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A family of stilbene-ethers as photolabile protecting groups for primary alcohols offers controlled deprotection based on choice of wavelength

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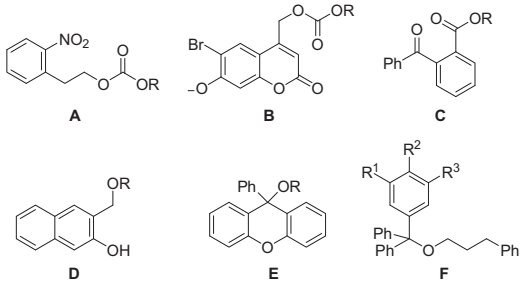
ABSTRACT

A novel stilbene-ether type of photolabile protecting group (PPG) for hydroxyl group has been developed. It contains a stable aryl ether group in the protected form and can be deprotected by acid-catalyzed photorearrangement under 300-nm irradiation. The selective deprotection has also been achieved by irradiation of the mixture of 4-alkoxystilbene and 2-(4-alkoxystyryl)furan at 365 nm.

1. Introduction

Photolabile protecting groups (PPGs) have several merits to the conventional protecting groups. Their advantages include spatial and temporal controls and orthogonal reaction conditions to most of thermal reactions, so that PPGs are widely used in the areas of organic synthesis, biochemically caged compounds, and solid-phase synthesis.[1] Some PPGs have been developed for the protection of hydroxyl group, including 2-nitrobenzene derivative **A**,[2] coumarin-4-ylmethoxycarbonyl **B**,[3] *o*-benzoylbenzoate ester **C**,[4] 3-hydroxy-2-naphthalenemethanol **D**,[5] 9-phenylxanthen-9-yl ether **E**,[6] and trityl ether **F**[7] (Scheme 1). In order to phototrigger deprotection reactions, these PPGs usually contain some acid- and base-sensitive functional groups, such as nitro, carbonate, ester, hydroxyl, and triphenyl ether groups.[8] Therefore, to develop a new type of PPG that can be stable under most of acidic and basic conditions is an important issue.

Aryl alkyl ether is a stable functional group to most of acidic and basic reaction conditions, but it is seldom used as a protecting group. That is because decomposition of aryl alkyl ethers usually needs strong reagents,[9] such as oxidants for methyl phenyl ether[10] and Lewis acids for isopropyl aryl ether.[11] However, a unique acid-catalyzed photorearrangement of stilbenyl ethers reported by Ho's group[12] has shown the ability to decompose aryl ethers under a mild condition (Scheme 2). One of the reported examples[12c] was the irradiation of 4-methoxystilbene **1**. When **1** was irradiated with 5 mM of hydrochloric acid in acetonitrile ([water] is ca. 73.6 mM),[13] 4-naphthan-2-yl-but-3-en-2-one **2** could be obtained. And when **1** was irradiated with 0.5 M of hydrochloric acid in water/acetonitrile ([water] is ca. 2.2 M)[13] solution, 1,4-dihydro-*2H*-phenanthren-3-one **3** would be formed as the major product. The proposed mechanism for the formation of compounds **2** and **3** shows multiple steps, including photocyclization, acid-catalyzed [1,9] and [1,3] hydrogen shift, 6e retro-electrocyclic reaction, and hydrolysis. The aromatization (**DHP1** to **DHP2** and **DHP2** to **N**) and hydrolysis



Scheme 1. Selected photolabile protecting groups of alcohols.

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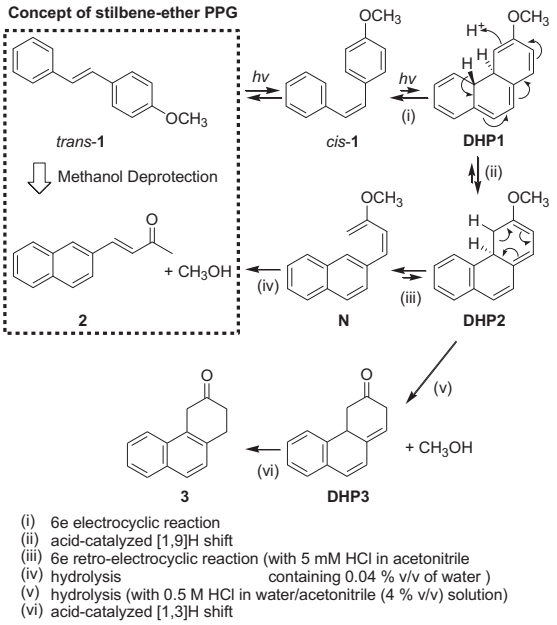
provide the driving force for this acid-catalyzed photorearrangement.



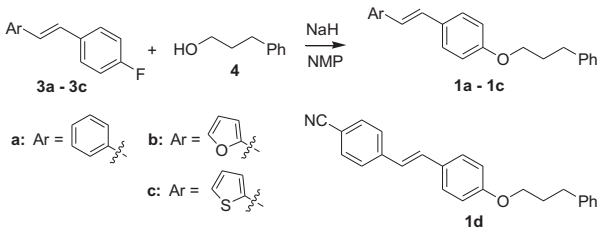
Scheme 2. Mechanism of acid-catalyzed photorearrangement of stilbenyl ethers and our concept of stilbene-ethers of PPG.

Our concept is to utilize stilbenyl ether as a protected form for alcohols and this acid-catalyzed photorearrangement as the deprotection step, which could change the aryl methyl ether group of compound **1** into the vinyl methyl ether group of intermediate **N**, and then release alcohol by hydrolysis of vinyl methyl ether (Scheme 2). Development of this stilbene-ether PPG contains several features: First, using aryl ether as a protecting group is very stable to most of thermal reaction conditions. Second, the deprotection condition is mild enough to keep the protected molecule from unwanted changes. Third, the necessity of catalytic acid for deprotection provides a safety-catch function.[2a] Fourth, the selective deprotection may be achieved by different photoreactivities of stilbene-type compounds under selected wavelength irradiation. To the best of our knowledge, this is the first case using the photoreaction of stilbene-type compounds in the field of PPGs. Therefore, we would like to report this family of stilbene-ethers to be a new type of PPG.

2. Results and discussion

2.1. Protection of primary alcohol

The preparations of **1a**–**c** are outlined in Scheme 3. The precursors **3a**–**c** were first synthesized by the Wittig reaction of 4-fluorobenzyl bromide and the appropriate aldehydes. Afterward the nucleophilic aromatic substitution[14] (S_NAr) of **3a**–**c** with 3-phenylpropanol **4** in presence of sodium hydride and *N*-methyl-2-pyrrolidone (NMP) afforded compounds **1a**–**c**, respectively. But compound **1d** could not be synthesized in the same manner. In order to prepare **1d**, an alternative synthetic method was offered by the Wittig reaction of 4-cyanobenzyl chloride and 4-(3-phenylpropoxy) benzaldehyde, which was synthesized from 4-hydroxybenzaldehyde and 3-phenyl-1-bromopropane. The synthetic yields of compounds **1a**–**d** are reported in Table 1. For the selection of irradiation wavelength, the absorption maxima of *trans* and *cis*-**1a**–**d** are also listed in Table 1.



