) in anhydrous THF (10 mL) were added anthranilic acid (105 mg, 0.79 mmol in 10 mL of anhydrous THF) and isoamyl nitrite (0.20 mL, 1.50 mmol in 10 mL of anhydrous THF) at 95 °C. After being stirred for 1−2 h, the reaction mixture was cooled to room temperature, and water was added. After dilution with diethyl ether, the organic layers were washed with satd $NaHCO_3$, dried with Na_2SO_4, and filtrated. The filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography using hexane−AcOEt (30/1) as a eluent to give **1b** (119 mg, 0.30 mmol) in 57% yield.

*1-[(tert-Butyldimethylsiloxy)methyl]-4-(triethylsilyl)-1,4-epoxy-1,4-dihydronaphthalene (**1b**):* yellow oil; IR (ATR) (cm^{-1}) 2953, 1462, 1253, 1097, 1006, 835, 752; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (dd, J = 6.0, 2.0 Hz, 1H), 7.15 (dd, J = 6.0, 2.0 Hz, 1H), 6.97−6.89 (m, 4H), 4.45 (d, J = 10.5 Hz, 1H), 4.27 (d, J = 10.5 Hz, 1H), 1.04 (t, J = 8.0 Hz, 9H), 0.93 (s, 9H), 0.84 (q, J = 8.0 Hz, 6H), 0.13 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$):δ 154.7, 151.2, 147.6, 142.6, 124.2, 124.1, 120.1, 119.8, 93.1, 85.9, 61.8, 25.8, 18.3, 7.6, 2.6, −5.3; ESI-HRMS m/z 425.2312 ([M + Na]$^+$), calcd for $C_{23}H_{38}O_2Si_2Na$ 425.2303.

*2.3. Synthetic Procedure of **1c**.* To a solution of 5-[(*tert*-butyldimethylsiloxy)methyl]-2-(triethylsilyl)furan (1.30g, 3.98 mmol) and 1,2-dibromo-4,5-dimethoxybenzene (590 mg, 1.99 mmol) in anhydrous THF (10 mL) was added 1.0 mL (2.6 mmol) of n-BuLi (2.6 M in hexanes) at −78 °C. After being stirred until the reaction was completed, the reaction mixture was added to water, diluted with diethyl ether, and washed with brine. After the solution was dried over Na_2SO_4 and filtrated, the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography using hexane−AcOEt (15/1) as a eluent to give **1c** (47 mg, 0.10 mmol) in 5% yield.

*1-[(tert-Butyldimethylsiloxy)methyl]-6,7-dimethoxy-l-4-(triethylsilyl)-1,4-epoxy-1,4-dihydronaphthalene (**1c**):* yellow pale oil; IR (ATR) (cm^{-1}) 2952, 1463, 1324, 1247, 1209, 1119, 1096, 834, 777, 730, 691; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (s, 1H), 6.98 (d, J = 5.6 Hz, 1H), 6.95 (d, J = 5.6 Hz, 1H), 6.85 (s, 1H), 4.40 (d, J = 11.2 Hz, 1H), 4.27 (d, J = 11.2 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 1.05 (t, J = 8.0 Hz, 9H), 0.94 (s, 9H), 0.84 (q, J = 8.0 Hz, 6H), 0.14 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 147.3, 145.3, 145.0, 144.3, 143.0, 107.4, 106.7, 93.2, 86.2, 62.0, 56.8, 56.2, 25.8, 18.2, 7.6, 2.6, −5.4; ESI-HRMS m/z 461.2550 ([M − H]$^-$), calcd for $C_{25}H_{41}O_4Si_2$: 461.2549.

*2.4. Synthetic Procedure of **4a**.* To a solution of the 2-[(*tert*-butyldimethylsiloxy)methyl]furan (1.06 g, 4.99 mmol; synthesized accoroding to ref 23) in anhydrous THF (20 mL) were added anthranilic acid (1.05 g, 7.66 mmol in 5 mL of anhydrous THF) and isoamyl nitrite (1.45 mL, 10.9 mmol in 5 mL of anhydrous THF) at 95 °C. After being stirred for 5 h, the reaction mixture was cooled to room temperature, and water was added. After dilution with diethyl ether, the organic layer was washed with satd $NaHCO_3$, dried with Na_2SO_4, and filtrated. The filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography using hexane−AcOEt (30/1) as a eluent to give **4a** (0.62 g, 2.16 mmol) in 43% yield.

*1-[(tert-Butyldimethylsiloxy)methyl]-1,4-epoxy-1,4-dihydronaphthalene (**4a**):* colorless oil; IR (ATR) (cm^{-1}) 2928, 2856, 1254, 1137, 1006, 978, 947, 835, 777, 755; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28−7.26 (m, 1H), 7.22−7.21 (m, 1H), 7.03 (dd, J = 6.0, 1.5 Hz, 1H), 6.97−6.95 (m, 3H), 5.69 (d, J = 1.5 Hz, 1H), 4.46 (d, J = 11.0 Hz, 1H), 4.31 (d, J = 11.0 Hz, 1H), 0.95 (s, 9H), 0.16 (s, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 152.4, 150.4, 145.5, 144.1, 126.2, 126.2, 121.2, 121.2, 94.8, 83.7, 62.7, 26.7, 19.5, −4.9; ESI-HRMS m/z 287.1474 ([M − H]$^-$), calcd for $C_{17}H_{23}O_2Si$ 287.1473.

*2.5. Synthetic Procedure of **4b**.* To a solution of 2-[(*tert*-butyldimethylsiloxy)methyl]furan (779 mg, 3.67 mmol) and 1,2,4,5-tetrabromobenzene (963 mg, 2.45 mmol) in anhydrous THF (30 mL) was added 1.17 mL (3.10 mmol) of n-BuLi (2.6 M in hexane) at −78 °C. After being stirred until reaction was completed, the reaction mixture was added to water, diluted with diethyl ether, and washed with brine. After the solution was dried over Na_2SO_4 and filtrated, the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography using hexane−AcOEt (20/1) as a eluent to give **1c** (397 mg, 0.86 mmol) in 35% yield.

*1-[(tert-Butyldimethylsiloxy)methyl]-6,7-dibromo-1,4-epoxy-1,4-dihydronaphthalene (**4b**):* pale yellow oil; IR (ATR) (cm^{-1}) 2928, 1255, 1099, 834, 776, 576; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.43 (s, 1H), 7.00 (dd, J = 5.4, 2.0 Hz, 1H), 6.92 (d, J = 5.4 Hz, 1H), 5.63 (d, J = 2.0 Hz, 1H), 4.37 (d, J = 11.6 Hz, 1H), 4.27 (d, J = 11.6 Hz, 1H), 0.94 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 150.7, 143.6, 142.8, 125.5, 125.1, 120.6, 120.4, 92.5, 81.6, 61.1, 25.8, 18.3, −5.4; ESI-HRMS m/z 466.9648 ([M + Na]$^+$), calcd for $C_{17}H_{22}O_2SiBr_2Na$ 466.9648.

