多聚磷酸催化的苄基芳基醚合成苄基酚的重排反应

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摘要 系统研究了多聚磷酸(PPA)催化的苄基芳基醚的重排反应,有效调整吸电子基团(EWG)和供电子基团(EDG)在酚部分或苄基部分取代位置,有利于重排反应和重排的区域选择性。重排反应遵循芳环上的取代引导规则。这种容易实现的重排反应方法对于酚的苄基化具有实际应用价值。

关键词 多聚磷酸;重排;脱保护;苄基芳基醚;苄基酚

Synthesis of Benzyl Phenol from Benzyl Aryl Ether by Polyphosphoric Acid-Catalyzed Benzyl Rearrangement

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Abstract The rearrangement activity of benzyl aryl ether catalyzed by polyphosphoric acid (PPA) was systematically investigated. Optimal structural tuning of substitutions of electron withdrawing group (EWG) and electron donating group (EDG) at phenolic moiety or benzyl moiety benefits the rearrangement and the regio-selectivity of the rearrangement obeyed the substitution directing rule at the aromatic ring. This readily available rearrangement method is of practical interest for the benzylation of diverse aromatic phenols.

Keywords polyphosphoric acid (PPA); rearrangement; deprotection; benzyl aryl ether; benzyl phenol

1 Introduction

Phenols work as versatile natural intermediates and are used as important synthetic building blocks for constructing pharmaceuticals, agrochemicals, additives, antioxidants, antiseptics and polymers^[1] since phenol possesses specific characteristics and plays an important role in re-dox reactions in nature. Diarylmethane is a valuable structural group of many important bioactive compounds such as sertraline, clemastine, nuvigil and lomerizine and it is useful structural moiety in organic synthesis and drug

discovery. Because of these, some benzylated phenols like lasofoxifene, detrol, corlopam, agrimophol and *etc.*, structurally associated with both of diarylmethane and phenol, are bioactive and used as drugs in clinic.

Friedel-Craft reaction and its related reactions^[2] of arene with benzyl halides and cross-coupling^[3] of aryl halides or special arenes with benzyl compounds are two complementary synthetic routes for the synthesis of diarylmethane. However, these methods are sometimes not suitable for the synthesis of benzylated phenol due to phenol group. The rearrangement of benzyl aryl ether is a valuable

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method to generate benzylated phenol with diarylmethane skeleton and phenol group, which was first introduced by Hartmann and Gattermann more than 120 years ago^[4] and up to 1952, Tarbell and Petropoulos^[5] described in detail the rearrangement of benzyl phenyl ether. Afterwards, the rearrangement is attracting considerable efforts in the synthesis.^[6] Bode and co-workers^[7] demonstrated the arylation of $\text{BF}_3 \cdot \text{OEt}_2$ -catalyzed benzyl hydroxamates. Paquin and coworkers^[8] developed the Friedel-Crafts alkylation of arenes with benzyl fluorides via the *in situ* generation of HF. And, later, Moran's group^[9] demonstrated the dehydrative Friedel-Crafts reactions of deactivated benzylic alcohols under super Brønsted acid catalysis. Antonchick's group^[10] disclosed a catalytic, metal-free intramolecular rearrangement of benzyl phenyl ethers using nitrosonium salt as a catalyst.

The rearrangement of some specific benzyl aryl ethers with acidic catalysts can offer acceptable rearrangement results; however, there is a lack of systematic study in the field. For versatile access to benzylated phenols, it is established that benzyl aryl ethers undergo benzyl rearrangement under the catalysis of polyphosphoric acid (PPA). Herein, we present our systematic investigation on PPA-catalyzed rearrangement of benzyl aryl ether in moderate to good yield (Scheme 1).

Scheme 1 Synthesis of **1aa** to **1al** and reaction process of benzyl rearrangement

2 Results and discussion

2.1 Reaction conditions for PPA-catalyzed benzyl rearrangement

The study of the benzyl rearrangement was first con-

ducted at room temperature (*ca.* 25 °C) by PPA-catalyzed reaction of 1-(4'-benzyloxy)-4-methoxybenzene (**1aa**)^[11a] and the reaction (Scheme 1 and Table 1, Entry 1) produced two rearranged products of **2aa** (*o*)^[11b,12b] as a major product (62% yield) and **2aa** (*m*)^[12b] as a minor product (7% yield), and trace amount of debenzylated product **3a**. The rearranged position of **2aa** (*o*) was determined by nuclear Overhauser effect spectroscopy (NOESY), in which there is nuclear Overhauser effect (NOE) between phenolic-OH and only one aromatic CH, NOE between CH_2 of Bn with one aromatic CH and weak NOE between phenolic-OH and CH_2 of Bn. Meanwhile, there are NOEs between OCH_3 with one or two aromatic CHs.