Scheme 3. Syntheses of **1a**–**c** and the structure of **1d**.

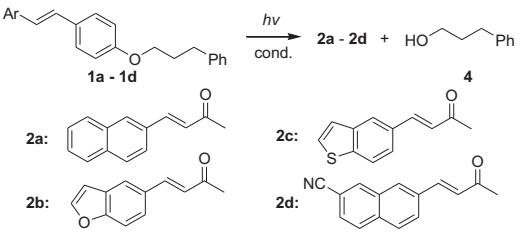
Table 1
Protection yields and absorption maxima of **1a**–**d**

Entry	Compound	λ_{abs}^{max} (*trans*)[a]	λ_{abs}^{max} (*cis*)[a]	Yield (%)
1	**1a**	311 nm	290 nm	87[b]
2	**1b**	321 nm	307 nm	64[b]
3	**1c**	331 nm	298 nm	89[b]
4	**1d**	337 nm	318 nm	66[c]

[a] 2.5×10^{-5} M in acetonitrile.
[b] The yields are determined after gravity chromatography purification twice.
[c] The yield includes *cis*- and *trans*-**1d**.

2.2. Deprotection

The deprotection was carried out by irradiation of N_2-purged solutions of **1a**–**d** at 300 nm ultraviolet light (Scheme 4), and the reaction conditions and the results are reported in Table 2. First, the irradiation of **1a** in a pure acetonitrile did not release alcohol **4** and only led to *trans*–*cis* isomerization (entry 1). When the irradiation of **1a** was took place in dichloromethane or acidic acetonitrile, the alcohol **4** would be released in moderate to good isolated yields (70–80%, entries 2–4). Deprotection of **1b** and **1c** also released alcohol **4** in good yields (74–88%, entries 5–8) after only 2-h and 4-h irradiation. Finally, irradiation of **1d** resulted in a poor result (55%, entry 9) after a prolonged irradiation time. The poor deprotection of compound **1d** may result from the substitution effect of cyano group on photocyclization reaction.[15]



Scheme 4. Deprotection of **1a**–**d**.

Table 2
Deprotection of **1a**–**d** by irradiation at 300 nm

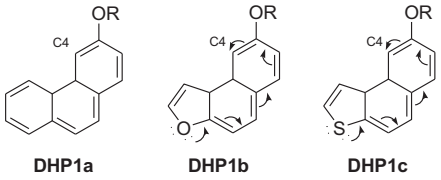
Entry	Compound	Solvent[a]	*hv* time (h)	Recovery of SM[b] (%)	Deprotection (%)[c]
1	**1a**	AN	6	88	0
2	**1a**	5 mM HCl/AN	6	27	70
3	**1a**	5 mM HCl/AN	10	8	76
4	**1a**	DCM	6	15	80
5	**1b**	5 mM HCl/AN	2	2	88
6	**1b**	DCM	2	0	81
7	**1c**	5 mM HCl/AN	4	9	74
8	**1c**	DCM	4	2	82
9	**1d**	5 mM HCl/AN	48	18	55

[a] AN: CH_3CN, DCM: CH_2Cl_2.
[b] SM: starting material *cis*/*trans*-**1a**–**d**.
[c] Isolated yield of released alcohol **4**.

It is worthy to mention that undehydrated dichloromethane could let this acid-catalyzed photorearrangement work well

without adding acid and moisture. Photolysis of dichloromethane generating hydrochloric acid at the interface between the UV light-exposed silica wall and the solvent has been reported.[16] We also used 2-(4-(*N*,*N*-dimethylamino)styryl)quinoline as acid–base indicator to prove the formation of acid in the cases of the irradiated dichloromethane and the irradiated dichloromethane solution of **1a** in the quartz tubes.[17] Besides, the residual water in common dichloromethane (usually 0.1 wt. %) could be the source of water for this photorearrangement because the concentration of residual water is ca. 73.6 mM, while the concentration of **1a** is just 3.2 mM in our cases.

The irradiation times of **1a**, **b**, and **c** (entries 3, 5, and 7 in Table 2) show that the photochemical reactivity is **1b**>**1c**>**1a**. This order of reactivity is consistent with that of Ho's work.[12a,b] Photochemical reactivity should be influenced by the reaction rate of the acid-catalyzed [1,9] hydrogen shift of **DHP1**, and this rate would be proportional to the electron density of C4 position (Scheme 5). Because **DHP1b** has oxygen atom with lone pairs of electrons to enhance the electron density on C4 atom, the reactivity of **1b** is the highest. The reactivity of **1c** is lower than **1b**, and that is because of the bad overlap of orbitals between sulfur and carbon atoms. Without the assistance of lone pairs of heteroatoms, **1a** has the lowest reactivity.



Scheme 5. Structure–reactivity correlation of **1a**, **b**, and **c**.

2.3. Selective deprotection

In order to investigate the possibility of selective deprotection based on choice of wavelength, the UV profiles of *cis*-**1a**–**1d**, which are the real starting materials for the photocyclization intermediates **DHP1**s (Scheme 2), are compared in Fig. 1. Compared with *cis*-**1a**, compounds **1b**–**1d** have longer wavelength absorptions and may be more reactive under 365-nm irradiation.

The deprotection of **1a**–**d**[18] under 365-nm irradiation in acidic acetonitrile was estimated by ^{1}H NMR of crude reaction mixture and the results are reported in Table 3. Photolysis of **1a** led to non-detectable deprotection after 3-h irradiation (entry 3), and only 16% deprotection after 24-h irradiation (entry 4). Irradiation of **1d**, whose *cis*-form has the longest wavelength end extending to 380 nm, was even more inactive at 365 nm (entry 12). An attempt on photochemical deprotection of **1d** at 419 nm was also failed to get a better result. However, a 3-h irradiation of **1b** and **1c** surprisingly led to more effective deprotection in 90% and 46% yields, respectively (entries 8 and 11). Finally, two quantitative experiments proved the high efficiency on deprotection of **1b** and **1c**: first, 6-h irradiation of **1b** at 365 nm leading to 91% deprotection; second, 8-h irradiation of **1c** at 365 nm leading to 84% deprotection.