*2.6. Synthetic Procedure of **6b**.* To a solution of 2,5-[(di-*tert*-butyldimethylsiloxy)methyl]furan (1.50 mL, 3.89 mmol) and 3,4-dibromoanisole (0.3 mL, 2.05 mmol) in anhydrous THF (10 mL) was added 1.0 mL (2.60 mmol) of n-BuLi (2.6 M in hexane) at −78 °C. After being stirred until the reaction was completed, the reaction mixture was added to water, diluted with diethyl ether, and washed with brine. After the solution was dried with Na_2SO_4 and filtrated, the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography using hexane−AcOEt (30/1) as a eluent to give **1c** (159 mg, 0.34 mmol) in 17% yield.

*1,4-[(Di-tert-butyldimethylsiloxy)methyl]-6-methoxy-1,4-epoxy-1,4-dihydronaphthalene (**6b**):* colorless oil; IR (ATR) (cm^{-1}) 2928, 2856, 1464, 1254, 1206, 1097, 1005, 832, 775; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, J = 8.0 Hz, 1H), 6.97 (d, J = 5.2 Hz, 1H), 6.94 (d, J = 5.2 Hz, 1H), 6.93 (d, J = 2.4 Hz, 1H), 6.41 (dd, J = 8.0, 2.4 Hz, 1H), 4.41−4.37 (m, 2H), 4.27−4.23 (m, 2H), 3.76 (s, 3H), 0.94 (s, 9H), 0.93 (s, 9H), 0.14 (s, 6H), 0.13 (s, 6H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 157.3, 153.2, 144.3, 143.1, 142.7, 119.6, 108.8, 107.3, 92.1, 91.9, 61.7, 61.7, 55.5, 25.9, 18.3, −5.3, −5.4; ESI-HRMS m/z 485.2523 ([M + Na]$^+$), calcd for $C_{25}H_{42}O_4Si_2Na$ 485.2514.

3. General Synthetic Procedures of Biarylmethanes and Fused Heterocyclic Arenes. *Typical Procedure Using Catalytic $FeCl_3$.* To a solution of the 4-substituted 1-(siloxymethyl)-1,4-epoxy-1,4-dihydronaphthalene (**1**, 0.2 mmol) in $(CH_2Cl)_2$ (1 mL) were added an arene (0.8 mmol) and $FeCl_3$ (0.01 mmol: 5 mol % of the substrate) and the mixture stirred at room temperature under argon. After an adequate reaction time, the mixture was quenched with water and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography to give the biarylmethane (**2**) or fused heterocyclic arene (**3**).

Typical Procedure Using TFAA. To a solution of a 4-substituted or unsubstituted 1-(siloxymethyl)-1,4-epoxy-1,4-dihydronaphthalene (**1** or **4**, 0.2 mmol) in $(CH_2Cl)_2$ (1 mL) was added an arene (0.8 mmol) and TFAA (0.2 mmol, 1 equiv of the substrate) and stirred at room temperature under argon. After an adequate reaction time, the mixture was quenched with water and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography to give the biarylmethane (**2** or **5**).

4. Spectroscopic Data of Products. *4-Methyl-2-[(2′,4′,6′-trimethoxyphenyl)methyl]naphthalen-1-ol* (***2a***). Compound **1a** (60.0 mg, 0.20 mmol), $FeCl_3$ (1.6 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (10/1) as a eluent, **2a** (59.3 mg, 0.18 mmol) was obtained in 88% yield: colorless solid; mp 122−127 °C; IR (ATR) (cm^{-1}) 3397, 2932, 2838, 1591, 1204, 1111, 944, 757; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.25 (m, 1H), 7.84−7.82 (m, 1H), 7.77 (s, 1H), 7.43−7.40 (m, 2H), 7.39 (s, 1H), 6.17 (s, 2H), 3.96 (s, 2H), 3.95 (s, 6H), 3.77 (s, 3H), 2.58 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$):δ 159.7, 157.7, 147.9, 132.2, 130.3, 125.2, 125.1, 124.7, 124.3, 123.7, 122.6, 119.5, 109.5, 91.1, 55.9, 55.3, 23.4, 18.8; ESI-HRMS m/z 361.1424 ([M + Na]$^+$), calcd for $C_{21}H_{22}O_4Na$ 361.1410.

2-[(2′,4′-Dimethoxyphenyl)methyl]-4-methylnaphthalen-1-ol (***2b***). Compound **1a** (56.6 mg, 0.19 mmol), $FeCl_3$ (1.6 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (10/1) as an eluent, **2b** (40.8 mg, 0.13 mmol) was obtained in 71% yield: colorless oil; IR (ATR) (cm^{-1}) 3383, 2937, 1613, 1582, 1506, 1207, 1148, 1029, 760; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28−8.26 (m, 1H), 7.85−7.83 (m, 1H), 7.45−7.43 (m, 2H), 7.34 (s, 1H), 7.25 (t, J = 8.0 Hz, 1H), 7.17 (s, 1H), 6.48−6.46 (m, 2H), 3.97 (s, 3H), 3.95 (s, 2H), 3.76 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 156.2, 147.5, 132.4, 130.7, 128.9, 125.8, 125.5, 125.4, 124.7, 123.8, 122.7, 121.1, 119.7, 105.5, 98.9, 55.9, 55.4, 30.3, 18.7; ESI-HRMS m/z 331.1294 ([M + Na]$^+$); Calcd for $C_{20}H_{20}O_3Na$: 331.1305.

2-[(4′-Methoxyphenyl)methyl]-4-methylnaphthalen-1-ol (***2c***). Compound **1a** (57.8 mg, 0.19 mmol), $FeCl_3$ (1.6 mg, 0.01 mmol) and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (15/1) as an eluent, **2c** (28.9 mg, 0.10 mmol) was obtained in 55% yield: red oil; IR (ATR) (cm^{-1}) 3501, 2926, 1510, 1387, 1245, 1033, 759; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15−8.12 (m, 1H), 7.93−7.91 (m, 1H), 7.52−7.45 (m, 2H), 7.17 (d, J = 8.8 Hz, 2H), 7.12 (s, 1H), 6.84 (d, J = 8.8 Hz, 2H), 4.99 (s, 1H), 4.07 (s, 2H), 3.78 (s, 3H), 2.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 147.5, 132.5, 131.2, 129.5, 129.3, 126.4, 125.5, 125.1, 125.0, 124.1, 121.7, 119.6, 114.3, 55.3, 36.0, 18.7; ESI-HRMS m/z 277.1237 ([M − H]$^-$), calcd for $C_{19}H_{17}O_2$ 277.1234.

