JOC The Journal of Organic Chemistry

Article

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Intramolecular Etherification and Polyene Cyclization of π-Activated Alcohols Promoted by Hot Water

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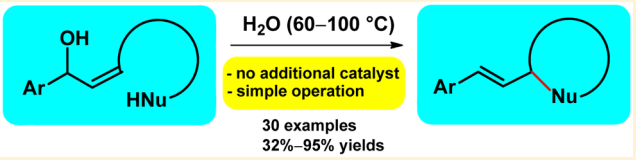
Supporting Information

ABSTRACT: Hot water, acting as a mildly acidic catalyst, efficiently promoted intramolecular direct nucleophilic substitution reactions of unsaturated alcohols with heteroatom or carbon nucleophiles. In a mixed solvent of water and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), polyene cyclizations using allylic alcohols as initiators gave the desired cyclized products, and in neat HFIP, a tricyclization reaction gave a tetracyclic product in 51% chemical yield.



INTRODUCTION

The use of direct nucleophilic substitution reactions of alcohols to build carbon−heteroatom and carbon−carbon bonds has obvious advantages. First, alcohols with a wide variety of chemical structures are abundant in the natural world, the structural motif of an alcohol can be readily incorporated into a target molecule by means of these reactions. Second, water is the only byproduct of the reaction. However, the poor leaving ability of the hydroxyl group disfavors direct nucleophilic substitution, and therefore alcohols generally have to be transformed into the corresponding halides, carboxylates, or sulfonates, which are better leaving groups, before reaction with a nucleophile. Various catalytic methods employing Lewis acid or Brønsted acid catalysts[1] or transition-metal catalysts[2] have been developed to mediate the direct nucleophilic substitutions of alcohols in organic solvents.

For S_N1 substitutions of alcohols, the use of water as the solvent generally used to be avoided because water was expected to instantly trap the carbocation intermediate and give back the starting material. However, by comparing the N parameters of π-systems and the N_1 parameters of water or aqueous−alcoholic solvent mixtures, Mayr et al. predicted that solvolytically generated carbocations could be trapped by π-nucleophiles ([Nuc] = 1 mol/L) in aqueous solution if the N of the corresponding π nucleophile is greater than the N_1 of the aqueous solvent.[3] In 2007 and 2008, Cozzi et al. showed that water can facilitate the departure of the hydroxyl group of an electron-rich benzylic alcohol, and the generated carbocation can react with carbon, sulfur, and nitrogen nucleophiles in water.[4] In addition, reactions of carbocations generated from less-electron-rich benzylic alcohols can be carried out in 2,2,2-trifluoroethanol, which is less nucleophilic than water.[4b] In 2012, the research groups of Nájera and Cozzi reported that perfluoroalcohols can promote direct nucleophilic substitution reactions of allylic alcohols and benzylic alcohols more effectively than water can.[5]

In addition to being an environmentally benign reaction medium, water has unique chemical and physical properties that allow it to catalyze organic reactions.[4,6] In previous studies, we showed that under refluxing conditions water can act as a mildly acidic catalyst to promote organic reactions traditionally catalyzed by Brønsted acid or Lewis acid catalysts.[7] Recently, we found that the S_N1 hydrolysis of allylic and benzylic alcohols occurs in hot water, and we systematically studied the effects of various reaction parameters on the outcome of this reaction.[7c] We were interested in determining whether an intramolecular heteroatom or carbon nucleophile could react with different kinds of π-stabilized carbocations preferentially over solvent water. Herein, we report that efficient intramolecular etherification and polyene cyclization reactions can be carried out in water or a mixed solvent of water and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) under refluxing conditions.

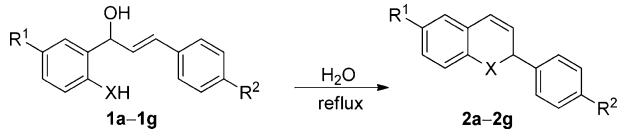
RESULTS AND DISCUSSION

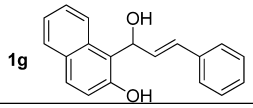
Intramolecular Etherifications Promoted by Hot Water. First, we tested various substrates to determine whether intramolecular etherification would take place in refluxing water without an additional catalyst (Table 1).[8] We found that the phenoxy group of substrate **1a** readily displaced the benzylic hydroxyl group to give 2*H*-chromene **2a** in 86% yield after 3 h (entry 1, Table 1).[9] Methoxy-substituted substrate **1b** gave a 95% yield of **2b** under the same conditions (entry 2), and substrates bearing electron-withdrawing groups on one or both of the phenyl rings (**1c**−**e**) gave slightly lower yields of the desired ethers (entries 3−5). Sulfonamide was also a suitable nucleophile: substrate **1f** gave 1,2-dihydroquinoline **2f** in 85% yield (entry 6). Photochromic compound **2g** could be prepared in 82% yield by reaction of substrate **1g** in refluxing water for 4 h (entry 7).[10]

Received: November 18, 2014

DOI: 10.1021/jo502636d
J. Org. Chem. XXXX, XXX, XXX−XXX

Table 1. Synthesis of 2*H*-Chromenes and 1,2-Dihydroquinoline[a]



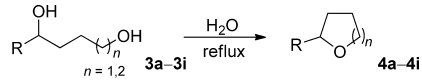
entry	substrate	time (h)	product	yield (%)[b]
1	**1a** (XH = OH, R^1 = H, R^2 = H)	3	**2a**	86
2	**1b** (XH = OH, R^1 = H, R^2 = OMe)	2	**2b**	95
3	**1c** (XH = OH, R^1 = Cl, R^2 = H)	3	**2c**	80
4	**1d** (XH = OH, R^1 = H, R^2 = CF_3)	4	**2d**	74
5	**1e** (XH = OH, R^1 = Cl, R^2 = Cl)	3	**2e**	76
6	**1f** (XH = NHTs, R^1 = H, R^2 = H)	3	**2f**	85
7	**1g** 	4	**2g**	82

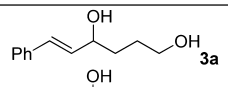
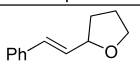
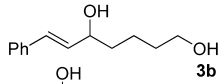
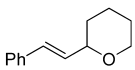
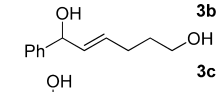
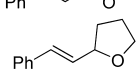
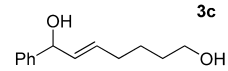
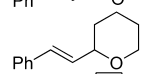
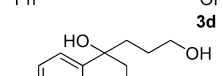
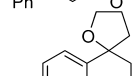
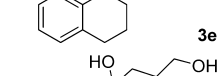
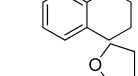
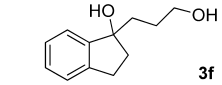
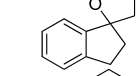
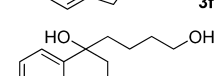
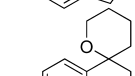
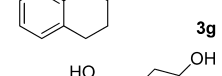
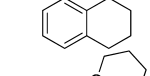
[a]Reaction conditions: 0.2 mmol of alcohol in H_2O (20 mL). [b]Isolated yield.

A relatively stable carbocation intermediate is crucial for an S_N1 substitution in water.[3] We found that intermolecular nucleophilic substitutions of cinnamic alcohol with various nucleophiles failed in water because the unstable carbocation was quenched by water before it could react with other nucleophiles. However, intramolecular substitution reactions of diols **3a–d**, which are structurally similar to cinnamic alcohol, did take place in water to give cyclic ethers **4a–d** in 70–79% yields (entries 1–4, Table 2, note that although **3c** has been reported to cyclize to **4a** in 91% yield with a boronic acid catalyst in CH_3NO_2 at room temperature, the isomeric **3a** only react slowly at 80 °C and give **4a** in 17% yield after 15 h[10]). Under the same reaction conditions, the etherifications of benzylic alcohols **3e–i** afforded spiro tetrahydrofurans and tetrahydropyrans **4e–i** in 79–85% yields (entries 5–9, the control experiments showed that **3g** did not react in refluxing methanol or 2-propanol, which indicated that the reactions did not initiate at raised temperature in a polar protic solvent and confirmed that water played a catalytic role in the reactions; see Supporting Information).