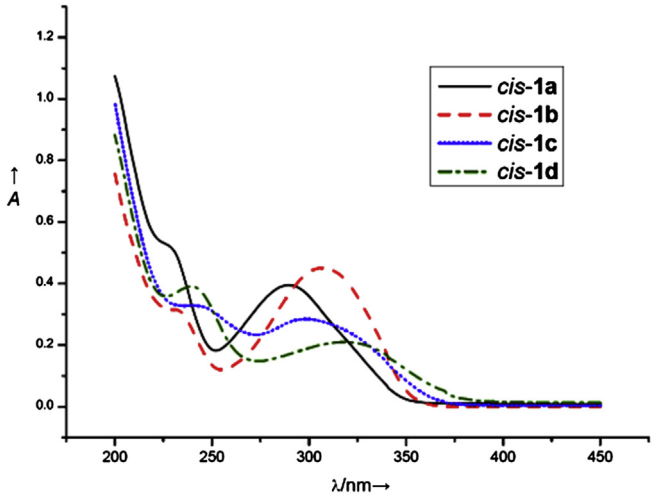


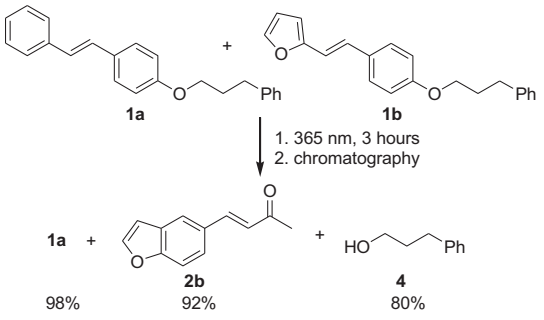
Fig. 1. UV–vis absorption spectra of *cis*-**1a**–**d** (2.5×10^{-5} M in acetonitrile).

Table 3
Deprotection of **1a**–**d** in acetonitrile solution containing 5 mM HCl by irradiation at 365 nm[a]

Entry	Compound	*hv* time (h)	Recovery of SM[b] (%)	Deprotection (%)
1	**1a**	1	100	0
2	**1a**	2	100	0
3	**1a**	3	100	0
4	**1a**	24	84	16
5	**1b**	0.5	86	14
6	**1b**	1.5	46	54
7	**1b**	2	28	72
8	**1b**	3	9	91
9	**1c**	1	91	9
10	**1c**	2	77	23
11	**1c**	3	53	47
12	**1d**	24	93	7

[a] Ratios were determined by ^{1}H NMR of crude reaction mixtures.
[b] SM: starting materials *cis*/*trans*-**1a**–**d**.

Compounds **1a** and **1b** showed remarkably different photoreactivities under 365-nm irradiation and could be used for selective deprotection. Photolysis of a 1:1 mixture of **1a** and **1b** at 365 nm for 3 h afforded **2b**, alcohol **4**, and the recycling **1a** in 92%, 80%, and 98% yields, respectively, after column chromatography (Scheme 6). None of deprotection of **1a** was observed. This excellent selectivity means there was no intermolecular energy transfer between the excited state of **1b** and the ground state of **1a**. Therefore, a successive control-release of two alcohols can be achieved by irradiating the mixture of 4-alkoxystilbene **1a** and 2-(4-alkoxystyryl) furan **1b**.



Scheme 6. Selective deprotection of **1a** and **b**.

2.4. Stability

The stability of compound **1a** under a variety of acidic and basic conditions is shown in Table 4. Treatment of **1a** with several strong bases, such as *n*-butyllithium, sodium hydride, potassium *tert*-butoxide, potassium hydroxide, at different temperatures led to the excellent recovery of **1a** (entries 1–9). In contrast, reactions of 3-phenylpropyl benzoate under basic conditions resulted in hydrolysis of the ester group.[19] When compound **1a** was reacted in acidic condition at the refluxing temperature of aqueous THF, no

Table 4
Stability of **1a** (0.06 M) under various conditions[a]

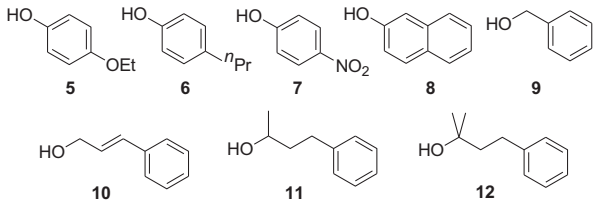
Entry	Reagent	Solvent	Condition[b]	Recovery of **1a** (%)
1	0.06 M ^{n}BuLi	THF	−78 °C, 4 h	98%
2	0.06 M ^{n}BuLi	THF	rt, 2 h	96%
3	0.15 M ^{n}BuLi	THF	rt, 2 h	95%
4	0.15 M NaH	NMP	rt, 2 h	95%
5	0.13 M NaH	NMP	50 °C, 2 h	96%
6	0.33 M ^{t}BuOK	THF	rt, 2 h	95%
7	0.35 M ^{t}BuOK	THF	Reflux, 2 h	98%
8	0.9 M KOH	H_2O/THF (1:1)	Reflux, 21 h	94%
9	2.2 M KOH	H_2O/THF (1:1)	Reflux, 2 h	99%
10[c]	3.0 M HCl	H_2O/THF (1:3)	Reflux, 2 h	99%
11[d]	1.2 M HCl	H_2O/THF (1:9)	Reflux, 2 h	95%

[a] General procedures: 0.06 M of **1a** in 5 mL of solvent was reacted under the above conditions. The recovery of **1a** was reported in isolated yields.
[b] rt: room temperature.
[c] [**1a**]=0.04 M.
[d] [**1a**]=0.03 M.

decomposition of stilbenyl ether happened (entry 10). This means that aryl alkyl ether is stable enough to many thermal reaction conditions, such as metal–halogen exchange, nucleophilic substitution, elimination reaction, acidic and basic hydrolysis of ester, and triphenylmethyl ether, etc.

2.5. Other alcohols

In order to extend the application of this stilbene-ether type of PPG, we have tried protections and deprotections of aryl alcohols **5**–**8**, benzyl alcohol **9**, allyl alcohol **10**, secondary alcohol **11**, and tertiary alcohol **12** (Scheme 7). The results are reported in Table 5. Protection of alcohols **5**, **6**, and **8** by the S_NAr reaction afforded protected compounds **1e**, **f**, and **g** in lower yields (38%–45%), and this may be because of the weaker nucleophilicity of phenoxide anion. Alcohol **7** was nearly not protected by the same reaction, because nitro group would weaken its nucleophilicity further. The protection of benzyl alcohol **9** yielded protected compound **1h** in a good yield (82%). But the protection of allyl alcohol **10** afforded compound **1i** in a very low yield (23%). This may be due to the instability of styrene part of alcohol **10** under high reaction temperature. Alcohols **11** and **12**, which were prepared by the reaction of 4-phenyl-2-butanone and methyl 3-phenylpropanoate with methylmagnesium bromide, also could not be protected by the same S_NAr reaction. The unsuccessful protection of **11** and **12** were possibly due to the repulsion of α-methyl group.



Scheme 7. Structures of alcohols **5**–**12**.