2-[(1′-Methoxynaphthalen-4′-yl)methyl]-4-methylnaphthalen-1-ol (***2d***). Compound **1a** (62.0 mg, 0.20 mmol), $FeCl_3$ (1.6 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (10/1) as an eluent, **2d** (61.8 mg, 0.17 mmol) was obtained in 83% yield: red oil; IR (ATR) (cm^{-1}) 3480, 2932, 1583, 1461, 1386, 1268, 1089, 906, 756; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33−8.30 (m, 1H), 8.16−8.13 (m, 1H), 8.01−7.99 (m, 1H), 7.91−7.89 (m, 1H), 7.50−7.43 (m, 4H), 7.11 (d, J = 8.0 Hz, 1H), 7.08 (s, 1H), 6.64 (d, J = 8.0 Hz, 1H), 5.22 (s, 1H), 4.42 (s, 2H), 3.93 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 147.7, 132.8, 132.5, 129.2, 126.8, 126.4, 126.4,126.2, 126.0, 125.5, 125.3, 125.1, 125.0, 124.1, 123.6, 122.7, 121.8, 118.6, 103.3, 55.4, 33.7, 18.8; ESI-HRMS m/z 351.1365 ([M + Na]$^+$), calcd for $C_{23}H_{20}O_2Na$ 351.1356.

2-[(2′-Methoxynaphthalen-1′-yl)methyl]-4-methylnaphthalen-1-ol (***2e***). Compound **1a** (31.2 mg, 0.10 mmol), $FeCl_3$ (0.8 mg, 0.005 mmol), and $(CH_2Cl)_2$ (0.5 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (10/1) as an eluent, **2e** (18.6 mg, 0.05 mmol) was obtained in 47% yield: colorless oil; IR (ATR) (cm^{-1}) 3352, 2938, 1579, 1512, 1465, 1386, 1247, 1079, 807, 760; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8.8 Hz, 1H), 8.26−8.24 (m, 1H), 7.83−7.76 (m, 4H), 7.56 (dt, J = 7.2, 1.6 Hz, 1H), 7.44−7.39 (m, 3H), 7.36 (t, J = 7.2 Hz, 1H), 7.32 (d, J = 8.8 Hz, 1H), 4.50 (s, 2H), 4.14 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 148.4, 133.1, 132.3, 130.0, 129.4, 128.8, 128.7, 126.8, 125.4, 125.3, 124.6, 123.9,123.8, 123.8, 123.7, 122.6, 121.3, 118.4, 112.9, 57.1, 26.2, 18.8; ESI-HRMS m/z 327.1377 ([M − H]$^-$), calcd for $C_{23}H_{19}O_2$ 327.1391.

3-[(1′-Hydroxy-4′-methylnaphthalen-2′-yl)methyl]-N-phenylindole (***2f***). Compound **1a** (59.7 mg, 0.19 mmol), $FeCl_3$ (1.5 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (10/1) as an eluent, **2f** (44.1 mg, 0.12 mmol) was obtained in 64% yield: yellow oil; IR (ATR) (cm^{-1}) 3469, 3063, 1596, 1499, 1455, 1218, 907, 734, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 7.6, 2.0 Hz, 1H), 7.91 (dd, J = 7.6, 2.0 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.49−7.38 (m, 6H), 7.27−7.20 (m, 3H), 7.14 (t, J = 8.0 Hz, 1H), 7.04 (s, 1H), 5.42 (s, 1H), 4.24 (s, 2H), 2.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 139.4, 136.6, 132.5, 129.5, 129.2, 128.5, 126.3, 126.3, 125.5, 125.2, 124.9, 124.1, 124.0, 123.0, 121.9, 120.3, 119.5, 118.4, 114.4, 110.7, 27.2, 18.8; ESI-HRMS m/z 386.1511 ([M + Na]$^+$), calcd for $C_{26}H_{21}NONa$ 386.1515.

2-[(1′-Hydroxy-4′-methylnaphthalen-2′-yl)methyl]benzo[b]-thiophene (***2g***). Compound **1a** (61.4 mg, 0.20 mmol), $FeCl_3$ (1.6 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (20/1) as an eluent, **2g** (21.5 mg, 0.07 mmol) was obtained in 34% yield: red oil; IR (ATR) (cm^{-1}) 3494, 3066, 1580, 1425, 1385, 1201, 906, 753, 725; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, J = 7.5, 2.0 Hz, 1H), 7.93 (dd, J = 7.5, 2.0 Hz, 1H), 7.86−7.84 (m, 1H), 7.81−7.79 (m, 1H), 7.51 (dt, J = 7.0, 2.0 Hz, 1H), 7.49 (dt, J = 7.0, 2.0 Hz, 1H), 7.38−7.34 (m, 2H), 7.15 (s, 1H), 6.98 (s, 1H), 5.15 (s, 1H), 4.27 (s, 2H), 2.59 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.5, 140.9, 138.5, 133.9, 132.6, 129.0, 126.7, 125.7, 125.1, 125.0, 124.6, 124.2, 124.2, 123.1, 122.9, 121.9, 121.6, 117.6, 30.2, 18.8; ESI-HRMS m/z 303.0852 ([M − H]$^-$), calcd for $C_{20}H_{15}OS$ 303.0849.

4-(Triethylsilyl)-2-[(2′,4′,6′-trimethoxyphenyl)methyl]-naphthalen-1-ol (***2ha***). Compound **1b** (58.3 mg, 0.14 mmol), $FeCl_3$ (1.2 mg, 0.007 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (10/1) as an eluent, **2ha** (46.1 mg, 0.11 mmol) was obtained in 75% yield: colorless solid; mp 119−121 °C; IR (ATR) (cm^{-1}) 3387, 2943, 1593, 1327, 1142, 1104, 758, 723; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29−8.27 (m, 1H), 8.00 (s, 1H), 7.94−7.92 (m, 1H), 7.78 (s, 1H), 7.39−7.36 (m, 2H), 6.17 (s, 2H), 3.99 (s, 2H), 3.94 (s, 6H), 3.78 (s, 3H), 0.98 (s, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 157.8, 151.0, 139.3, 137.7, 127.3, 125.3, 125.0, 124.1, 124.0, 122.9, 119.1, 109.4, 91.1,55.9, 55.4, 23.8, 7.8, 4.7, 0.0; ESI-HRMS m/z 461.2126 ([M + Na]$^+$), calcd for $C_{26}H_{34}O_4SiNa$ 461.2119.