Spiroketal enol ether derivatives have been synthesized by intramolecular cyclization of 2-furylcarbinols.[11] Here we found that in refluxing water, 2-furylcarbinol **5a** gave spiroacetal enol ether **6a** in 62% yield, together with a side product with higher polarity than **6a**. This side product was determined to be fused cyclopentenone **7a**, which was generated from **6a** through a thermal 4π electrocyclic rearrangement reaction described by Piancatelli et al.[12] A control experiment confirmed that **6a** could be quantitatively transformed into **7a** in refluxing water for 12 h. When the temperature of the cyclization reaction of **5a** was lowered to 60 °C, a higher yield **6a** (77%) was obtained, and the yield of **7a** was reduced to 10% (entry 1, Table 3). A higher yield of **7a** (91%) could be achieved by refluxing **5a** in water for 24 h. 2-Furylcarbinols **5b** and **5c**, which bear electron-donating or electron-withdrawing groups, respectively, on the phenyl ring showed reactivities similar to that of **5a** at 60 °C and under refluxing conditions (entries 3–6). Reaction of styrenyl-substituted enol ether **5d** at 60 °C gave a 1:2 mixture of spiroacetal enol ethers (*E*)- and (*Z*)-**6d** (entry 7), and

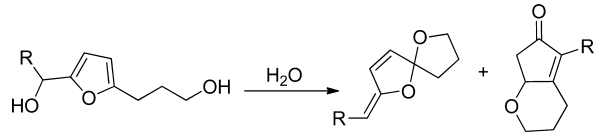
Table 2. Intramolecular Etherification in Water[a]

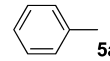
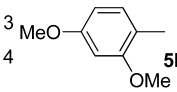
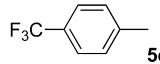
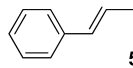


entry	substrate	time (h)	product	yield (%)[b]
1	 **3a**	2	 **4a**	75
2	 **3b**	2	 **4b**	70
3	 **3c**	3	 **4a**	72
4	 **3d**	3	 **4b**	79
5	 **3e**	3	 **4e**	83
6	 **3f**	3	 **4f**	79
7	 **3g**	3	 **4g**	81
8	 **3h**	3	 **4h**	81
9	 **3i**	3	 **4i**	85

[a]Reaction conditions: 0.2 mmol of alcohol in H_2O (20 mL). [b]Isolated yield.

Table 3. Synthesis of Spiroketal Enol Ethers and Fused Cyclopentenones in Water[a]



entry	R	temp (°C)	time (h)	yield(%)[b]
1	 **5a**	60	6	**6a** (77%) + **7a** (10%)
2		reflux	24	**7a** (91%)
3	 **5b**	60	4	**6b** (79%) +**7b** (12%)
4		reflux	24	**7b** (82%)
5	 **5c**	60	6	**6c** (82%) + **7c** (3%)
6		reflux	24	**7c** (87%)
7	 **5d**	60	5	**6d** (71%) + **7d** (8%) *E*/*Z* = 1:2
8		reflux	24	**7d** (86%)
9	 **5e**	60	4	**6e** (76%) + **7e** (12%)
10		reflux	24	**7e** (70%)

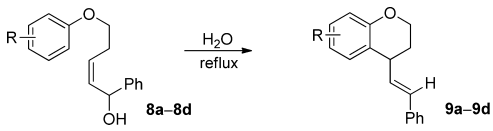
[a]Reaction conditions: 0.2 mmol substrate in H_2O (20 mL). [b]Isolated yields.

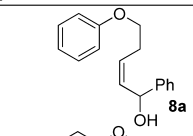
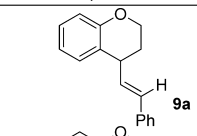
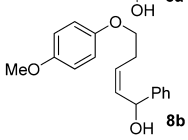
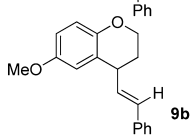
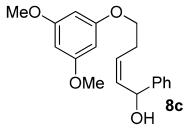
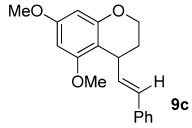
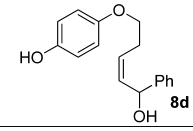
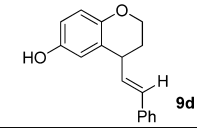
reaction of thiophene-substituted substrate **5e** gave **6e** in 76% yield at 60 °C and gave the natural product chrycorin (**7e**) in 70% yield under refluxing conditions (entry 10).[13]

DOI: 10.1021/jo502636d
J. Org. Chem. XXXX, XXX, XXX–XXX

We next turned our attention to intramolecular nucleophilic substitution reactions with carbon nucleophiles.[1o,14] We found that intramolecular Friedel–Crafts reactions of alcohols **8a–c** proceeded in refluxing water, but the yields of the cyclized products were only 11–23% after 24 h (data not shown). However, substrate **8d**, which bears a hydroxyl group on the phenyl ring, gave a 65% yield of the cyclization product under the same conditions (entry 4, Table 4). We conjectured that

Table 4. Intramolecular Direct Nucleophilic Substitution by a Phenyl Ring[a]



entry	substrate	time (h)	product	yield (%)[b,c]
1	 **8a**	24	 **9a**	80
2	 **8b**	20	 **9b**	90
3	 **8c**	16	 **9c**	85
4[d]	 **8d**	18	 **9d**	65

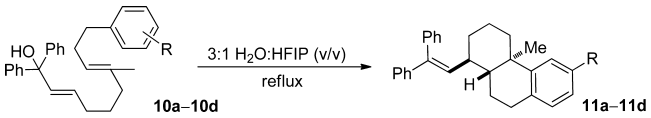
[a]Reaction conditions: 0.05 mmol of substrate in refluxing H_2O (50 mL). [b]Isolated yield. [c]*E*/*Z* isomer ratio >20:1. [d]Reaction conditions: 0.2 mmol of substrate in H_2O (20 mL) under a N_2 atmosphere.

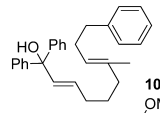
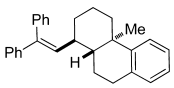
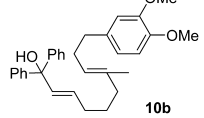
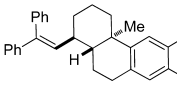
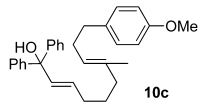
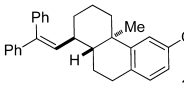
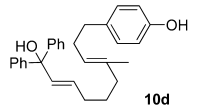
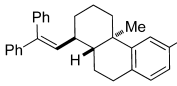
the poor aqueous solubility of substrates **8a–c** might have slowed their reactions,[7f,15] and by reducing the concentrations of **8a–c**, we were able to obtain 80–90% yields of the desired cyclization products within 24 h (entries 1–3).

Two reviewers raised a question about whether the reactions were actually catalyzed by the glass surface and water was just a polar solvent. Theoretically, the possibility that the reactions were catalyzed by the glass surface does exist because the glass surface is slightly acidic (the pK_a of silanol is estimated to be 13.6) and some types of laboratory glassware may leach Lewis-acidic metals into aqueous solution. The controlled experiments were then performed in PFA round-bottom flasks[16] and base-washed round-bottom flasks using compounds **5a** and **8b** as the substrates (see Supporting Information). The experimental results showed that the reactions could proceed well in PFA or base-washed round-bottom flasks. The chemical yields obtained from base-washed and acetone-washed reaction flasks were comparable, but the reactions employing PFA reaction flasks were slightly slower than reactions employing glass reaction flasks (the chemical yields were 85–95% of the average yields obtained from glass reaction flasks). The possible reason might be the less efficient heat transfer while using a PFA reaction flask. Or it might be that the PFA surface disturbs the self-ionization of water, which is similar to the addition of an organic solvent to water.[17] Recently, Professor Jamison reported studies on the epoxide-opening cyclizations templated by a preformed tetrahydropyran ring (promoted by neutral water at 70 °C). The controlled experiment performed in polypropylene tube furnished similar endo/exo selectivity suggesting that the glass surface was not responsible for the observed high endo selectivity.[18]

Intramolecular Polyene Cyclizations of Allylic Alcohols Promoted by Hot Water. There has been long-standing interest in nonenzymatic polyene cyclization reactions for the rapid construction of polycyclic frameworks. Polyene cyclizations are usually carried out in nonprotic solvents that do not trap the carbocation intermediate. We were interested to see whether polyene cyclization with an allylic alcohol as initiator groups could be carried out in water.[19] An initial experiment showed that allylic alcohol **10a** was unreactive in refluxing water. We speculated that the failure of the reaction might have been due to insufficient solvation of the hydrophobic substrate in the aqueous solution. Therefore, we added a small amount of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), which is a better hydrogen-bond donor and has higher ionizing power than water, as well as better ability to solubilize organic compounds. At a H_2O:HFIP ratio of 3:1 (v/v), a cyclization cascade afforded an 80% yield of a dicyclized product with very high diastereoselectivity (entry 1, Table 5). Allylic alcohols **10b** and

Table 5. Intramolecular Dicyclization Reactions[a]



entry	substrate	time (h)	product	yield (%)[b,c]
1	 **10a**	10	 **11a**	80 dr = 25:1:1:0.5
2	 **10b**	8	 **11b**	78 dr = 24:1:1:0.35
3	 **10c**	8	 **11c**	76 dr = 25:1:1:0.25
4[d]	 **10d**	6	 **11d**	82 dr = 24:1:2:0.35

[a]Reaction conditions: 0.1 mmol of substrate in refluxing 3:1 H_2O:HFIP (v/v, 5 mL). [b]Isolated yield. [c]The diastereomeric (dr) ratio was determined by ^1H NMR spectroscopy. [d]Under a N_2 atmosphere.