Deprotection of compounds **1e**–**i** by the acid-catalyzed photorearrangement showed good results (75%–90% yields). But due to the lower protection yields, this stilbene-ether type of photolabile protecting group is improper used for the protection of aryl, secondary, and tertiary alcohols.

3. Conclusion

In conclusion, we demonstrated a novel stilbene-ether type of PPG for primary alcohols, including 3-phenylpropanol and benzyl alcohol. This PPG contains stable aryl alkyl ether as a protecting functional group and has remarkable stability under strong acidic and basic conditions. The protection procedure can be carried out by S_NAr reaction of a corresponding fluoro-compound in a good yield, and the deprotection can easily complete by photolysis in a catalytically acidic condition. This PPG also has the ability of control-release when a mixture of 4-alkoxystilbene **1a** and 2-(4-alkoxystyryl)furan **1b** was irradiated under 365 nm first and then 300 nm. In the further study, the multiple control-release function of a mixture sample that contains this stilbene-ether type and other types of PPGs will be estimated.

Table 5
Protection of **5**–**12** with **3a** by S_NAr reaction and deprotection in acetonitrile solution containing 5 mM HCl by irradiation at 300 nm[a]

Entry	Alcohols	Protected forms	Protection yields (%)[b]	Deprotections (%)[c]
1	**5**	**1e**	45	85
2	**6**	**1f**	45	90
3	**7**	—	0	—
4	**8**	**1g**	38	80
5	**9**	**1h**	82	83
6	**10**	**1i**	23	75
7	**11**	—	0	—
8	**12**	—	0	—

[a] Isolated yields.
[b] The protection method is the S_NAr reaction of **3a** and alcohols **5**–**12** in presence of sodium hydride and NMP.
[c] The deprotection method is irradiation an acidic acetonitrile solution of **1e**–**i** at 300 nm for 6 h.

4. Experimental section

4.1. General information

The photochemical reactor, equipped a merry-go-round apparatus encompassed with 16 monochromatic light tubes (300 nm and 365 nm), was made by a local company. The average temperature inside the photochemical reactor during operation is about 40 °C. The quartz tubes of photolysis were 1.3 cm in diameter and 20 cm in length. NMR spectra were measured on a Bruker AVIII 500 MHz FT-NMR with chloroform-d_1 as the standard (7.26 ppm for ^{1}H NMR and 77.0 ppm for ^{13}C NMR). Mass spectra were recorded on a Finnigan MAT 95S Mass spectrometer. UV–vis spectra were recorded on a JASCO V-630 Spectrophotometer. Column chromatography used silica gel with 60–120 mesh. Anhydrous *N*-methyl-2-pyrrolidone (NMP) of AcroSeal packaging was purchase from Acros Company. All other solvent and commercial reagents used as obtained without further purification. The preparation of 5 mM HCl in CH_3CN was by simple dilution of concentrated aqueous hydrochloride with acetonitrile solution.

4.2. Synthesis of precursors *trans*-3a–c

The synthesis of *trans*-**3a** is used as an example: a mixture of 4.0 g (2.78 mmol) of 4-fluorobenzyl chloride and 8.73 g (3.30 mmol) triphenylphosphine in 12 mL of benzene was refluxed for 2 days to yield white solid. Collect the solid by suction filtration and (4-fluorobenzyl)-triphenylphosphonium salt was obtained in 82% yield. Afterward, a mixture of 9.97 g (2.5 mmol) of the previous salt, 2.37 g (2.2 mmol) of benzaldehyde, and 0.82 g (3.11 mmol) of 18-crown-6 in 56 mL of dichloromethane was stirred violently and 27 mL of 50% aqueous solution of K_2CO_3 was added slowly. After addition, the reaction was stirred at room temperature for 3 days. And then the reaction mixture was poured into water and extracted with ethyl acetate for three times. The organic layers were combined and dried with anhydrous $MgSO_4$. The organic solvent was

removed under reduced pressure and the residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1:10) to afford *cis* and *trans*-**3a** in a 95.1% yield. Refluxing the previous mixture with catalytic iodine in benzene for 3 h and then purify the resulting products by column chromatography on silica gel (ethyl acetate/hexane=1:10) afforded *trans*-**3a** in 92% yield.

The synthesis of *trans*-**3b** and **3c** were in the same manner.

*4.2.1. trans-4-Fluorostilbene (trans-**3a**).*[20] Yield 92%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J=7.0 Hz, 2H), 7.48 (dd, J=8.7, 5.5 Hz, 2H), 7.36 (t, J=7.8 Hz, 2H), 7.26 (t, J=7.4 Hz, 1H), 7.08 (d, J=16.4 Hz, 1H), 7.05 (t, J=8.7 Hz, 2H), 7.02 (d, J=16.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.35 (d, $^1J_{F-C}$=245.7 Hz), 137.19, 133.54 (d, $^4J_{F-C}$=3.2 Hz), 128.69, 128.52 (d, $^5J_{F-C}$=2.7 Hz), 127.97 (d, $^3J_{F-C}$=7.9 Hz), 127.66, 127.50, 126.44, 115.60 (d, $^2J_{F-C}$=21.8 Hz).

*4.2.2. trans-4-Fluorostyrylfuran (trans-**3b**).*[21] Yield 80%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, J=5.5, 2.1 Hz, 2H), 7.40 (d, J=1.45 Hz, 1H), 7.03 (t, J=8.8 Hz, 2H), 6.99 (d, J=16.2 Hz, 1H), 6.80 (d, J=16.2 Hz, 1H), 6.42 (dd, J=3.3, 1.9 Hz, 1H), 6.34 (d, J=3.25 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.29 (d, $^1J_{F-C}$=245.6 Hz), 153.09, 142.13, 133.22 (d, $^4J_{F-C}$=3.2 Hz), 127.78 (d, $^3J_{F-C}$=7.9 Hz), 125.93, 116.34 (d, $^5J_{F-C}$=2.2 Hz), 115.64 (d, $^2J_{F-C}$=21.3 Hz), 111.63, 108.53.

*4.2.3. trans-4-Fluorostyrylthiophene (trans-**3c**).*[22] Yield 83%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (dd, J=8.6, 5.4 Hz, 2H), 7.19 (d, J=5.1 Hz, 1H), 7.14 (d, J=16.1 Hz, 1H), 7.06 (d, J=3.4 Hz, 1H), 7.04 (t, J=8.9 Hz, 2H), 7.00 (dd, J=5.1, 3.6 Hz, 1H), 6.89 (d, J=16.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.31 (d, $^1J_{F-C}$=246.2 Hz), 142.67, 133.18 (d, $^4J_{F-C}$=3.6 Hz), 127.76 (d, $^3J_{F-C}$=7.8 Hz), 127.60, 127.13, 126.05, 124.32, 121.60 (d, $^5J_{F-C}$=2.5 Hz), 115.65 (d, $^2J_{F-C}$=21.8 Hz).