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2-[(2′,4′,6′-Trimethoxyphenyl)methyl]naphthalen-1-ol ***(2hb)***. Compound **1b** (81.8 mg, 0.20 mmol), $FeBr_3$ (3.0 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 3.0 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (5/1) as an eluent, **2hb** (42.7 mg, 0.13 mmol) was obtained in 66% yield: colorless solid; mp 122−126 °C; IR (ATR) (cm^{-1}) 3377, 2940, 1591, 1452, 1142, 1110, 944, 781; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24−8.21 (m, 1H), 7.94 (s, 1H), 7.70−7.69 (m, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.40−7.35 (m, 2H), 7.30 (d, *J* = 8.4 Hz, 1H), 6.16 (s, 2H), 3.99 (s, 2H), 3.93 (s, 6H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 157.9, 149.7, 133.6, 130.1, 127.2, 125.4, 125.2, 124.7, 122.3, 120.1, 119.0, 109.5, 91.3, 56.1, 55.5, 23.7;ESI-HRMS *m*/*z* 347.1256 ($[M + Na]^+$), calcd for $C_{20}H_{20}O_4Na$ 347.1254.

3-[(1′-Hydroxynaphthalen-2′-yl)methyl]-N-phenylindole ***(2i)***. Compound **1b** (81.0 mg, 0.20 mmol), $FeCl_3$ (1.6 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (10/1) as an eluent, **2i** (69.2 mg, 0.15 mmol) was obtained in 72% yield: red oil; IR (ATR) (cm^{-1}) 3052, 2292, 1657, 1594, 1499, 1455, 1329, 906, 727; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16−8.13 (m, 1H), 8.04−8.02 (m, 1H), 7.75−7.70 (m, 2H), 7.56 (t, *J* = 7.2 Hz, 2H), 7.53−7.46 (m, 5H), 7.37−7.33 (m, 1H), 7.28 (s, 1H), 7.23 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.16 (dt, *J* = 8.0, 1.2 Hz, 1H), 6.73 (s, 1H), 4.11 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.4, 185.3, 150.2, 136.2, 139.5, 135.3, 133.7, 133.6, 132.3, 132.2, 129.6, 128.4, 127.2, 126.6, 126.4, 126.1, 124.2, 122.8, 120.4, 119.1, 111.6, 110.8, 25.2; ESI-HRMS *m*/*z* 348.1392 ($[M - H]^-$), calcd for $C_{25}H_{18}NO$ 348.1394.

6,7-Dimethoxy-2-[(2′,4′,6′-trimethoxyphenyl)methyl]-naphthalen-1-ol ***(2j)***. Compound **1c** (47.0 mg, 0.10 mmol), $FeCl_3$ (0.8 mg, 0.005 mmol), and $(CH_2Cl)_2$ (0.5 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (5/1) as an eluent, **2j** (24.1 mg, 0.06 mmol) was obtained in 63% yield: yellow oil; IR (ATR) (cm^{-1}) 3381, 2940, 2836, 1609, 1953, 1510, 1487, 1456, 1253, 1230, 1156, 1111, 728; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s,1H), 7.51 (s, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.01 (s, 1H), 6.16 (s, 2H), 4.00 (s, 3H), 3.96 (s, 2H), 3.95 (s, 3H), 3.94 (s, 6H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 157.7, 149.0, 148.7, 148.5, 129.2, 128.3, 120.0, 118.8, 117.5, 109.5, 105.8, 101.1, 91.1, 55.9, 55.8, 55.7, 55.4, 23.5; ESI-HRMS *m*/*z* 407.1456 ($[M + Na]^+$), calcd for $C_{22}H_{24}O_6Na$ 407.1465.

Product ***3a***. Compound **1a** (57.2 mg, 0.19 mmol), $FeCl_3$ (1.5 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (20/1) as an eluent, **3a** (40.4 mg, 0.14 mmol) was obtained in 74% yield: pale yellow solid; M.p.116−117 °C; IR (ATR) (cm^{-1}) 2891, 1596, 1509, 1417, 1241, 1178, 1148, 1096, 1013, 743; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14−8.12 (m, 1H), 7.86−7.83 (m, 1H), 7.58 (d, *J* = 6.8 Hz, 1H), 7.43 (t, *J* = 3.8 Hz, 1H), 7.40 (t, *J* = 3.8 Hz, 1H), 7.12 (dt, *J* = 7.8, 1.2 Hz, 1H), 7.09 (s, 1H), 6.86 (t, *J* = 7.6 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 5.92 (d, *J* = 7.6 Hz, 1H), 5.42−5.39 (m, 1H), 3.29 (dd, *J* = 15.6, 4.2 Hz, 1H), 3.23 (dd, *J* = 15.6, 4.2 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 148.5, 132.3, 130.9, 127.8, 127.5, 126.3, 126.1, 125.9, 125.4, 125.1, 124.0, 121.7, 120.9, 117.6, 109.9, 82.8, 79.3, 29.1, 18.8; ESI-HRMS *m*/*z* 287.1081 ($[M - H]^-$), calcd for $C_{20}H_{15}O_2$ 287.1078.

Product ***3b***. Compound **1a** (60.8 mg, 0.20 mmol), $FeCl_3$ (1.6 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (30/1) as an eluent, **3b** (51.4 mg, 0.18 mmol) was obtained in 90% yield: colorless oil; IR (ATR) (cm^{-1}) 2931, 1582, 1417, 1107, 755, 730; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.25 (m, 1H), 7.86−7.83 (m, 1H), 7.59−7.58 (m, 1H), 7.44−7.42 (m, 2H), 7.23−7.21 (m, 3H), 6.97 (s, 1H), 5.64 (d, *J* = 6.4 Hz, 1H), 3.14−3.00 (m, 3H), 2.85−2.80 (m, 1H), 2.66−2.60 (m, 1H), 2.55 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4, 143.0, 142.5, 132.1, 128.6, 127.9, 126.8, 125.7, 125.5, 125.2, 125.2, 125.1, 124.8, 123.9, 122.0, 115.9, 81.4, 37.7, 37.1, 27.8, 18.7; ESI-HRMS *m*/*z* 285.1276 ($[M - H]^-$), calcd for $C_{21}H_{17}O$ 285.1285.

3,4-Dihydro-6-methyl-2-phenyl-2H-naphtho[1,2-b]pyran ***(3c)***. Compound **1a** (60.9 mg, 0.20 mmol), $FeCl_3$ (1.6 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 2.0 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (15/1) as an eluent, **3c** (38.8 mg, 0.16 mmol) was obtained in 77% yield: colorless oil; IR (ATR) (cm^{-1}) 2924, 1580, 1416, 1386, 1107, 756, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 6.8 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.51−7.45 (m, 4H), 7.42−7.38 (m, 2H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.01 (s, 1H), 5.21 (dd, *J* = 9.6, 2.4 Hz, 1H), 3.10−3.02 (m, 1H), 2.84−2.78 (m, 1H), 2.59 (s, 3H), 2.35−2.28 (m, 1H), 2.20−2.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 142.1, 132.1, 128.4, 127.9, 127.6, 125.8, 125.5, 125.5, 125.4, 124.9, 123.9, 122.0, 114.9, 77.5, 30.1, 24.9, 18.6; ESI-HRMS *m*/*z* 273.1286 ($[M - H]^-$), calcd for $C_{20}H_{17}O$ 273.1285.