10c, which bear one or two methoxy groups on the phenyl ring, gave similar yields and diastereoselectivities (entries 2 and 3), and the formation of **11c** was confirmed by X-ray crystallography (Figure 1). It is noteworthy that the current method, unlike the method using a Lewis acid catalyst, did not require the protection of the phenoxy group in **10d** (entry 4).

Refluxing of alcohol **12** in the above-described mixed solvent resulted in the formation of the trans,trans-tricyclized product **13** and the trans,cis-tricyclized product **14** in 26% total yield, along with a mixture of mono- and dicyclized products in 21%

DOI: 10.1021/jo502636d
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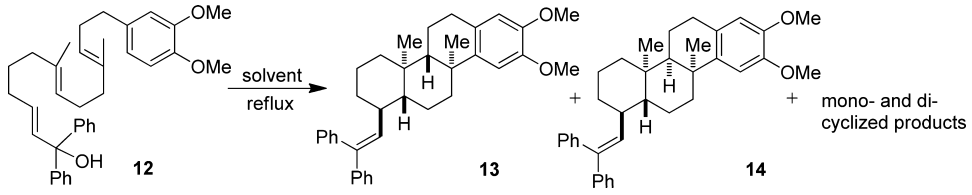
Table 6. Intramolecular Tricyclization Reactions[a]



entry	solvent	time (h)	yield (%)[b,c] 13 + 14/13:14	yield (%)[b,c] mono- and dicyclized products
1	3:1 H_2O:HFIP (v/v)	12	26 (2.7:1)	21
2	1:1 H_2O:HFIP (v/v)	10	31 (2.5:1)	22
3	1:2 H_2O:HFIP (v/v)	6	32 (2.5:1)	25
4	HFIP	3	51 (3:1)	23

[a]Reaction conditions: 0.1 mmol of substrate in mixed solvent or pure HFIP (5 mL) under refluxing conditions. [b]Isolated yield. [c]The diastereomeric ratio was determined by ^{1}H NMR spectroscopy.

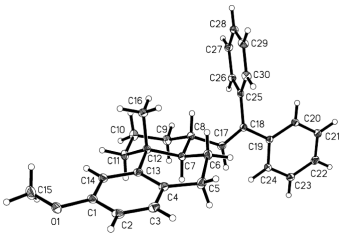


Figure 1. ORTEP diagram of **11c**.

total yield (entry 1, Table 6). Increasing the volume ratio of HFIP increased the speed of the reaction as well as the total yield of the tricyclization products (entries 2 and 3); the yield reached 51% in pure HFIP (entry 4). The mixture of mono- and dicyclized products could be transformed into tricyclized products in 72% yield by treatment with trifluoroacetic acid; thus the combined yield of tricyclized products obtained from the reaction in entry 4 was 68%.[19b,j]

CONCLUSION

In summary, intramolecular direct nucleophilic substitutions of unsaturated alcohols could be realized in water without an additional catalyst. In a mixed solvent of water and HFIP, polyene cyclizations using allylic alcohols as the initiator gave the desired cyclized products, and the use of neat HFIP afforded tricyclization products in a high yield that was comparable to the yields obtained by catalysis with Lewis acids or Brønsted acids. The unique catalytic effects of water and HFIP demonstrated here can be expected to facilitate the extensive use of these solvents as reaction media and promoters in organic synthesis.

EXPERIMENTAL SECTION

General Methods. Unless specially indicated, all reactions were carried out in aerial atmosphere. Water used in the reactions was from Milli-Q Ultrapure Water Purification System or Watson's distilled water (pH = 5.5–6.5). Reaction temperatures reported in the tables were the temperatures of the oil bath. Organic solvents used were purified by standard methods. Flash column chromatographies were performed using the indicated solvent system on Qingdao–Haiyang silica gel (200–300 mesh). Melting points were measured using open capillary tubes and are uncorrected. All of the compounds were characterized by ^{1}H and ^{13}C NMR peaks recorded are relative to internal standards: TMS (δ = 0.00) for ^{1}H NMR and $CDCl_3$ (δ = 77.00) for ^{13}C NMR spectra. High resolution mass spectral analyses (HRMS) were performed on a high resolution ESI–FTICR mass spectrometer.

*Preparation of Substrates **1a–g**.* Substrates **1a–e**,[20] **1f,g**[21] were prepared according to previously reported procedures.

*(E)-2-(1-Hydroxy-3-(4-methoxyphenyl)allyl)phenol (**1b**).* Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.65 (d, J = 2.8 Hz, 1H), 3.80 (s, 3H), 5.52 (d, J = 7.2 Hz, 1H), 6.35 (dd, J = 15.8, 7.3 Hz, 1H), 6.58 (d, J = 15.8 Hz, 1H), 6.83–6.87 (m, 3H), 6.91 (d, J = 8.1 Hz, 1H), 7.05 (d, J = 7.6 Hz, 1H), 7.20 (t, J = 7.4 Hz, 1H), 7.31–7.33 (m, 2H), 7.92 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.6, 155.5, 131.8, 129.3, 128.7, 128.0, 127.6, 126.7, 125.7, 120.0, 117.3, 114.0, 76.7, 55.3; HRMS (ESI) for $C_{16}H_{16}O_3Na$ calcd for $[M + Na]^+$ m/z 279.0997, found 279.0995.

*(E)-2-(1-Hydroxy-3-(4-(trifluoromethyl)phenyl)allyl)phenol (**1d**).* Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.25 (br s, 1H), 5.54 (d, J = 6.2 Hz, 1H), 6.54 (dd, J = 15.8, 6.2 Hz, 1H), 6.64 (d, J = 15.9 Hz, 1H), 6.86–6.91 (m, 2H), 7.05 (dd, J = 7.5, 1.2 Hz, 1H), 7.21 (t, J = 7.2 Hz, 1H), 7.41–7.45 (m, 2H), 7.53–7.55 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.2, 139.5, 131.6, 130.0, 129.6, 127.6, 126.8, 125.5 (q, J = 3.9 Hz), 125.4, 125.4, 120.3, 117.3, 75.7; HRMS (ESI) for $C_{16}H_{12}F_3O_2$ calcd for $[M - H]^+$ m/z 293.0789, found 293.0792.

*(E)-4-Chloro-2-(3-(4-chlorophenyl)-1-hydroxyallyl)phenol (**1e**).* Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.86 (d, J = 3.2 Hz, 1H), 5.48 (dd, J = 6.8, 2.7 Hz, 1H), 6.38 (dd, J = 15.8, 7.0 Hz, 1H), 6.59 (d, J = 15.8 Hz, 1H), 6.83 (d, J = 8.6 Hz, 1H), 7.01 (d, J = 2.5 Hz, 1H), 7.15 (dd, J = 8.6, 2.6 Hz, 1H), 7.27–7.32 (m, 4H), 7.83 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.1, 134.2, 134.0, 131.3, 129.2, 128.8, 128.8, 128.0, 127.2, 126.8, 124.8, 118.7, 75.7; HRMS (ESI) for $C_{15}H_{11}Cl_2O_2$ calcd for $[M - H]^+$ m/z 293.0136, found 293.0145.

*(E)-1-(1-Hydroxy-3-phenylallyl)naphthalen-2-ol (**1g**).* Yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.98 (d, J = 2.4 Hz, 1H), 6.34 (d, J = 5.5 Hz, 1H), 6.51 (dd, J = 15.8, 6.5 Hz, 1H), 6.67 (d, J = 15.8 Hz, 1H), 7.14 (d, J = 8.9 Hz, 1H), 7.20–7.25 (m, 2H), 7.29–7.38 (m, 3H), 7.42–7.51 (m, 2H), 7.70–7.77 (m, 3H), 9.04 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.3, 135.9, 131.8, 130.1, 128.9, 128.5, 128.0, 127.1, 126.8, 126.7, 123.0, 121.0, 119.8, 115.3, 72.8; HRMS (ESI) for $C_{19}H_{16}O_2Na$ calcd for $[M + Na]^+$ m/z 299.1048, found 299.1043.