4.3. Protection: compounds *trans*-1a–c and 1e–i

The synthesis of *trans*-**1a** is used as an example: A mixture of 3-phenyl-1-propanol **4** (0.2 g, 1.47 mmol), sodium hydride (60% purity, 0.194 g, 8.08 mmol) was sealed quickly in a flask with a septum. And then 2 mL of anhydrous NMP was added with a syringe. The reaction mixture was stirred in an ice-water bath for 30 min, and then at room temperature for another 30 min. Afterward, a solution of *trans*-1-fluoro-4-styrylbenzene (*trans*-**3a**, 0.35 g, 1.76 mmol) and anhydrous NMP (2.5 mL) was added with a syringe at room temperature. And then the reaction mixture was stirred at 100 °C for overnight. After completion of the reaction, the reaction was poured into water and extracted with ethyl acetate for three times. The organic layers were combined and dried with anhydrous $MgSO_4$. The residue was obtained by removing organic solvent under reduced pressure, and then purified by column chromatography on silica gel (hexane, then ethyl acetate/hexane=1:10) to afford *trans*-**1a** in 87% yield.

The syntheses of *trans*-**1b**, **1c**, and **1e–i** were in the same manner.

*4.3.1. trans-1-(3-Phenylpropoxy)-4-styrylbenzene (trans-**1a**).* Yield 87%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J=7.6 Hz, 2H), 7.44 (d, J=8.7 Hz, 2H), 7.35 (t, J=7.8 Hz, 2H), 7.30 (t, J=7.4 Hz, 2H), 7.25–7.18 (m, 4H), 7.07 (d, J=16.3 Hz, 1H), 6.98 (d, J=16.3 Hz, 1H), 6.89 (d, J=8.7 Hz, 2H), 3.99 (t, J=6.3 Hz, 2H), 2.83 (t, J=7.5 Hz, 2H), 2.12 (p, J=7.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.77, 141.47, 137.68, 130.07, 128.62, 128.51, 128.41, 128.26, 127.69, 127.17, 126.54, 126.23, 125.94, 114.75, 66.95, 32.13, 30.81. MS (EI, 70 eV) m/e 315 (M^++1, 4), 314 (M^+, 98), 196 (100), 91 (49). HRMS ($C_{23}H_{22}O$) calcd: 314.1665, found: 314.1667.

*4.3.2. trans-2-{2-[4-(3-Phenylpropoxy)-phenyl]-vinyl}-furan (trans-**1b**).* Yield 64%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J=8.6 Hz, 2H), 7.38 (s, 1H), 7.30 (t, J=7.5 Hz, 2H), 7.23–7.19 (m, 3H), 6.99 (d, J=16.2 Hz, 1H), 6.87 (d, J=8.6 Hz, 2H), 6.77 (d, J=16.2 Hz, 1H), 6.41 (dd, J=3.3, 1.9 Hz, 1H), 6.30 (d, J=3.3 Hz, 1H), 3.98 (t, J=6.4 Hz, 2H), 2.82 (t, J=7.8 Hz, 2H), 2.12 (p, J=7.0, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.73, 153.57, 141.71, 141.45, 129.73, 128.51, 128.41, 127.52, 126.81, 125.93, 114.74, 114.56, 111.53, 107.61, 66.93, 32.12, 30.80. MS (EI, 70 eV) m/e 305 (M^++1, 5), 304 (M^+, 100), 186 (87), 91 (43). HRMS ($C_{21}H_{20}O_2$) calcd: 304.1458, found: 304.1458.

*4.3.3. trans-2-{2-[4-(3-Phenylpropoxy)-phenyl]-vinyl}-thiophene (trans-**1c**).* Yield 89%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J=8.7 Hz, 2H), 7.29 (t, J=7.5 Hz, 2H), 7.23–7.19 (m, 3H), 7.15 (d, J=4.9 Hz, 1H), 7.10 (d, J=16.0 Hz, 1H), 7.02 (d, J=3.4 Hz, 1H), 6.99 (dd, J=4.9, 3.4 Hz, 1H), 6.88 (d, J=16.0 Hz, 1H), 6.87 (d, J=8.7 Hz, 2H), 3.98 (t, J=6.3 Hz, 2H), 2.82 (t, J=7.8 Hz, 2H), 2.12 (p, J=6.9 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.74, 143.28, 141.45, 129.67, 128.51, 128.42, 128.01, 127.50, 125.94, 125.33, 123.68, 119.71, 114.76, 114.48, 66.93, 32.12, 30.80. MS (EI, 70 eV) m/e 321 (M^++1, 5), 320 (M^+, 100), 202 (99), 91 (41). HRMS ($C_{21}H_{20}OS$) calcd: 320.1229, found: 320.1230.

*4.3.4. trans-1-Ethoxy-4-(4-styrylphenoxy)benzene (trans-**1e**).* Yield 45% (145 °C for 21 h). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J=7.4 Hz, 2H), 7.45 (d, J=8.7 Hz, 2H), 7.36 (t, J=7.5 Hz, 2H), 7.25 (t, J=7.4 Hz, 1H), 7.07 (d, J=16.3 Hz, 1H), 7.00 (d, J=16.3 Hz, 1H), 6.99 (d, J=9.0 Hz, 2H), 6.94 (d, J=8.7 Hz, 2H), 6.89 (d, J=9.0 Hz, 2H), 4.03 (q, J=7.0 Hz, 2H), 1.43 (t, J=7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.21, 155.37, 149.86, 137.47, 131.80, 128.65, 127.97, 127.75, 127.45, 127.38, 126.33, 120.83, 117.73, 115.52, 63.91, 14.88. MS (EI, 70 eV) m/z 316 (M^+, 100), 288 (18), 178 (20), 152 (8).

*4.3.5. trans-1-Propyl-4-(4-styrylphenoxy)benzene (trans-**1f**).* Yield 45% (180 °C for 2 days). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J=7.3 Hz, 2H), 7.47 (d, J=8.7 Hz, 2H), 7.35 (t, J=7.9 Hz, 2H), 7.25 (t, J=7.3 Hz, 1H), 7.15 (d, J=8.5 Hz, 2H), 7.09 (d, J=16.4 Hz, 1H), 7.01 (d, J=16.4 Hz, 1H), 6.98 (d, J=8.7 Hz, 2H), 6.96 (d, J=8.5 Hz, 2H), 2.58 (t, J=7.8 Hz, 2H), 1.69–1.61 (m, 2H), 0.96 (t, J=7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.42, 154.76, 137.94, 137.45, 132.20, 129.65, 128.66, 127.97, 127.78, 127.62, 127.42, 126.35, 119.02, 118.57, 37.32, 24.65, 13.78.