Product ***3d***. Compound **1b** (61.2 mg, 0.15 mmol), $FeCl_3$ (1.3 mg, 0.007 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 2.0 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (20/1) as an eluent, **3d** (8.3 mg, 0.02 mmol) was obtained in 14% yield: yellow oil; IR (ATR) (cm^{-1}) 2952, 1599, 1478, 1240, 978, 728; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19−8.16 (m, 1H), 7.98−7.94 (m, 1H), 7.60 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.42−7.36 (m, 3H), 7.17 (dt, *J* = 7.5, 1.4 Hz, 1H), 6.90 (dt, *J* = 7.5, 1.4 Hz, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 5.88 (d, *J* = 7.2 Hz, 1H), 5.40−5.36 (m, 1H), 3.34 (dd, *J* = 15.6, 4.2 Hz, 1H), 3.27 (dd, *J* = 15.6, 4.2 Hz, 1H), 0.96−0.94 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 151.3, 137.7, 135.8, 131.0, 127.9, 127.6, 126.3, 126.2, 125.8, 125.3, 124.8, 122.0, 121.0, 116.2, 110.1, 82.5, 78.9, 28.9, 7.7, 4.5; ESI-HRMS *m*/*z* 387.1783 ($[M - H]^-$), calcd for $C_{25}H_{28}O_2Si$: 387.1786.

4-[(2′,4′,6′-Trimethoxyphenyl)methyl]-naphthalen-1-ol ***(5a)***. Compound **4a** (58.6 mg, 0.20 mmol), TFAA (28 μL, 0.20 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 2.0 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (5/1) as an eluent, **5a** (65.6 mg, 0.20 mmol) was obtained in quantitative yield: colorless solid; mp 126−129 °C; IR (ATR) (cm^{-1}) 3374, 1590, 1200, 1144, 1116, 812, 761; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.2 Hz, 1H), 8.19 (d, *J* = 8.2 Hz, 1H), 7.58−7.54 (m, 1H), 7.51−7.47 (m, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 6.63 (d, *J* = 7.6 Hz, 1H), 6.21 (s, 2H), 4.96 (s, 1H), 4.29 (s, 2H), 3.85 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 159.3, 149.5, 133.2, 129.5, 126.0, 124.6, 124.5, 123.9, 123.8, 122.0, 108.8, 108.2, 90.7,55.7, 55.3, 24.7; ESI-HRMS *m*/*z* 347.1245 ($[M + Na]^+$), calcd for $C_{20}H_{20}O_4Na$ 347.1254.

4-[(1′-Methoxynaphthalen-4′-yl)methyl]-naphthalen-1-ol ***(5b)***. Compound **4a** (60.9 mg, 0.21 mmol), TFAA (28 μL, 0.20 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 2.0 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (5/1) as an eluent, **5b** (48.9 mg, 0.16 mmol) was obtained in 74% yield: colorless solid; mp 126−129 °C; IR (ATR) (cm^{-1}) 3519, 1585, 1463, 1381, 1267, 1242, 1091, 757; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35−8.32 (m, 1H), 8.27−8.24 (m, 1H), 8.00−7.94 (m, 2H), 7.52−7.46 (m, 4H), 6.96 (d, *J* = 7.8 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 6.67−6.64 (m, 2H), 4.69 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 150.2, 133.2, 133.0, 128.8, 128.2, 126.8, 126.8, 126.5, 125.9, 125.0, 124.9, 124.7, 124.0, 123.8, 122.5, 122.2, 108.2, 103.5,55.4, 34.8; ESI-HRMS *m*/*z* 337.1188 ($[M + Na]^+$), calcd for $C_{22}H_{18}O_2Na$ 337.1199.

4-[(2′-Methoxynaphthalen-1′-yl)methyl]-naphthalen-1-ol ***(5c)***. Compound **4a** (55.1 mg, 0.19 mmol), TFAA (27 μL, 0.19 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 2.0 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (10/1) as an eluent, **5c** (22.1 mg, 0.07 mmol) was obtained in 36% yield: colorless solid; mp 145−148 °C; IR (ATR) (cm^{-1}) 3380, 2926, 1586, 1511, 1384, 1250, 1089, 743; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.6 Hz, 1H), 8.25 (d, *J* = 8.6 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.84−7.82 (m, 1H), 7.69−7.64 (m, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 8.8 Hz, 1H), 7.34−7.29 (m, 2H), 6.47 (d, *J* = 7.6 Hz, 1H), 6.41 (d, *J* = 7.6 Hz, 1H), 5.00 (s, 1H), 4.81 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 149.7, 133.8, 133.1, 129.3, 128.6, 128.4, 128.3, 126.4, 124.9, 124.6, 124.4,124.4, 124.0, 123.4, 123.4,122.3, 120.8, 113.7, 108.2, 56.8, 27.0; ESI-HRMS *m*/*z* 337.1195 ([M + Na]$^+$), calcd for $C_{22}H_{18}O_2Na$ 337.1199.

*3-[(1′-Hydroxynaphthalen-4-yl)methyl]-N-phenylindol (**5d**).* Compound **4a** (56.7 mg, 0.19 mmol), TFAA (28 μL, 0.20 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 3.0 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (10/1) as an eluent, **5d** (78.8 mg, 0.19 mmol) was obtained in quantitative yield: red oil: IR (ATR) (cm^{-1}) 3508, 3046, 1499, 1455, 905, 728; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23−8.22 (m, 1H), 8.06−8.05 (m, 1H), 7.68 (d, *J* = 7.0 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.47−7.45 (m, 2H), 7.41−7.35 (m, 4H), 7.25−7.20 (m, 3H), 7.17 (t, *J* = 7.0 Hz, 1H), 6.81 (s, 1H), 6.69 (d, *J* = 7.5 Hz, 1H), 5.27 (s, 1H), 4.49 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 139.7, 136.0, 133.1, 129.4,, 129.4, 128.9, 128.7, 126.4, 126.4, 126.0, 124.9, 124.7, 124.4, 124.0, 122.5, 122.1, 119.9, 119.4, 116.8, 110.5, 108.1, 28.4; ESI-HRMS *m*/*z* 372.1360 ([M + Na]$^+$), calcd for $C_{25}H_{19}NONa$ 372.1359.