General procedure for Intramolecular Etherifications in Table 1. *2-Phenyl-2H-chromene (**2a**).*[22] Substrate **1a** (45 mg, 0.2 mmol) was suspended in water (20 mL), and then the mixture was heated under refluxing condition. After the reaction was completed as determined by TLC, the reaction mixture was cooled to room temperature and was extracted with EtOAc (3 × 30 mL). The organic phase was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (EtOAc/petroleum ether = 1:25) to give the desired product **2a** (36 mg, 86% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.80 (dd, J = 9.8, 3.4 Hz, 1H), 5.91–5.92 (m, 1H), 6.53 (dd, J = 9.8, 1.7 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.86 (td, J = 7.4, 0.8 Hz, 1H), 7.01 (dd, J = 7.4, 1.6 Hz, 1H), 7.11 (td, J =

DOI: 10.1021/jo502636d
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7.8, 1.6 Hz, 1H), 7.32−7.47 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.1, 140.8, 129.4, 128.6, 128.3, 127.0, 126.6, 124.8, 124.0, 121.3, 121.1, 116.0, 77.3.

*2-(4-Methoxyphenyl)-2H-chromene (**2b**).*[22] Following the general procedure (45 mg, 95% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.80 (s, 3H), 5.78 (dd, J = 9.8, 3.4 Hz, 1H), 5.86−5.87 (m, 1H), 6.54 (dd, J = 9.8, 1.0 Hz, 1H), 6.75 (d, J = 8.0 Hz, 1H), 6.83−6.90 (m, 3H), 7.01 (dd, J = 7.4, 1.3 Hz, 1H), 7.09 (td, J = 7.8, 1.5 Hz, 1H), 7.37−7.40 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.7, 153.1, 132.9, 129.4, 128.6, 126.5, 124.9, 124.0, 121.3, 121.0, 116.0, 114.0, 76.8, 55.3.

*6-Chloro-2-phenyl-2H-chromene (**2c**).*[22] Following the general procedure (39 mg, 80% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.86 (dd, J = 9.8, 3.5 Hz, 1H), 5.90−5.91 (m, 1H), 6.48 (dd, J = 9.8, 1.4 Hz, 1H), 6.71 (d, J = 8.5 Hz, 1H), 6.99−7.06 (m, 2H), 7.32−7.44 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.6, 140.2, 129.0, 128.7, 128.6, 127.0, 126.1, 126.0, 125.8, 123.1, 122.6, 117.3, 77.3.

*2-(4-(Trifluoromethyl)phenyl)-2H-chromene (**2d**).*[22] Following the general procedure (41 mg, 74% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.79 (dd, J = 9.8, 3.5 Hz, 1H), 5.94−5.99 (m, 1H), 6.56 (dd, J = 9.8, 1.3 Hz, 1H), 6.81 (d, J = 8.1 Hz, 1H), 6.89 (dt, J = 7.4, 1.0 Hz, 1H), 7.02 (dd, J = 7.4, 1.4 Hz, 1H), 7.14 (td, J = 8.0, 1.6 Hz, 1H), 7.56−7.64 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.8, 144.7, 129.7, 127.1, 126.8, 125.6 (q, J = 3.5 Hz), 124.5, 123.9, 121.5, 121.1, 116.0, 76.2.

*6-Chloro-2-(4-chlorophenyl)-2H-chromene (**2e**).*[22] Following the general procedure (42 mg, 76% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.82 (dd, J = 9.8, 3.5 Hz, 1H), 5.87 (dd, J = 3.5, 1.6 Hz, 1H), 6.50 (dd, J = 9.8, 1.1 Hz, 1H), 6.70 (d, J = 8.6 Hz, 1H), 6.99 (d, J = 2.5 Hz, 1H), 7.05 (dd, J = 8.6, 2.5 Hz, 1H), 7.32−7.37 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.3, 138.6, 134.4, 129.2, 128.9, 128.4, 126.2, 126.0, 125.4, 123.5, 122.4, 117.3, 76.4.

*2-Phenyl-1-tosyl-1,2-dihydroquinoline (**2f**).*[23] Following the general procedure (61 mg, 85% yield). White solid: mp = 124−125 °C (lit.[3] mp = 125 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.35 (s, 3H), 5.88 (dd, J = 9.6, 6.0 Hz, 1H), 6.02 (d, J = 6.0 Hz, 1H), 6.28 (d, J = 9.6 Hz, 1H), 6.96 (d, J = 7.2 Hz, 1H), 7.08−7.14 (m, 3H), 7.18−7.24 (m, 4H), 7.33−7.34 (m, 4H), 7.64 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.4, 138.3, 136.1, 132.9, 129.1, 128.6, 128.4, 128.2, 127.9, 127.6, 127.4, 127.2, 126.5, 126.4, 126.2, 125.5, 56.9, 21.5.

*3-Phenyl-3H-benzo[f]chromene (**2g**).*[24] Following the general procedure (42 mg, 82% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.93 (dd, J = 9.8, 3.7 Hz, 1H), 5.97−5.98 (m, 1H), 7.07 (d, J = 8.8 Hz, 1H), 7.23 (s, 1H), 7.32−7.38 (m, 4H), 7.46−7.51 (m, 3H), 7.64 (d, J = 8.8 Hz, 1H), 7.73 (d, J = 8.2 Hz, 1H), 7.97 (d, J = 8.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.2, 140.5, 129.8, 129.7, 129.3, 128.6, 128.5, 128.4, 127.1, 126.6, 123.6, 123.4, 121.2, 120.2, 118.0, 114.1, 76.9.

*Preparation of Substrates **3a−i**.* Substrates **3a−d**[10] were prepared according to previously reported procedures.

*1-(3-Hydroxypropyl)-1,2,3,4-tetrahydronaphthalen-1-ol (**3e**).* A solution of *i*-PrMgCl (2.75 mL, 2.0 M in THF, 5.5 mmol) was added to a THF (10 mL) solution of 3-iodopropan-1-ol (930 mg, 5.5 mmol) at −78 °C. After 5 min, a hexane solution of *n*-BuLi (4.38 mL, 2.4 M in hexanes, 10.5 mmol) was added, and then to it was added 1-tetralone (730 mg, 5.0 mmol). After 30 min, a saturated aqueous NH_4Cl (10 mL) solution was added, and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/petroleum ether = 1:1) to afford the desired product **3e** (823 mg, 80% yield). White solid: mp = 84−85 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.59−2.14 (m, 10H), 2.70−2.88 (m, 2H), 3.62−3.75 (m, 2H), 7.06−7.24 (m, 3H), 7.56 (d, J = 9.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.6, 136.5, 128.9, 127.1, 126.3, 126.1, 72.3, 63.3, 39.1, 35.9, 29.7, 27.3, 19.8; HRMS (ESI) for $C_{13}H_{17}O_2$ calcd for $[M - H]^-$ m/z 205.1229, found 205.1227.

*1-(3-Hydroxypropyl)-2,3-dihydro-1H-inden-1-ol (**3f**).* Prepared using the similar procedure of **3e**. White solid: mp = 69−70 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.67−1.86 (m, 3H), 1.96−2.04 (m, 1H), 2.08−2.16 (m, 1H), 2.26−2.33 (m, 1H), 2.43 (br s, 2H), 2.78−2.86 (m, 1H), 2.96−3.04 (m, 1H), 3.69 (t, J = 5.6 Hz, 2H), 7.22−7.24 (m, 3H), 7.34−7.37 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.5, 142.8, 128.2, 126.7, 125.0, 122.9, 83.3, 63.2, 40.2, 37.2, 29.4, 27.6; HRMS (ESI) for $C_{12}H_{16}O_2Na$ calcd for $[M + Na]^+$ m/z 215.1048, found 215.1043.

*1-(4-Hydroxybutyl)-1,2,3,4-tetrahydronaphthalen-1-ol (**3g**).* Prepared using the similar procedure of **3e**. Colorless viscous oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.29−1.59 (m, 5H), 1.79−1.89 (m, 5H), 1.99−2.07 (m, 2H), 2.69−2.83 (m, 2H), 3.62 (t, J = 6.4 Hz, 2H), 7.07 (d, J = 7.2 Hz, 1H), 7.15−7.20 (m, 2H), 7.51 (d, J = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.4, 136.6, 128.8, 127.0, 126.2, 126.1, 72.4, 62.5, 41.9, 35.9, 32.9, 29.8, 20.2, 19.8; HRMS (ESI) for $C_{14}H_{20}O_2Na$ calcd for $[M + Na]^+$ m/z 243.1361, found 243.1356.

*1-(4-Hydroxybutyl)-2,3-dihydro-1H-inden-1-ol (**3h**).* Prepared using the similar procedure of **3e**. Colorless viscous oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.38−1.61 (m, 4H), 1.70−1.78 (m, 1H), 1.87−1.95 (m, 2H), 2.04−2.11 (m, 1H), 2.16 (br s, 1H), 2.25−2.32 (m, 1H), 2.77−2.85 (m, 1H), 2.95−3.02 (m, 1H), 3.62 (t, J = 6.0 Hz, 2H), 7.21−7.32 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.5, 142.8, 127.9, 126.4, 124.7, 122.8, 83.4, 62.0, 39.7, 32.7, 29.4, 20.2; HRMS (ESI) for $C_{13}H_{17}O_2$ calcd for $[M - H]^-$ m/z 205.1229, found 205.1236.