*4.3.6. trans-2-(4-Styrylphenoxy)naphthalene (trans-**1g**).* Yield 38% (160 °C for 21 h). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (t, J=8.9 Hz, 2H), 7.72 (d, J=8.2 Hz, 1H), 7.52 (d, J=8.7 Hz, 2H), 7.52–7.50 (m, 2H), 7.47 (ddd, J=8.3, 7.0, 1.2 Hz, 1H), 7.41 (ddd, J=8.3, 7.0, 1.4 Hz, 1H), 7.38–7.35 (m, 3H), 7.29–7.24 (m, 2H), 7.11 (d, J=16.3 Hz, 1H), 7.07 (d, J=8.7 Hz, 2H), 7.05 (d, J=16.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.81, 154.91, 137.39, 134.32, 132.79, 130.23, 129.91, 128.68, 127.96, 127.91, 127.87, 127.74, 127.51, 127.14, 126.56, 126.39, 124.76, 119.96, 119.25, 114.24. MS (EI, 70 eV) m/z 323 (M^++1, 22), 322 (M^+, 100), 178 (10), 127 (12), 115 (8).

*4.3.7. 1-Benzyloxy-4-styryl-benzene (trans-**1h**).* Yield 82% (160 °C for 21 h). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J=7.2 Hz, 2H), 7.47–7.44 (m, 4H), 7.40 (t, J=7.7 Hz, 2H), 7.37–7.33 (m, 3H), 7.24 (t, J=7.4 Hz, 1H), 7.07 (d, J=16.4 Hz, 1H), 6.98 (d, J=16.4 Hz, 1H), 6.98 (d, J=8.8 Hz, 2H), 5.01 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.49, 137.61, 136.89, 130.39, 128.63, 128.60, 128.16, 127.99, 127.71, 127.46, 127.22, 126.74, 126.25, 115.08, 70.06.

*4.3.8. 1-(Cinnamyloxy)-4-(trans-styryl)benzene (trans-**1i**).* Yield 23% (100 °C for 21 h). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J=7.5 Hz, 2H), 7.46 (d, J=8.7 Hz, 2H), 7.41 (d, J=7.5 Hz, 2H), 7.35 (d, J=7.3 Hz, 2H), 7.33 (d, J=7.3 Hz, 2H), 7.27–7.22 (m, 2H), 7.07 (d, J=16.3 Hz, 1H), 6.98 (d, J=16.3 Hz, 1H), 6.96 (d, J=8.7 Hz, 2H), 6.75 (d, J=16.0 Hz, 1H), 6.43 (dt, J=16.0, 5.8 Hz, 1H), 4.73 (dd, J=5.8, 1.3 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.34, 137.63, 136.39, 133.13, 130.37, 128.63, 128.59, 128.17, 127.93, 127.73, 127.22, 126.73, 126.58,

126.25, 124.32, 115.01, 68.71. MS (EI, 70 eV) *m*/*z* 312 (M^+, 18), 195 (8), 165 (24), 117 (100), 191 (22).

4.4. Preparation of compounds *cis*-1a–c

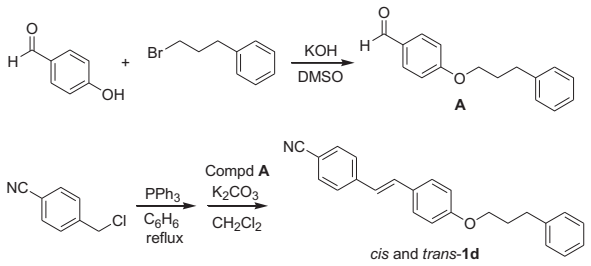
A 100 mL of acetonitrile solution containing 0.1 g of compound **1** was divided into five quartz tubes (1.3 cm×20 cm), and then sealed the tubes with septa. After excluding oxygen by bubbling with N_2 for 30 min, the tubes were irradiated at 300 nm for 2 h. The reaction mixtures were collected and the solvent was removed under reduced pressure. Then compound *cis*-**1** was isolated by column chromatography on silica gel (hexane).

*4.4.1. cis-1-(3-Phenylpropoxy)-4-styrylbenzene (cis-**1a**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.15 (m, 12H), 6.73 (d, *J*=8.7 Hz, 2H), 6.53 (d, *J*=12.3 Hz, 1H), 6.50 (d, *J*=12.3 Hz, 1H), 3.94 (t, *J*=6.3 Hz, 2H), 2.80 (t, *J*=7.8 Hz, 2H), 2.09 (p, *J*=7.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.14, 141.50, 137.64, 130.11, 129.80, 129.58, 128.80, 128.67, 128.49, 128.40, 128.20, 126.86, 125.92, 114.18, 66.86, 32.15, 30.82. MS (EI, 70 eV) *m*/*e* 315 (M^++1, 10), 314 (M^+, 53), 196 (100), 91 (55). HRMS ($C_{23}H_{22}O$) calcd: 314.1665, found: 314.1666.

*4.4.2. cis-2-{2-[4-(3-Phenylpropoxy)-phenyl]-vinyl}-furan (cis-**1b**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J*=8.7 Hz, 2H), 7.34 (s, 1H), 7.32 (t, *J*=7.5 Hz, 2H), 7.26–7.21 (m, 3H), 6.89 (d, *J*=8.7 Hz, 2H), 6.43 (d, *J*=12.6 Hz, 1H), 6.36 (dd, *J*=3.4, 1.8 Hz, 1H), 6.31 (d, *J*=12.6 Hz, 1H), 6.31 (d, *J*=3.4 Hz, 1H), 4.01 (t, *J*=6.3 Hz, 2H), 2.85 (t, *J*=7.8 Hz, 2H), 2.15 (p, *J*=7.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.37, 152.36, 141.50, 141.31, 130.04, 129.68, 128.51, 128.41, 127.75, 125.92, 116.57, 114.09, 111.14, 109.52, 66.86, 32.15, 30.83. MS (EI, 70 eV) *m*/*e* 305 (M^++1, 9), 304 (M^+, 100), 186 (93), 91 (72). HRMS ($C_{21}H_{20}O_2$) calcd: 304.1458, found: 304.1462.

*4.4.3. cis-2-{2-[4-(3-Phenylpropoxy)-phenyl]-vinyl}-thiophene (cis-**1c**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.30 (m, 4H), 7.27–7.21 (m, 3H), 7.12 (d, *J*=5.0 Hz, 1H), 7.01 (d, *J*=3.5 Hz, 1H), 6.92 (dd, *J*=5.0, 3.5 Hz, 1H), 6.89 (d, *J*=8.6 Hz, 2H), 6.65 (d, *J*=11.9 Hz, 1H), 6.54 (d, *J*=11.9 Hz, 1H), 4.01 (t, *J*=6.3 Hz, 2H), 2.85 (t, *J*=7.9 Hz, 2H), 2.15 (p, *J*=7.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.51, 141.49, 140.02, 130.06, 129.43, 128.80, 128.49, 128.39, 127.77, 126.40, 125.91, 125.15, 122.38, 114.46, 66.85, 32.15, 30.82. MS (EI, 70 eV) *m*/*e* 321 (M^++1, 4), 320 (M^+, 98), 202 (100), 91 (59). HRMS ($C_{21}H_{20}OS$) calcd: 320.1229, found: 320.1231.