*6,7-Dibromo-4-[(2′,4′,6′-trimethoxyphenyl)methyl]naphthalen-1-ol (**5e**).* Compound **4b** (83.3 mg, 0.19 mmol), TFAA (28 μL, 0.20 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 2.0 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (2/1) as an eluent, **5e** (45.0 mg, 0.10 mmol) was obtained in 52% yield: yellow oil; IR (ATR) (cm^{-1}) 3396, 2937, 2837, 1596, 1454, 1416, 1203, 1148, 1118, 812, 732; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.46 (s, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 6.17 (s, 2H), 5.09 (s, 1H), 4.18 (s, 2H), 3.82 (s, 3H), 3.77 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 160.0, 159.0, 148.7, 133.1, 129.5, 129.5,127.1, 126.8, 124.5, 122.5, 120.6, 109.4, 108.6, 90.7, 55.7, 55.3, 25.0; ESI-HRMS *m*/*z* 502.9457 ([M + Na]$^+$), calcd for $C_{20}H_{18}O_4Br_2Na$ 502.9464.

*2,4-Bis[(2′,4′,6′-trimethoxyphenyl)methyl]naphthalen-1-ol (**7a**).* Compound **6a** (83.6 mg, 0.19 mmol), $FeCl_3$ (1.6 mg, 0.01 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (5/1) as an eluent, **7a** (62.4 mg, 0.13 mmol) was obtained in 65% yield: colorless solid; mp 117−118 °C; IR (ATR) (cm^{-1})3486, 2937, 1623, 1584, 1513, 1421, 1387, 1269, 1091, 904, 726; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 7.8 Hz, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.74 (s, 1H), 7.45 (t, *J* = 7.0 Hz, 1H), 7.41 (t, *J* = 7.0 Hz, 1H), 6.94 (s, 1H), 6.25 (s, 2H), 6.08, (s, 1H), 4.26 (s, 3H), 3.88 (s, 3H), 3.83 (s, 2H), 3.76−3.74 (m, 9H), 3.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 159.5, 157.7, 147.7, 132.0, 127.8, 127.6, 125.2, 124.9, 124.0, 123.3, 122.6, 119.4, 109.7, 109.4, 90.9, 90.7, 90.6, 55.8, 55.7, 55.6, 55.4, 24.6, 23.5; ESI-HRMS *m*/*z* 527.2037 ([M + Na]$^+$), calcd for $C_{30}H_{32}O_7Na$ 527.2040.

*2,4-Bis[(1′-methoxynaphthalen-4′-yl)methyl]naphthalen-1-ol (**7b**).* Compound **6a** (43.2 mg, 0.10 mmol), $FeCl_3$ (0.8 mg, 0.005 mmol), and $(CH_2Cl)_2$ (0.5 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (5/1) as an eluent, **7b** (40.7 mg, 0.08 mmol) was obtained in 84% yield: pale yellow oil; IR (ATR) (cm^{-1}) 2394, 1584, 1461, 1387, 1267, 1090, 760; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.0 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.19 (d, *J* = 9.0 Hz, 1H), 7.93 (t, *J* = 7.0 Hz, 2H), 7.83 (d, *J* = 7.0 Hz, 1H), 7.49−7.41 (m, 5H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 6.92−6.91 (m, 2H), 6.61 (d, *J* = 8.0 Hz, 2H), 5.29 (s, 1H), 4.67 (s, 2H), 4.32 (s, 2H), 3.94 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 154.2, 148.4, 132.8, 132.7, 132.2, 130.1, 128.6, 128.2, 126.7, 126.4, 126.2, 126.1, 125.8, 125.8, 125.2, 125.0, 124.9, 124.9, 124.0, 124.0, 123.7, 123.7, 122.6, 122.5, 122.0, 118.6, 103.3, 103.1, 55.4, 55.4, 34.7, 34.2; ESI-HRMS *m*/*z* 507.1930 ([M + Na]$^+$), calcd for $C_{34}H_{28}O_3Na$ 507.1931.

*2,4-Bis[(3′-N-phenylindolyl)methyl]-naphthalen-1-ol (**7c**).* Compound **6a** (32.3 mg, 0.07 mmol), $FeCl_3$ (0.6 mg, 0.004 mmol) and $(CH_2Cl)_2$ (0.5 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (15/1) as an eluent, **7c** (26.5 mg, 0.05 mmol) was obtained in 68% yield: yellow oil; IR (ATR) (cm^{-1}) 3481, 3051, 1596, 1498, 1455, 906, 730; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20−8.18 (m, 1H), 8.07−8.04 (m, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.57−7.51 (m, 3H), 7.43−7.34 (m, 11H), 7.28−7.17 (m, 4H), 7.13 (dt, *J* = 4.4, 1.2 Hz, 1H), 7.08−7.05 (m, 2H), 6.84 (s, 1H), 5.49 (s, 1H), 4.53 (s, 2H), 4.25 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 139.8, 139.4, 136.6, 136.1, 132.2, 129.6, 129.5, 129.4, 128.9, 128.5, 128.4, 126.4, 126.3, 126.0, 125.9, 125.7, 125.4, 124.9, 124.3, 124.1, 124.0, 123.0, 122.5, 122.0, 120.3, 120.0, 119.5, 119.4, 118.5, 117.0, 114.4, 110.7, 110.5, 28.4, 27.3; ESI-HRMS *m*/*z* 577.2246 ([M + Na]$^+$), calcd for $C_{40}H_{30}N_2ONa$ 577.2250.

*2,4-Bis[(2′,4′,6′-trimethoxyphenyl)methyl]-7-methoxynaphthalen-1-ol (**7d**).* Compound **6b** (46.7 mg, 0.10 mmol), $FeCl_3$ (0.8 mg, 0.005 mmol), and $(CH_2Cl)_2$ (0.5 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (5/1) as an eluent, **7d** (38.4 mg, 0.07 mmol) was obtained in 72% yield: pale yellow oil; IR (ATR) (cm^{-1}) 3411, 2936, 1590, 1418, 1207, 1108, 1034, 799; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 9.2 Hz, 1H), 7.68 (s, 1H), 7.56 (d, *J* = 2.6 Hz, 1H), 7.11 (dd, *J* = 9.2, 2.6 Hz, 1H), 6.83 (s, 1H), 6.24 (s, 2H), 6.09 (s, 2H), 4.23 (s, 2H), 3.93 (s, 3H), 3.87 (s, 3H), 3.82 (s, 2H), 3.76 (s, 6H), 3.74 (s, 3H), 3.70 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 159.5, 159.5, 157.7, 156.6, 146.8, 127.8, 127.5, 126.1, 125.6, 125.1, 120.1, 117.3, 109.8, 109.6, 100.9, 90.9, 90.7, 55.8, 55.7,55.5, 55.4, 55.3, 24.6, 23.6; ESI-HRMS *m*/*z* 557.2138 ([M + Na]$^+$), calcd for $C_{31}H_{34}O_8Na$ 557.2146.