*9-(3-Hydroxypropyl)-9,10-dihydroanthracen-9-ol (**3i**).* Prepared using the similar procedure of **3e**. Light yellow solid: mp = 131−132 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.38−1.45 (m, 2H), 1.76−1.79 (m, 2H), 2.03 (br s, 1H), 2.96 (br s, 1H), 3.47 (t, J = 6.2 Hz, 2H), 3.88−4.03 (m, 2H), 7.23−7.32 (m, 6H), 7.75 (d, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.8, 133.9, 127.3, 126.9, 126.5, 124.9, 74.1, 62.9, 39.9, 35.0, 27.1; HRMS (ESI) for $C_{17}H_{18}O_2Na$ calcd for $[M + Na]^+$ m/z 277.1204, found 277.1202.

General Procedure for Intramolecular Etherifications in Table 2. *(E)-2-Styryltetrahydrofuran (**4a**).*[10] Substrate **3a** (39 mg, 0.2 mmol) was suspended in water (20 mL), and then the mixture was heated under refluxing condition. After the reaction was completed as determined by TLC, the reaction mixture was cooled to room temperature and was extracted with EtOAc (3 × 30 mL). The organic phase was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (EtOAc/petroleum ether = 1:50) to give the desired product **4a** (27 mg, 75% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.69−1.76 (m, 1H), 1.90−2.01 (m, 2H), 2.08−2.17 (m, 1H), 3.81−3.87 (m, 1H), 3.94−4.00 (m, 1H), 4.45−4.50 (m, 1H), 6.21 (dd, J = 15.8, 6.6 Hz, 1H), 6.58 (d, J = 15.8 Hz, 1H), 7.20−7.24 (m, 1H), 7.28−7.32 (m, 2H), 7.37−7.39 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.8, 130.5, 130.4, 128.5, 127.4, 126.4, 79.6, 68.1, 32.4, 25.9.

*(E)-2-Styryltetrahydro-2H-pyran (**4b**).*[10] Following the general procedure (26 mg, 70% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.21−1.81 (m, 6H), 3.47 (t, J = 14.0 Hz, 1H), 3.87−4.01 (m, 2H), 6.14 (dd, J = 21.2, 7.6 Hz, 1H), 6.51 (d, J = 21.2 Hz, 1H), 7.14−7.31 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.0, 130.8, 129.7, 128.4, 127.4, 126.4, 78.0, 68.4, 32.2, 25.8, 23.4.

*Spiro[furan-2(3H),1′(2′H)-naphthalene] (**4e**).*[25] Following the general procedure (31 mg, 83% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.72−1.83 (m, 1H), 1.85−1.88 (m, 2H), 1.93−2.15 (m, 5H), 2.73−2.82 (m, 2H), 4.00−4.05 (m, 1H), 4.11−4.16 (m, 1H), 7.04 (d, J = 7.5 Hz, 1H), 7.11−7.20 (m, 2H), 7.40 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.6, 136.8, 128.4, 126.7, 126.4, 126.1, 82.8, 68.4, 40.4, 35.9, 29.3, 26.6, 21.1.

*Spiro[tetrahydrofuran-2,1′-indan] (**4f**).*[26] Following the general procedure (27 mg, 79% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.08−2.25 (m, 6H), 2.77−2.84 (m, 1H), 2.97−3.04 (m, 1H), 3.95−4.02 (m, 2H), 7.22−7.29 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.6, 143.2, 127.9, 126.6, 124.7, 122.7, 91.8, 67.9, 39.6, 37.1, 29.7, 26.6.

*Spiro[1H-2-benzopyran-1,1′-cyclohexane] (**4g**).*[27] Following the general procedure (33 mg, 81% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.56−1.94 (m, 9H), 2.34−2.40 (m, 1H), 2.70−

DOI: 10.1021/jo502636d
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2.86 (m, 2H), 3.80−3.84 (m, 2H), 7.03 (d, J = 7.2 Hz, 1H), 7.13 (td, J = 7.6, 1.6 Hz, 1H), 7.22 (t, J = 7.2 Hz, 1H), 7.63 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.7, 136.6, 128.3, 127.0, 126.7, 126.1, 73.8, 61.7, 36.0, 29.8, 28.9, 25.8, 20.0.

*Spiro[cyclohexane-1,1′(3′H)-isobenzofuran] (**4h**).*[28] Following the general procedure (31 mg, 81% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.60−1.86 (m, 6H), 2.24−2.28 (m, 2H), 2.78−2.85 (m, 1H), 2.99−3.03 (m, 1H), 3.69−3.89 (m, 2H), 7.22−7.39 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.6, 142.7, 128.1, 126.6, 124.7, 123.2, 85.0, 63.6, 34.6, 34.1, 29.6, 25.8, 21.0.

*4′,5′-Dihydro-3′H,10H-spiro[anthracene-9,2′-furan] (**4i**).* Following the general procedure (40 mg, 85% yield). White solid: mp = 58−59 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.97−2.10 (m, 4H), 3.95 (dd, J = 17.8, 15.8 Hz, 2H), 4.45 (t, J = 6.4 Hz, 2H), 7.19−7.23 (m, 2H), 7.27−7.31 (m, 4H), 7.57−7.61 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.2, 134.2, 127.1, 126.4, 126.3, 123.3, 83.8, 70.8, 39.9, 35.9, 25.6; HRMS (ESI) for $C_{17}H_{17}O$ calcd for $[M + H]^+$ m/z 237.1279, found 237.1270.

*Preparation of Substrates **5a−e**.* Substrates **5a−e** were prepared according to previously reported procedures.[11d]

*3-(5-((2,4-Dimethoxyphenyl)(hydroxy)methyl)furan-2-yl)propan-1-ol (**5b**).* Yellow solid: mp = 83−86 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.42 (br s, 1H), 1.86−1.93 (m, 2H), 2.72 (t, J = 7.2 Hz, 2H), 2.97 (br s, 1H), 3.68 (dd, J = 10.8, 6.0 Hz, 2H), 3.81 (s, 3H), 3.82 (s, 3H), 5.92−5.94 (m, 3H), 6.47−6.50 (m, 2H), 7.21 (d, J = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.6, 157.9, 155.2, 154.3, 128.7, 121.9, 107.5, 105.6, 104.2, 98.8, 66.2, 62.1, 55.5, 55.4, 31.0, 24.4; HRMS (ESI) for $C_{16}H_{20}O_5Na$ calcd for $[M + Na]^+$ m/z 315.1208, found 315.1211.

General Procedure for the Synthesis of Spiroketal Enol Ethers and Cyclopentenones in Table 3. *2-Benzylidene-1,6-dioxaspiro[4.4]non-3-ene (**6a**).*[29] Substrate **5a** (47 mg, 0.2 mmol) was suspended in water (20 mL), and then the mixture was stirred at 60 °C, After the reaction was completed as determined by TLC, the reaction mixture was cooled to room temperature and was extracted with EtOAc (3 × 30 mL). The organic phase was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (EtOAc/petroleum ether = 1:7) to give products **6a** (33 mg, 77% yield) and **7a** (5 mg, 10% yield). Compound **6a**; Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.95−2.06 (m, 2H), 2.12−2.32 (m, 2H), 3.93 (q, J = 7.6 Hz, 1H), 4.15−4.20 (m, 1H), 5.32 (s, 1H), 5.95 (d, J = 5.6 Hz, 1H), 6.26 (d, J = 5.6 Hz, 1H), 7.03−7.21 (m, 3H), 7.54 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.9, 136.1, 130.9, 129.8, 128.2, 128.1, 125.6, 121.0, 101.2, 69.0, 35.9, 24.5.

*5-Phenyl-3,4,7,7a-tetrahydrocyclopenta[b]pyran-6(2H)-one (**7a**).*[30] Following general procedure (39 mg, 91% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.81−1.88 (m, 2H), 2.49 (dd, J = 18.4, 2.4 Hz, 1H), 2.53−2.59 (m, 1H), 2.87 (dd, J = 18.4, 6.4 Hz, 1H), 3.06−3.10 (m, 1H), 3.74−3.81 (m, 1H), 4.06−4.11 (m, 1H), 4.53−4.55 (m, 1H), 7.26−7.44 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 202.7, 168.7, 138.2, 130.2, 129.0, 128.3, 128.1, 75.6, 57.4, 42.0, 26.8, 26.5.