4.5. Synthesis of compounds *cis* and *trans*-1d



*4.5.1. Synthesis of **A**.* A mixture of 5 g (4.1 mmol) of 4-hydroxybenzaldehyde and grounded 9.44 g (0.17 mol) of KOH in 62 mL of DMSO was stirred at room temperature for 30 min, and then 12.17 g (1.5 mol) of 1-bromo-3-phenylpropane was added slowly into the previous solution. After addition, the reaction was stirred for another 90 min. Afterward, the reaction was poured into water and extracted with dichloromethane for three times. The organic layers were combined and dried with anhydrous $MgSO_4$. And then the organic solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1:5) to afford 4-(3-phenylpropoxy)-benzaldehyde **A** in 96.3% yield.

*4.5.2. The Wittig reaction to synthesize cis and trans-**1d**.* A mixture of 2.01 g (1.33 mmol) of 4-chloromethylbenzonitrile and 4.44 g (1.96 mmol) PPh_3 in 12 mL of benzene was refluxed for 2 days to produce white solid. Collect the solid by suction filtration and (4-cyanobenzyl)triphenylphosphonium salt was obtained in 89.3% yield. Afterward, a mixture of 4.88 g (1.82 mmol) of the previous salt, 2.6 g (1.08 mmol) of compound **A**, and 0.38 g (1.45 mmol) of 18-crown-6 in 25 mL of dichloromethane was stirred violently and 12 mL of 50% aqueous solution of K_2CO_3 were added slowly After addition, the reaction was stirred at room temperature for 3 days. And then the reaction mixture was poured into water and extracted with ethyl acetate for three times. The organic layers were combined and dried with anhydrous $MgSO_4$. The organic solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1:10) to afford the mixture of *cis* and *trans*-**1d** in a 66.1% yield. Some of *cis* and *trans* isomers were readily isolated by further purification.

*4.5.3. 4-(3-Phenylpropoxy)-benzaldehyde (**A**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.89 (s, 1H), 7.84 (d, *J*=8.7 Hz, 2H), 7.31 (t, *J*=7.5 Hz, 2H), 7.23–7.21 (m, 3H), 6.99 (d, *J*=8.7 Hz, 2H), 4.06 (t, *J*=6.3 Hz, 2H), 2.84 (t, *J*=7.6 Hz, 2H), 2.16 (p, *J*=6.9, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.80, 164.10, 141.09, 131.98, 129.87, 128.48, 126.07, 114.76, 67.25, 32.00, 30.55.

*4.5.4. cis-4-{2-[4-(3-Phenylpropoxy)-phenyl]-vinyl}-benzonitrile (cis-**1d**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J*=8.2 Hz, 2H), 7.36 (d, *J*=8.2 Hz, 2H), 7.30 (t, *J*=7.6 Hz, 2H), 7.24–7.2 (m, 3H), 7.13 (d, *J*=8.6 Hz, 2H), 6.78 (d, *J*=8.6 Hz, 2H), 6.69 (d, *J*=12.2 Hz, 1H), 6.47 (d, *J*=12.2 Hz, 1H), 3.96 (t, *J*=6.3 Hz, 2H), 2.82 (t, *J*=7.6 Hz, 2H), 2.12 (p, *J*=7.0, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.68, 142.51, 141.36, 132.82, 131.97, 130.11, 129.43, 128.44, 128.39, 126.70, 125.93, 118.97, 114.39, 110.15, 66.88, 32.08, 30.72. MS (EI, 70 eV) *m*/*e* 340 (M^++1, 5), 339 (M^+, 64), 221 (97), 91 (100). HRMS ($C_{24}H_{21}ON$) calcd: 339.1618, found: 339.1625.

*4.5.5. trans-4-{2-[4-(3-Phenylpropoxy)-phenyl]-vinyl}-benzonitrile (trans-**1d**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J*=8.4 Hz, 2H), 7.55 (d, *J*=8.4 Hz, 2H), 7.46 (d, *J*=8.7 Hz, 2H), 7.30 (t, *J*=7.4 Hz, 2H), 7.24–7.19 (m, 3H), 7.17 (d, *J*=16.3 Hz, 1H), 6.95 (d, *J*=16.3 Hz, 1H), 6.91 (d, *J*=8.7 Hz, 2H), 4.00 (t, *J*=6.3 Hz, 2H), 2.83 (t, *J*=7.6 Hz, 2H), 2.13 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.54, 142.24, 141.35, 132.42, 131.99, 128.96, 128.49, 128.42, 128.24, 126.52, 125.97, 124.44, 119.13, 114.85, 109.99, 66.96, 32.08, 30.73. MS (EI, 70 eV) *m*/*e* 340 (M^++1, 4), 339 (M^+, 53), 221 (85), 91 (100). HRMS ($C_{24}H_{21}ON$) calcd: 339.1618, found: 339.1615.

4.6. Deprotection of compounds 1a–i

A 100 mL of acetonitrile solution containing 0.1 g of compound **1** and 5 mM HCl was divided into five quartz tubes (1.3 cm×20 cm), and then the tubes were sealed with septa. After excluding oxygen by 30 min of bubbling with N_2, the tubes were irradiated at 300 nm for 6 h. The reaction mixtures were then collected, and neutralized with aqueous sodium hydroxide. The resulting solution was extracted with ethyl acetate, and then organic layers were combined and dried with anhydrous $MgSO_4$. The residue was obtained by removing organic solvent under reduced pressure, and then purified by column chromatography on silica gel (ethyl acetate/hexane=1:10) to afford 3-phenyl-1-propanol **4** and the side product **2**.

*4.6.1. trans-4-(Naphthalen-2-yl)-but-3-en-2-one (trans-**2a**).*[12a] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.87–7.82 (m, 3H), 7.69–7.65 (m, 2H), 7.53–7.51 (m, 2H), 6.83 (d, J=16.2 Hz, 1H), 2.42 (s, 3H).

*4.6.2. trans-4-(Benzo[b]furan-5-yl)-but-3-en-2-one (trans-**2b**).*[12a,c] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.64 (d, J=2.2 Hz, 1H), 7.61 (d, J=16.2 Hz, 1H), 7.49 (d, J=0.9 Hz, 2H), 6.77 (d, J=2.2 Hz, 1H), 6.71 (d, J=16.2 Hz, 1H), 2.38 (s, 3H).