*Product **8a**.* Compound **6a** (41.2 mg, 0.10 mmol), $FeCl_3$ (0.8 mg, 0.005 mmol), and $(CH_2Cl)_2$ (0.5 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (15/1) as an eluent, **8a** (19.8 mg, 0.05 mmol) was obtained in 54% yield: yellow oil; IR (ATR) (cm^{-1}) 3065, 2925, 1600, 1511, 1478, 1388, 1241, 1106, 750; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.5 Hz, 1H), 7.89 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.43−7.37 (m, 4H), 7.21−7.18 (m, 2H), 7.17−7.13 (m, 2H), 6.88 (t, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 9.0 Hz, 1H), 6.19 (s, 1H), 5.94 (d, *J* = 7.5 Hz, 1H), 5.43−5.39 (m, 1H), 4.48 (d, *J* = 16.5 Hz, 1H), 4.39 (d, *J* = 16.5 Hz, 1H), 3.30 (dd, *J* = 15.8, 4.0 Hz, 1H), 3.25 (dd, *J* = 15.8, 4.0 Hz, 1H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 157.8, 154.7, 149.5, 131.7, 131.0, 128.8, 128.4, 126.5, 126.3, 126.2, 126.0, 125.9, 125.3, 123.8, 123.3, 122.4, 121.9, 121.0, 120.3 117.4, 110.9, 110.0, 103.6, 82.5, 79.2, 32.0, 29.0; ESI-HRMS *m*/*z* 403.1330 ([M − H]$^-$), calcd for $C_{28}H_{19}O_3$ 403.1340.

*Product **8b**.* Compound **6b** (26.7 mg, 0.06 mmol), $FeCl_3$ (0.8 mg, 0.005 mmol), and $(CH_2Cl)_2$ (0.5 mL) were used, and the reaction was carried out at room temperature for 0.5 h. After purification of the crude product by silica gel column chromatography using hexane−AcOEt (10/1) as an eluent, **8b** (6.4 mg, 0.01 mmol) was obtained in 21% yield: yellow oil; IR (ATR) (cm^{-1}) 2930, 1601, 1454, 1254, 1222, 751; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 9.2 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 2.8 Hz, 1H), 7.40 (dt, *J* = 5.6, 1.2 Hz, 2H), 7.21−7.13 (m, 3H), 7.06−7.03 (m, 2H), 6.88 (dt, *J* = 7.2, 1.2 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.17 (s, 1H), 5.93 (d, *J* = 7.6 Hz, 1H), 5.42−5.39 (m, 1H), 4.43 (d, *J* = 16.4 Hz, 1H), 4.35 (d, *J* = 17.2 Hz, 1H), 3.92 (s, 3H), 3.29 (dd, *J* = 15.6, 4.0 Hz, 1H), 3.23 (dd, *J* = 15.6, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 157.9, 157.4, 154.8, 148.6, 131.1, 128.8, 127.3, 127.3, 126.7, 126.1, 126.0, 125.6, 123.9, 123.3, 122.4, 121.0, 120.3, 118.4, 118.3, 110.9, 110.1, 103.6, 100.3, 82.7, 79.4, 55.3, 32.1, 29.2; ESI-HRMS *m*/*z* 457.1414 ([M + Na]$^+$) calcd for $C_{29}H_{22}O_4Na$ 457.1410.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthetic method for substrates and spectroscopic data of substrates and products. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00434.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Rokita, S. E. *Quinone Methides*; John Wiley & Sons: Edison, NJ, 2009; Vol. *1*,.

(2) For reviews, see: (a) Van De Water, R. W.; Pettus, T. R. R. *Tetrahedron* **2002**, *58*, 5367−5405. (b) Bai, W.-J.; David, J. G.; Feng, Z.-G.; Weaver, M. G.; Wu, K.-L.; Pettus, T. R. R. *Acc. Chem. Res.* **2014**, *47*, 3665−3664.

(3) Examples of 1-naphthoquinone-2-methides: (a) Sabie, R.; Fillion, H.; Pinatel, H.; Fent, B. *J. Heterocycl. Chem.* **1990**, *27*, 1893−1897. (b) Bouaziz, Z.; Fillion, H.; Pinatel, H. *J. Heterocycl. Chem.* **1993**, *30*, 41−44.

(4) Examples using 2-naphthoquinone-1-methides: (a) Marshall, J. A.; Pike, M. T. *Tetrahedron Lett.* **1965**, *35*, 3107−3114. (b) Katritzky, A. R.; Lan, X. *Synthesis* **1992**, 761−764. (c) Asherson, J. L.; Bilgic, O.; Young, D. W. *J. Chem. Soc., Perkin Trans. 1* **1981**, 3041−3047.

(5) 2-Naphthoquinone-3-methides could selectively react with alkyl vinyl ether to afford the benzo[*g*]chroman analogues. See: (a) Kostikov, A. P.; Popik, V. V. *J. Org. Chem.* **2007**, *72*, 9190−9194. (b) Kulikov, A.; Arumugam, S.; Popik, V. V. *J. Org. Chem.* **2008**, *73*, 7611−7615. (c) Arumugam, S.; Popik, V. V. *J. Am. Chem. Soc.* **2009**, *131*, 11892−11899. (d) Arumugam, S.; Popik, V. V. *J. Am. Chem. Soc.* **2011**, *133*, 5573−5579.

(6) Antonio, M. D.; Doria, F.; Richter, S. N.; Bertipaglia, C.; Mella, M.; Sissi, C.; Palumbo, M.; Freccero, M. *J. Am. Chem. Soc.* **2009**, *131*, 13132−13141.

(7) (a) Itoigawa, M.; Ito, C.; Tan, H. T.-W.; Okuda, M.; Tokuda, H.; Nishino, H.; Furukawa, H. *Cancer Lett.* **2001**, *174*, 135−139. (b) Wen, B.; Doneanu, C. E.; Gartner, C. A.; Roberts, A. G.; Atkins, W. M.; Nelson, S. D. *Biochemistry* **2005**, *44*, 1833−1845. (c) Gartner, C. G.; Wen, B.; Wan, J.; Becker, R. S.; Jones, G., II; Gygi, S. P.; Nelson, S. D. *Biochemistry* **2005**, *44*, 1846−1855. (d) Claessens, S.; Kesteleyn, B.; Van, T. N.; De Kimpe, N. *Tetrahedron* **2006**, *62*, 8419−8424. (e) Lee, Y. R.; kim, Y. M. *Helv. Chim. Acta* **2007**, *90*, 2401−2413. (f) Itokawa, H.; Ibraheim, Z. Z.; Qiao, Y.-F.; Takeya, K. *Chem. Pharm. Bull.* **1993**, *41*, 1869−1872. (g) Singh, R.; Geetanjali; Chauhan, S. M. S. *Chem. Biodiversity* **2004**, *1*, 1241−1264. (h) Lumb, J.-P.; Choong, K. C.; Trauner, D. *J. Am. Chem. Soc.* **2008**, *130*, 9230−9231. (i) Chiou, W.-F.; Li, S.-Y.; Ho, L.-K.; Hsien, M.-L.; Don, M.-J. *Eur. J. Med. Chem.* **2002**, *37*, 69−75.