*2-(2,4-Dimethoxybenzylidene)-1,6-dioxaspiro[4.4]non-3-ene (**6b**).* Following general procedure (43 mg, 79% yield). Yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.04−2.08 (m, 2H), 2.20−2.29 (m, 2H), 3.82 (s, 6H), 3.99−4.04 (m, 1H), 4.22−4.26 (m, 1H), 5.76 (s, 1H), 5.96 (s, 1H), 6.36−6.42 (m, 2H), 6.51 (d, J = 8.4 Hz, 1H), 8.03 (d, J = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.8, 157.0, 154.7, 130.2, 129.8, 129.2, 120.8, 118.0, 104.5, 98.1, 94.1, 68.9, 55.5, 55.3, 36.0, 24.6; HRMS (ESI) for $C_{16}H_{19}O_4$ calcd for $[M + H]^+$ m/z 275.1283, found 275.1280.

*5-(2,4-Dimethoxyphenyl)-3,4,7,7a-tetrahydrocyclopenta[b]-pyran-6(2H)-one (**7b**).* Following general procedure (45 mg, 82% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.75−1.89 (m, 2H), 2.36−2.49 (m, 2H), 2.70−2.88 (m, 2H), 3.72−3.76 (m, 4H), 3.82 (s, 3H), 4.08 (d, J = 11.4 Hz, 1H), 4.54 (d, J = 3.0 Hz, 1H), 6.50 (s, 1H), 6.55 (d, J = 8.3 Hz, 1H), 7.09 (d, J = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.1, 170.0, 161.1, 157.9, 135.1, 131.6, 111.8, 104.4, 98.8, 75.7, 67.4, 55.4, 42.0, 27.3, 26.8; HRMS (ESI) for $C_{16}H_{18}O_4Na$ calcd for $[M + Na]^+$ m/z 297.1103, found 297.1108.

*2-(4-(Trifluoromethyl)benzylidene)-1,6-dioxaspiro[4.4]non-3-ene (**6c**).*[31] Following general procedure (46 mg, 82% yield). Yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.01−2.16 (m, 2H), 2.20−2.40 (m, 2H), 3.97−4.32 (m, 2H), 5.42 (s, 1H), 6.12 (d, J = 5.5 Hz, 1H), 6.35 (d, J = 5.6 Hz, 1H), 7.52 (d, J = 8.2 Hz, 2H), 7.69 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.7, 139.8, 132.5, 129.6, 128.0, 127.2, 125.8, 125.1 (q, J = 3.4 Hz), 121.4, 99.9, 69.4, 35.9, 24.6.

*5-(4-(Trifluoromethyl)phenyl)-3,4,7,7a-tetrahydrocyclopenta[b]-pyran-6(2H)-one (**7c**).*[31] Following general procedure (49 mg, 87% yield). Pale yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.81−1.89 (m, 2H), 2.50−2.64 (m, 2H), 2.90 (dd, J = 18.4, 6.4 Hz, 1H), 3.03−3.07 (m, 1H), 3.79 (td, J = 11.6, 3.2 Hz, 1H), 4.09−4.12 (m, 1H), 4.62 (dd, J = 6.4, 3.2 Hz, 1H), 7.43 (d, J = 7.6 Hz, 2H), 7.68 (d, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 202.2, 170.2, 137.1, 133.9, 130.3, 130.0, 129.4, 125.3 (q, J = 3.4 Hz), 75.6, 67.4, 42.0, 26.8, 26.6.

*2-(3-Phenylallylidene)-1,6-dioxaspiro[4.4]non-3-ene (**6d**, E/Z = 1:2).*[32] Following general procedure (34 mg, 71% yield). Yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.07−2.34 (m, 4H), 3.98−4.01 (m, 1H), 4.17−4.25 (m, 1H), 5.38 (d, J = 11.2 Hz, 0.66H, *Z*-isomer), 5.79 (d, J = 11.6 Hz, 0.33H, *E*-isomer), 6.03 (s, 0.63H, *Z*-isomer), 6.12 (s, 0.30H, *E*-isomer), 6.27−6.30 (m, 0.60H, *Z*-isomer), 6.38−6.46 (m, 1H), 6.79−6.94 (m, 0.66H), 7.12−7.42 (m, 6H).

*(E)-5-Styryl-3,4,7,7a-tetrahydrocyclopenta[b]pyran-6(2H)-one (**7d**).*[30] Following general procedure (41 mg, 86% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.86−1.97 (m, 2H), 2.42 (dd, J = 18.4, 2.8 Hz, 1H), 2.50 (td, J = 13.2, 6.4 Hz, 1H), 2.80 (dd, J = 18.4, 6.4 Hz, 1H), 3.16 (dt, J = 14.4, 2.0 Hz, 1H), 3.74 (td, J = 11.6, 2.8 Hz, 1H), 4.08 (dt, J = 11.6, 2.0 Hz, 1H), 4.44 (d, J = 5.6 Hz, 1H), 6.74 (d, J = 16.4 Hz, 1H), 7.26−7.28 (m, 1H), 7.32−7.36 (m, 2H), 7.48−7.50 (m, 2H), 7.76 (d, J = 16.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.2, 168.1, 137.3, 134.5, 133.1, 128.6, 128.1, 126.6, 116.1, 75.3, 67.2, 42.4, 26.8, 25.9.

*2-(Thiophen-2-ylmethylene)-1,6-dioxaspiro[4.4]non-3-ene (**6e**).*[29] Following general procedure (33 mg, 76% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.04−2.17 (m, 2H), 2.20−2.27 (m, 1H), 2.33−2.46 (m, 1H), 4.01−4.06 (m, 1H), 4.28 (td, J = 8.0, 3.2 Hz, 1H), 5.76 (s, 1H), 6.07 (d, J = 5.6 Hz, 1H), 6.35 (d, J = 5.6 Hz, 1H), 6.95−6.98 (m, 1H), 7.05 (d, J = 3.6 Hz, 1H), 7.17 (d, J = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.3, 139.2, 131.3, 128.5, 126.7, 124.9, 124.2, 120.7, 95.3, 69.0, 35.9, 24.4.

*5-(Thiophen-2-yl)-3,4,7,7a-tetrahydrocyclopenta[b]pyran-6(2H)-one (chrycorin) (**7e**).*[30] Following general procedure (31 mg, 70% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.87−1.94 (m, 2H), 2.48 (dd, J = 18.4, 2.8 Hz, 1H), 2.58−2.66 (m, 1H), 2.88 (dd, J = 18.4, 6.4 Hz, 1H), 3.43−3.47 (m, 1H), 3.75−3.82 (m, 1H), 4.08−4.11 (m, 1H), 4.52−4.53 (m, 1H), 7.10−7.13 (m, 1H), 7.41 (d, J = 3.2 Hz, 1H), 7.50 (d, J = 3.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.6, 166.4, 131.2, 131.1, 127.9, 127.0, 126.6, 75.5, 67.3, 41.8, 26.8, 26.4.

*Preparation of Substrates **8a−d**.* Substrates **8a−d** were prepared according to previously reported procedures.[10]

*(E)-5-(4-Methoxyphenoxy)-1-phenylpent-2-en-1-ol (**8b**).* Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.10 (s, 1H), 2.51 (q, J = 5.9 Hz, 2H), 3.75 (s, 3H), 3.95 (t, J = 6.5 Hz, 2H), 5.17 (br s, 1H), 5.76−5.88 (m, 2H), 6.81 (s, 4H), 7.24−7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.8, 152.9, 143.0, 134.7, 128.5, 127.8, 127.6, 126.2, 115.5, 114.6, 74.9, 67.8, 55.7, 32.2; HRMS (ESI) for $C_{18}H_{20}NaO_3$ calcd for $[M + Na]^+$ m/z 307.1310, found 307.1301.

*(E)-5-(3,5-Dimethoxyphenoxy)-1-phenylpent-2-en-1-ol (**8c**).* Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.97 (br s, 1H), 2.54 (q, J = 6.2 Hz, 2H), 3.76 (s, 6H), 3.97 (t, J = 6.6 Hz, 2H), 5.20 (d, J = 4.9 Hz, 1H), 5.78−5.90 (m, 2H), 6.07−6.08 (m, 3H), 7.26−7.30 (m, 1H), 7.33−7.39 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.5, 160.7, 142.9, 134.8, 128.5, 127.7, 127.6, 126.2, 93.4, 93.0, 75.0, 67.1, 55.3, 32.1; HRMS (ESI) for $C_{19}H_{23}O_4$ calcd for $[M + H]^-$ m/z 315.1596, found 315.1591.

*(E)-4-((5-Hydroxy-5-phenylpent-3-en-1-yl)oxy)phenol (**8d**).* White solid: mp = 100−102 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.99 (br s, 1H), 2.52 (q, J = 6.3 Hz, 2H), 3.94 (t, J = 6.6 Hz, 2H), 4.84 (br s, 1H),

DOI: 10.1021/jo502636d
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5.21 (d, J = 5.6 Hz, 1H), 5.78−5.90 (m, 2H), 6.73−6.78 (m, 4H), 7.28−7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.9, 149.6, 142.9, 134.6, 128.5, 128.0, 127.7, 126.2, 116.0, 115.7, 75.0, 67.8, 32.2; HRMS (ESI) for $C_{17}H_{17}O_3$ calcd for $[M - H]^-$ m/z 269.1178, found 269.1188.