*4.6.3. trans-4-(Benzo[b]thiophen-5-yl)-but-3-en-2-one (trans-**2c**).*[12a,c] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.86 (d, J=8.4 Hz, 1H), 7.62 (d, J=16.3 Hz, 1H), 7.53 (d, J=8.4 Hz, 1H), 7.48 (d, J=5.4 Hz, 1H), 7.34 (d, J=5.4 Hz, 1H), 6.78 (d, J=16.3 Hz, 1H), 2.39 (s, 3H).

*4.6.4. trans-7-(3-Oxo-but-1-enyl)-naphthalene-2-carbonitrile (trans-**2d**).* ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.00 (s, 1H), 7.93 (d, J=7.7 Hz, 1H), 7.91 (d, J=7.7 Hz, 1H), 7.84 (dd, J=8.6, 1.2 Hz, 1H), 7.67 (d, J=16.2 Hz, 1H), 7.66 (dd, J=8.6, 1.2 Hz, 1H), 6.87 (d, J=16.2 Hz, 1H), 2.44 (s, 3H). MS (EI, 70 eV) m/e 222 (M^++1, 5), 221 (M^+, 38), 206 (100), 178 (44), 151 (54). HRMS ($C_{15}H_{11}ON$) calcd: 221.0835, found: 221.0837.

4.7. Selective deprotection of compounds 1a and b

A 100 mL of acetonitrile solution containing 0.05 g of compound **1a**, 0.05 g of **1b**, and 5 mM HCl was prepared and divided into five quartz tubes (1.3 cm×20 cm), and then the tubes were sealed with septa. After excluding oxygen by 30 min of bubbling with N_2, the tubes were irradiated at 365 nm for 3 h. The reaction mixtures were then collected, and neutralized with aqueous sodium hydroxide. The resulting solution was extracted with ethyl acetate, and then organic layers were combined and dried with anhydrous $MgSO_4$. After removing organic solvent under reduced pressure, the residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1:10) to afford the recycling **1a**, 3-phenyl-1-propanol **4**, and the side product **2b** in 98%, 80%, and 92% yields, respectively.

4.8. Stability test of compound *trans*-1a

Reacted 0.1 g of *trans*-**1a** under the reaction conditions listed in Table 3. After reaction, the mixture was added into a large amount of water. The resulting solution was extracted with ethyl acetate for three times, and then the organic layers were combined and dried with anhydrous $MgSO_4$. After removing organic solvent under reduced pressure, the residue was purified by column chromatography on silica gel (hexane) to recover *trans*-**1a**. (The isolated yields are listed in Table 3.)

4.9. Synthesis of 3-phenylpropyl benzoate[23]

Stirred the mixture of 0.82 g (6.0 mmol) of 3-phenyl-1-propanol, 1.68 g (11.95 mmol) of benzoyl chloride, and 0.92 g (9.0 mmol) of aluminum oxide in a flask at room temperature for 4 h and then suction filtrate the reaction mixture with ethyl acetate. Collected the filtration, removed solvent under reduced pressure, and then purified the residue by column chromatography on silica gel (ethyl acetate/hexane=1:15). The ester, 3-phenylpropyl benzoate, was obtained in an 82% yield.

4.9.1. 3-Phenylpropyl benzoate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J=8.0 Hz, 2H), 7.58 (t, J=7.5 Hz, 1H), 7.46 (t, J=7.8 Hz, 2H), 7.32 (t, J=7.6 Hz, 2H), 7.25–7.20 (m, 3H), 4.37 (t, J=6.5 Hz, 2H), 2.81 (t, J=7.8 Hz, 2H), 2016–2.10 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.58, 141.17, 132.85, 130.37, 129.53, 128.45, 128.42, 128.32, 126.01, 64.25, 32.29, 30.28.

4.10. Synthesis of secondary and tertiary alcohols

*4.10.1. 4-Phenylbutan-2-ol (**11**).* To a stirred THF solution (15 mL) of 3-phenylpropanal 1.0 g (7.5 mmol), 7.5 mL of methylmagnesium bromide (1 M in THF) was added dropwise at 0 °C. After addition, the reaction mixture was stirred for 1 h and then diluted with brine and extracted with ethyl acetate. The organic layers were combined, dried with $MgSO_4$, and concentrated by reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1:5) to afford 4-phenylbutan-2-ol in a 65.6% yield.

*4.10.1.1. 4-Phenylbutan-2-ol (**11**).*[24] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (t, J=7.5 Hz, 2H), 7.19 (d, J=7.0 Hz, 2H), 7.17 (t, J=7.3 Hz, 1H), 3.82 (sextet, J=6.2 Hz, 1H), 2.74 (ddd, J=13.6, 9.3, 6.3 Hz, 1H), 2.65 (ddd, J=13.6, 9.3, 7.1 Hz, 1H), 1.81–1.70 (m, 2H), 1.22 (d, J=6.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.02, 128.37, 125.78, 67.49, 40.80, 32.10, 23.57.

*4.10.2. 2-Methyl-4-phenylbutan-2-ol (**12**).* To a stirred of THF solution (12 mL) of methyl 3-phenylpropanoate 1.0 g (6.1 mmol), 12.2 mL of methylmagnesium bromide (1 M in THF) was added dropwise at 0 °C. After addition, the reaction mixture was stirred for 1 h and then diluted with brine and extracted with ethyl acetate. The organic layers were combined, dried with $MgSO_4$, and concentrated by reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1:5) to afford 2-methyl-4-phenylbutan-2-ol in a 54.0% yield.

*4.10.2.1. 2-Methyl-4-phenylbutan-2-ol (**12**).*[25] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (t, J=7.5 Hz, 2H), 7.19 (d, J=7.6 Hz, 2H), 7.16 (t, J=7.3 Hz, 1H), 2.71–2.67 (m, 2H), 1.80–1.76 (m, 2H), 1.28 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.50, 128.39, 128.29, 125.73, 70.90, 45.72, 30.73, 29.35, 29.27.

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Supplementary data

^{1}H and ^{13}C NMR spectra of *cis* and *trans*-**1a**–**d**, *trans*-**1e**–**i**, *trans*-**3a**–**c**, **5**, and **6**, ^{1}H NMR spectra of *trans*-**2a**–**d**, and a test experiment for examining the formation of acid are included in Supplementary data. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.06.074.

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18. The absorbances of **1a**–**c** at 365 nm in the reaction concentration (~3.2 mM) are 0.096, 0.554, and 1.798, respectively.
19. The consumptions of starting material after the reactions of 3-phenylpropyl benzoate (0.08 M) under some basic conditions are described as follows: 100% for THF solution containing 0.33 M ^{t}BuOK at room temperature for 2 h, 68% for NMP solution with 0.13 M NaH at room temperature for 2 h, and 54% for a mixture solution of water and THF (1:1) containing 0.9 M KOH at refluxing temperature for 21 h.
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