(8) Batt, D. G.; Maynard, G. D.; Petraitis, J. J.; Shaw, J. E.; Galbraith, W.; Harris, R. R. *J. Med. Chem.* **1990**, *33*, 360−370.

(9) (a) Michne, W. F.; Guiles, J. W.; Treasurywala, A. M.; Castonguay, L. A.; Weigelt, C. A.; Oconnor, B.; Volberg, W. A.; Grant, A. M.; Chadwick, C. C.; Krafte, D. S.; Hill, R. J. *J. Med. Chem.* **1995**, *38*, 1877−1883. (b) Huffman, J. W.; Mabon, R.; Wu, M.-J.; Lu, J.; Hart, R.; Hurst, D. P.; Reggio, P. H.; Wiley, J. L.; Martin, B. R. *Bioorg. Med. Chem.* **2003**, *11*, 539−549. (c) Morikawa, T.; Xie, H.; Matsuda, H.; Wang, T.; Yoshikawa, M. *Chem. Pharm. Bull.* **2006**, *54*, 506−513.

(10) (a) Sawama, Y.; Nagata, S.; Yabe, Y.; Morita, K.; Monguchi, Y.; Sajiki, H. *Chem.—Eur. J.* **2012**, *18*, 16608−16611. (b) Sawama, Y.; Shibata, K.; Sawama, Y.; Takubo, M.; Monguchi, Y.; Krause, N.; Sajiki, H. *Org. Lett.* **2013**, *15*, 5282−5285. (c) Sawama, Y.; Shishido, Y.; Kawajiri, T.; Goto, R.; Monguchi, Y.; Sajiki, H. *Chem.—Eur. J.* **2014**, *20*, 510−516. (d) Sawama, Y.; Goto, R.; Nagata, S.; Shishido, Y.; Monguchi, Y.; Sajiki, H. *Chem.—Eur. J.* **2014**, *20*, 2631−2636. (e) Sawama, Y.; Masuda, M.; Asai, S.; Goto, R.; Nagata, S.; Nishimura, S.; Monguchi, Y.; Sajiki, H. *Org. Lett.* **2015**, *17*, 434−437.

(11) (a) Sawama, Y.; Kawamoto, K.; Satake, H.; Krause, N.; Kita, Y. *Synlett* **2010**, *14*, 2151−2155. (b) Sawama, Y.; Ogata, Y.; Kawamoto, K.; Satake, H.; Shibata, K.; Monguchi, Y.; Sajiki, H.; Kita, Y. *Adv. Synth. Catal.* **2013**, *355*, 517−528. (c) Sawama, Y.; Asai, S.; Kawajiri, T.; Monguchi, Y.; Sajiki, H. *Chem.—Eur. J.* **2015**, *21*, 2222−2229.

(12) Sawama, Y.; Shishido, Y.; Yanase, T.; Kawamoto, K.; Goto, R.; Monguchi, Y.; Sajiki, H. *Angew. Chem., Int. Ed.* **2013**, *52*, 1515−1519.

(13) $FeCl_3$ was used as a catalyst for Friedel−Crafts reactions. For examples, see refs 10c and 11c and: (a) Iovel, I.; Mertins, K.; Kischel, J.; Zapf, A.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 3913−3917. (b) Wang, B.-Q.; Xiang, S.-K.; Sun, Z.-P.; Guan, B.-T.; Hu, P.; Zhao, K.-Q.; Shi, Z.-J. *Tetrahedron Lett.* **2008**, *49*, 4310−4312. (c) Stadler, D.; Bach, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 7557−7559.

(14) 2,4-Bisbenzyl-1-phenol derivatives are also important as bioactive compounds; see: (a) Lasswell, W. L., Jr.; Hufford, C. D. *J. Org. Chem.* **1977**, *42*, 1295−1302. (b) Nakatani, N.; Ichimaru, M.; Moriyasu, M.; Kato, A. *Biol. Pharm. Bull.* **2005**, *28*, 83−86.

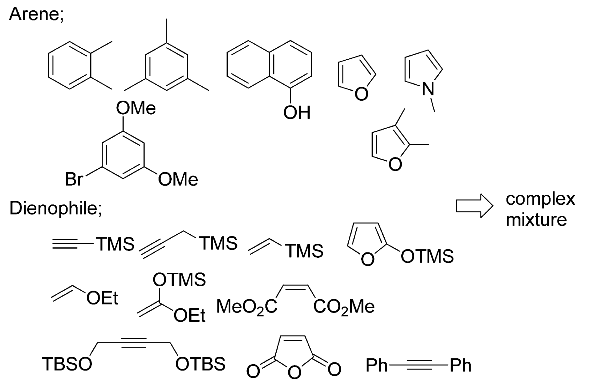
(15) A (*tert*-butyldimethylsiloxy)methyl group was found to be the most effective substituent at the 1-position of the 1,4-epoxy-1,4-dihydronaphthalene nucleus to generate the *o*-NQM derivatives **A**. See ref 12.

(16) $AuCl_3$ also effectively activates the benzylic C−O bonds. See refs 10 and 11 and: Sawama, Y.; Sawama, Y.; Krause, N. *Org. Lett.* **2009**, *11*, 5034−5037.

(17) Regioisomers were not obtained.

(18) The reaction using the unprotected indole gave a complex mixture.

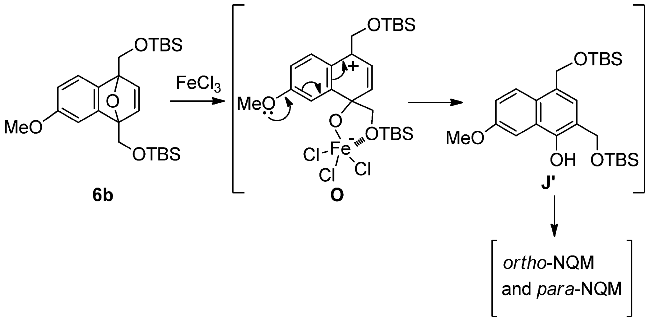
(19) Inapplicable arenes and dienophiles under the present reaction are described below.



(20) During the reaction using **1** and **4**, the intermediates, such as **E** and **I**, were never observed because the reaction was smoothly completed.

(21) The siloxy group at the benzylic position is smoothly eliminated to generate the corresponding carbocation intermediate. See refs 10a and 10c.

(22) The carbocation intermediate **O** was selectively generated due to the stabilization of an electron-donating methoxy group.



(23) Martín-Matute, B.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2003**, *125*, 5757−5766.