General Procedure for the Intramolecular Friedel−Crafts Reactions in Table 4. *(E)-4-Styrylchroman (**9a**).*[10] Substrate **8a** (13 mg, 0.05 mmol) was suspended in water (50 mL) and then the mixture was heated under refluxing condition. After the reaction was completed for 24 h, the reaction mixture was cooled to room temperature and was extracted with EtOAc (3 × 75 mL). The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (EtOAc/petroleum ether = 1:20) to give the desired product **9a** (10 mg, 80% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.94−2.02 (m, 1H), 2.12−2.20 (m, 1H), 3.68 (q, J = 7.2 Hz, 1H), 4.16−4.21 (m, 1H), 4.24−4.29 (m, 1H), 6.24 (dd, J = 15.6, 8.0 Hz, 1H), 6.44 (d, J = 15.6 Hz, 1H), 6.83−6.87 (m, 2H), 7.11−7.23 (m, 3H), 7.28−7.37 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.5, 137.0, 133.1, 131.6, 130.1, 128.5, 127.9, 127.3, 126.2, 123.7, 120.2, 116.8, 64.0, 38.5, 29.0.

*(E)-6-Methoxy-4-styrylchroman (**9b**).* Following general procedure (12 mg, 90% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.92−2.00 (m, 1H), 2.12−2.19 (m, 1H), 3.66 (q, J = 7.1 Hz, 1H), 3.71 (s, 3H), 4.12−4.17 (m, 1H), 4.20−4.26 (m, 1H), 6.24 (dd, J = 15.7, 8.1 Hz, 1H), 6.46 (d, J = 15.8 Hz, 1H), 6.68−6.79 (m, 3H), 7.21−7.24 (m, 1H), 7.29−7.38 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.2, 148.6, 137.0, 133.0, 131.6, 128.5, 127.4, 126.2, 124.3, 117.4, 114.6, 114.0, 64.0, 55.7, 38.9, 29.2; HRMS (ESI) for $C_{18}H_{18}NaO_2$ calcd for $[M + Na]^+$ m/z 289.1204, found 289.1193.

*(E)-5,7-Dimethoxy-4-styrylchroman (**9c**).* Following general procedure (12 mg, 85% yield). White solid: mp = 49−50 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.87−1.91 (m, 1H), 2.08−2.17 (m, 1H), 3.73 (s, 3H), 3.76−3.78 (m, 4H), 4.07−4.13 (m, 1H), 4.19−4.23 (m, 1H), 6.06−6.08 (m, 2H), 6.15 (d, J = 16.0 Hz, 1H), 6.32 (dd, J = 15.8, 6.0 Hz, 1H), 7.15−7.19 (m, 1H), 7.25−7.33 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.8, 158.9, 155.8, 137.6, 133.2, 130.4, 128.4, 126.9, 126.1, 104.7, 93.2, 91.4, 62.2, 55.5, 55.2, 31.2, 27.3; HRMS (ESI) for $C_{19}H_{20}NaO_3$ calcd for $[M + Na]^+$ m/z 319.1310, found 319.1302.

*(E)-4-Styrylchroman-6-ol (**9d**).* Substrate **8d** (54 mg, 0.2 mmol) was suspended in water (20 mL), and then the mixture was heated under refluxing condition. After the reaction was completed, the reaction mixture was cooled to room temperature and was extracted with EtOAc (3 × 30 mL). The organic phase was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (EtOAc/petroleum ether = 1:7) to give the desired product **9d** (33 mg, 65% yield). White solid: mp = 79−82 °C (decomp); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.91−2.17 (m, 2H), 3.59−3.65 (m, 1H), 4.10−4.26 (m, 2H), 4.55 (br s, 1H), 6.20 (dd, J = 15.8, 8.2 Hz, 1H), 6.46 (d, J = 15.8 Hz, 1H), 6.62−6.64 (m, 2H), 6.72 (d, J = 8.4 Hz, 1H), 7.21−7.25 (m, 1H), 7.29−7.38 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.9, 148.5, 136.9, 132.8, 131.7, 128.6, 127.4, 126.2, 124.6, 117.5, 116.0, 115.2, 64.2, 38.8, 29.1; HRMS (ESI) for $C_{17}H_{15}O_2$ calcd for $[M - H]^-$ m/z 251.1072, found 251.1075.

*Preparation of Substrates **10a−d** and **12**.* Substrates **10a−d**,[10] **12**[10] were prepared according to previously reported procedures.

*(2E,7E)-10-(3,4-Dimethoxyphenyl)-7-methyl-1,1-diphenyldeca-2,7-dien-1-ol (**10b**).* Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.44−1.59 (m, 5H), 1.98 (t, J = 7.4 Hz, 2H), 2.06 (q, J = 7.4 Hz, 2H), 2.25−2.33 (m, 3H), 2.58 (t, J = 7.3 Hz, 2H), 3.83 (s, 3H), 3.85 (s, 3H), 5.14 (t, J = 7.4 Hz, 1H), 5.57−5.64 (m, 1H), 6.07 (d, J = 15.4 Hz, 1H), 6.67−6.81 (m, 3H), 7.23−7.37 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.6, 147.0, 146.4, 135.8, 135.4, 135.0, 130.9, 128.0, 127.0, 126.8, 123.9, 120.2, 111.7, 111.0, 79.0, 55.8, 55.7, 39.1, 35.6, 31.7, 30.0, 27.4, 15.9; HRMS (ESI) for $C_{31}H_{36}NaO_3$ calcd for $[M + Na]^+$ m/z 479.2562, found 479.2558.

*(2E,7E)-10-(4-Methoxyphenyl)-7-methyl-1,1-diphenyldeca-2,7-dien-1-ol (**10c**).* Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.44−1.52 (m, 5H), 1.97 (t, J = 7.4 Hz, 2H), 2.05 (q, J = 7.3 Hz, 2H), 2.23−2.30 (m, 3H), 2.56 (t, J = 7.3 Hz, 2H), 3.76 (s, 3H), 5.13 (t, J = 6.8 Hz, 1H), 5.57−5.64 (m, 1H), 6.07 (d, J = 15.4 Hz, 1H), 6.80 (d, J = 8.5 Hz, 2H), 7.09 (d, J = 8.5 Hz, 2H), 7.23−7.38 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.6, 146.4, 135.8, 135.4, 134.4, 131.0, 129.3, 128.5, 128.0, 127.0, 126.9, 126.5, 124.0, 113.6, 79.0, 55.2, 39.1, 35.1, 31.7, 30.1, 27.3, 15.8; HRMS (ESI) for $C_{30}H_{34}NaO_2$ calcd for $[M + Na]^+$ m/z 449.2457, found 449.2451.

*4-((3E,8E)-10-Hydroxy-4-methyl-10,10-diphenyldeca-3,8-dien-1-yl)phenol (**10d**).* Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.41−1.49 (m, 5H), 1.93−2.02 (m, 4H), 2.24 (q, J = 7.2 Hz, 2H), 2.54 (t, J = 7.6 Hz, 2H), 5.09 (t, J = 6.8 Hz, 1H), 5.54−5.61 (m, 1H), 6.04 (d, J = 15.4 Hz, 1H), 6.68 (d, J = 7.6 Hz, 2H), 7.00 (d, J = 8.4 Hz, 2H), 7.22−7.37 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.5, 146.3, 135.7, 135.4, 134.4, 131.1, 129.5, 128.0, 127.1, 126.9, 124.0, 115.0, 79.1, 39.1, 35.0, 31.6, 29.9, 27.3, 15.8; HRMS (ESI) for $C_{29}H_{32}NaO_2$ calcd for $[M + Na]^+$ m/z 435.2300, found 435.2299.

*(2E,7E,11E)-14-(3,4-Dimethoxyphenyl)-7,11-dimethyl-1,1-diphenyltetradeca-2,7,11-trien-1-ol (**12**).* Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.48−1.57 (m, 8H), 1.96−2.11 (m, 8H), 2.25−2.32 (m, 3H), 2.56−2.60 (m, 2H), 3.84 (s, 3H), 3.87 (s, 3H), 5.08 (t, J = 6.6 Hz, 1H), 5.17 (t, J = 6.7 Hz, 1H), 5.59−5.66 (m, 1H), 6.09 (d, J = 15.4 Hz, 1H), 6.71−6.78 (m, 3H), 7.22−7.38 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.6, 147.0, 146.4, 135.8, 135.7, 135.0, 134.7, 130.9, 128.0, 127.0, 126.8, 124.4, 123.6, 120.2, 111.8, 111.1, 79.0, 55.9, 55.7, 39.7, 39.1, 35.6, 31.7, 30.1, 27.4, 26.6, 16.0, 15.8; HRMS (ESI) for $C_{36}H_{44}O_3Na$ calcd for $[M + Na]^+$ m/z 547.3188, found 547.3184.

General Procedure for the Polyene Cyclization Reactions in Table 5. *(1S,4aS,10aS)-1-(2,2-Diphenylvinyl)-6,7-dimethoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (**11b**).* Substrate **10b** (44 mg, 0.1 mmol) was suspended in the mixed solution of water and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (5 mL, V_{H2O}:V_{HFIP} = 3:1), and then the mixture was stirred in a 95 °C oil bath. After the reaction was completed as determined by TLC, the reaction mixture was cooled to room temperature and was extracted with EtOAc (3 × 30 mL). The organic phase was dried over $MgSO_4$ and then concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (EtOAc/petroleum ether = 1:6) to give the desired product **11b** (33 mg, 78% yield). The dr ratio was determined from the ^{1}H NMR spectrum of the crude product. Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.93 (s, 3H), 1.23−1.27 (m, 1H), 1.38−1.45 (m, 3H), 1.52−1.58 (m, 1H), 1.65−1.74 (m, 2H), 1.94−1.99 (m, 1H), 2.14−2.32 (m, 2H), 2.68−2.81 (m, 2H), 3.82 (s, 3H), 3.83 (s, 3H), 5.86 (d, J = 10.0 Hz, 1H), 6.53 (s, 1H), 6.76 (s, 1H), 7.16−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.8, 146.8, 142.6, 141.0, 140.5, 134.0, 134.9, 129.7, 128.1, 128.0, 127.0, 126.8, 126.7, 111.6, 108.1, 56.0, 55.7, 47.4, 38.2, 38.0, 36.7, 33.5, 29.4, 23.2, 22.6, 21.5; HRMS (ESI) for $C_{31}H_{35}O_2$ calcd for $[M + H]^+$ m/z 439.2637, found 439.2635.

*1-(2,2-Diphenylvinyl)-6-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (**11c**).* Following general procedure (31 mg, 76% yield). The single crystal of **11c** was grown from EtOAc. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99 (s, 3H), 1.24−1.35 (m, 1H), 1.43−1.53 (m, 3H), 1.55−1.63 (m, 1H), 1.71−1.79 (m, 2H), 2.01−2.04 (m, 1H), 2.22−2.37 (m, 2H), 2.83−2.86 (m, 2H), 3.82 (s, 3H), 5.92 (d, J = 10.1 Hz, 1H), 6.73 (dd, J = 8.3, 2.4 Hz, 1H), 6.87 (d, J = 2.4 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 7.16−7.45 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.5, 149.2, 142.6, 141.0, 140.5, 134.9, 129.9, 129.7, 128.2, 128.1, 127.6, 127.0, 126.8, 110.8, 110.4, 55.2, 47.1, 38.4, 37.7, 37.2, 33.5, 28.8, 23.2, 22.6, 21.5; HRMS (ESI) for $C_{30}H_{33}O$ calcd for $[M + H]^+$ m/z 409.2531, found 409.2524.

*8-(2,2-Diphenylvinyl)-4b-methyl-4b,5,6,7,8,8a,9,10-octahydrophenanthren-3-ol (**11d**).* Following general procedure (32 mg, 82% yield). Colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.90 (s, 3H), 1.21−1.27 (m, 1H), 1.33−1.43 (m, 3H), 1.45−1.55 (m, 1H), 1.63−1.73 (m, 2H), 1.94−1.96 (m, 1H), 2.05−2.10 (m, 1H), 2.27−2.45 (m, 1H), 2.75−2.77 (m, 2H), 4.74−4.80 (m, 1H), 5.85 (d, J = 10.0 Hz, 1H), 6.54−6.57 (m, 1H), 6.72 (d, J = 1.4 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 7.18−7.37 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.2, 149.4, 142.6, 141.0, 140.4, 134.9, 130.1, 129.7, 128.2, 128.1, 127.6, 127.0, 126.8, 126.8, 112.7, 111.3, 47.0, 38.3, 37.6, 37.0, 33.4, 28.8, 23.1,

DOI: 10.1021/jo502636d
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22.6, 21.4; HRMS (ESI) for $C_{29}H_{31}O$ calcd for $[M + H]^+$ m/z 395.2375, found 395.2378.

General Procedure for the Tricyclization Reactions in Table 6. Allylic alcohol **12** (52 mg, 0.1 mmol) was suspended in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (5 mL), and then the mixture was stirred under refluxing condition. After the reaction was completed as determined by TLC, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (CH_2Cl_2/petroleum ether = 2:5) to give the crude tetracyclic products **13** and **14** and mono- and dicyclized byproducts. The crude tetracyclic products were further purified by preparative HPLC on ODS-C_{18} (flow: 10 mL/min; 26.08 min (**14**), 28.31 min (**13**); 99% CH_3CN, 1% H_2O, 25 °C).

*(1S,4aS,4bR,10bR,12aS)-1-(2,2-Diphenylvinyl)-8,9-dimethoxy-4a,10b-dimethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysene (**13**).* White solid (20 mg, 39% yield): mp = 82−89 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.67 (s, 3H), 0.88 (td, J = 12.4, 5.2 Hz, 1H), 0.99−1.03 (m, 1H), 1.16 (s, 3H), 1.18−1.22 (m, 1H), 1.26−1.28 (m, 1H), 1.34 (qd, J = 13.2, 2.7 Hz, 1H), 1.42−1.54 (m, 3H), 1.60−1.66 (m, 2H), 1.77−1.79 (m, 2H), 1.83−1.87 (m, 1H), 2.16 (qd, J = 10.9, 3.6 Hz, 1H), 2.27 (dt, J = 12.7, 3.0 Hz, 1H), 2.73−2.86 (m, 2H), 3.82 (s, 3H), 3.83 (s, 3H), 5.80 (d, J = 10.1 Hz, 1H), 6.51 (s, 1H), 6.74 (s, 1H), 7.17−7.24 (m, 7H), 7.29−7.39 (m, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 147.0, 146.7, 142.7, 142.5, 140.6, 140.5, 135.4, 129.7, 128.1, 128.0, 127.2, 127.0, 126.7, 126.8, 111.2, 107.8, 56.0, 55.7, 53.3, 52.4, 39.9, 38.8, 37.8, 37.5, 36.8, 33.8, 30.3, 25.8, 23.5, 20.7, 18.1, 13.6; HRMS (ESI) for $C_{36}H_{42}O_2Na$ calcd for $[M + Na]^+$ m/z 529.3083, found 529.3079.

*(1S,4aS,4bS,10bR,12aS)-1-(2,2-Diphenylvinyl)-8,9-dimethoxy-4a,10b-dimethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysene (**14**).* White solid (6 mg, 13% yield): mp = 91−96 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.98 (s, 3H), 1.16−1.20 (m, 3H), 1.23−1.30 (m, 1H), 1.33−1.37 (m, 1H), 1.47 (s, 3H), 1.48−1.72 (m, 7H), 1.80−1.83 (m, 1H), 2.08−2.14 (m, 2H), 2.60−2.70 (m, 2H), 3.83 (s, 6H), 5.75 (d, J = 10.1 Hz, 1H), 6.47 (s, 1H), 6.77 (s, 1H), 7.15−7.24 (m, 7H), 7.30−7.39 (m, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 147.1, 146.4, 142.7, 140.7, 140.6, 135.4, 129.7, 128.6, 128.1, 128.0, 126.9, 126.7, 110.7, 110.4, 56.1, 55.7, 54.3, 44.9, 39.3, 38.6, 38.3, 37.6, 36.9, 33.6, 32.0, 31.3, 24.4, 22.6, 21.5, 21.1; HRMS (ESI) for $C_{36}H_{42}O_2Na$ calcd for $[M + Na]^+$ m/z 529.3083, found 529.3074.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of the products listed in Tables 1−6. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was financially supported by the NSFC (21072098, 21372119), the National Natural Science Foundation of China Innovation Group (21121002), and the Tianjin Natural Science Foundation (14JCYBJC20200). We thank Professor Chi Zhang at Nankai University for helpful discussions.

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(16) The PFA round-bottom flask was purchased from Vitlab (PFA: fluoropolymers which are copolymers of tetrafluoroethylene (C_2F_4) and perfluoroethers ($CF_2F_3OR^f$, where R^f is a perfluorinated group such as trifluoromethyl)).
(17) At room temperature, the pK_a* value of water (K_a* is the apparent ionization constant of water) changes from 14 to 14.60 in an aqueous solution containing 20 vol % of 1,4-dioxane and further to 16 in an aqueous solution containing 60 vol % of 1,4-dioxane. Please see: Woolley, E. M.; Hurkot, D. G.; Hepler, L. G. *J. Phys. Chem.* **1970**, *74*, 3908−3913.
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