To explore the reaction conditions, the rearrangement of **1aa** was carried out in the presence of a series of acidic catalysts in different solvents at 25 °C (Table 1). As PPA in 1,2-dichloroethane (DCE) (Table 1, Entry 1), PPA in dichloromethane (DCM) and toluene (Table 1, Entries 2, 11) also afforded **2aa** (*o*) as a major product and **2aa** (*m*) as a minor product with 10% yield of **3a**. However, trifluoroacetic acid (TFA) in DCE (Table 1, Entry 6) catalyzed the reaction to produce 50% yield of **2aa** (*o*) and **2aa** (*m*) in total and 30% yield of **3a**, and anhydrous AlCl_3 in DCM (Table 1, Entry 9) resulted in 40% yield of **2aa** (*o*) and 30% yield of **3a**. Anhydrous ZnCl_2 only produced trace amount of **3a** (Table 1, Entry 10) and no reaction happened by H_3PO_4 (Table 1, Entry 3), pyridinium 4-toluenesulfonate (PPTS) (Table 1, Entry 4), $\text{TsOH} \cdot \text{H}_2\text{O}$ (Table 1, Entry 5) and cond. HCl (Table 1, Entries 7 and 8). It is interesting and important that ether solvents (Table 1, Entries 17~20) of tetrahydrofuran (THF), dioxane, 1,2-dimethoxyethane (DME) and ethyl ether were not benign solvents for the rearrangement catalyzed by PPA.

In general, TFA and anhydrous AlCl_3 are not as effective as PPA in the benzyl rearrangement due to its production of appreciable **3a**, and PPA was determined to be the optimal catalyst. The PPA-catalyzed rearrangement is tolerated solvents of DCE, DCM and toluene, and DCE was the first choice of the reaction solvent used in this study.

2.2 Effects of substitutions at phenolic moiety

The effects of the substitutions at phenolic moiety and benzyl moiety on the rearrangement reactivity are presented in Table 2.

The electron donating group (EDG) of OMe in benzyl moiety promotes the rearrangement and deprotection (Table 2), resulting that *p*-methoxybenzyl (PMB) ($\text{R}^2 = \text{OMe}$) is more easily rearranged or/and deprotected than benzyl (Bn) ($\text{R}^2 = \text{H}$) at lower temperature and in shorter reaction time, but the rearranged yields of Bn phenyl ethers **1aa**,^[11a] **1ba**,^[13a] **1ca**,^[15a] **1ea**,^[17] **1fa**,^[18a] and **1ga**,^[19a] are better than those of PMB phenyl ethers **1ab**,^[12a] **1bb**,^[14a] **1cb**,^[15b] **1eb**, **1fb**,^[18c] and **1gb**.^[19b] These results can be reasoned from higher stabilizing capacity of OMe for the formation of partial positive ion of PMB and on the other hand, more stable partial positive ion of PMB possesses less electrophilic ability than less stable partial positive ion of Bn

Table 1 Influence of catalysts and solvents on the benzyl rearrangement at 25 °C

Entry	Catalyst	Solvent ^a	Time/h	Ratio ^b /%			
				2aa (o) ^c	2aa (m) ^d	3a	Unreacted 1aa
1 ^e	PPA	DCE	72	62	7	Trace	Trace
2	PPA	Dry DCM	180	60	10	10	20
3	H ₃ PO ₄ (≥85%)	DCE	60	NR	NR	NR	100
4	PPTS	DCE	60	NR	NR	NR	100
5	TsOH·H ₂ O	DCE	60	NR	NR	NR	100
6	TFA	DCE	126	40	10	30	10
7	Cond. HCl	DCE	40	NR	NR	NR	100
8	Cond. HCl	Dry DCM	80	NR	NR	NR	100
9	Anhydrous AlCl ₃	Dry DCM	10	40	Trace	30	0
10	Anhydrous ZnCl ₂	Dry DCM	168	NR	NR	Trace	>95
11 ^e	PPA	Toluene	96	65	20	10	Trace
12	PPA	THF	96	NR	NR	NR	100
13	PPA	Dioxane	120	—	—	Trace	>95
14	PPA	DME	124	—	—	Trace	80
15	PPA	Ethyl ether	96	NR	NR	NR	100

^a The solvent was used directly or treated for anhydrous goal before use. Asterisk (*) denotes minor regioisomer. ^b The ratio was estimated by TLC except Entries 1 and 11. —, NR, and trace represent not detectable, no reaction and lower than 5%, respectively. ^c *ortho* to hydroxy. ^d *meta* to hydroxy. ^e Isolated yields.

Table 2 Effects of EWG and EDG substitutions at phenolic moiety on the rearrangement^a

 2aa , 69%, 70 °C, 11 h, <i>o</i> : <i>m</i> = 9:1	 2ab , 60%, 15 °C, 4.5 h	 2ba , 77%, 70 °C, 20 h, <i>o</i> : <i>p</i> = 4:1	 2bb , 58%, 15 °C, 3 h	 2ca , 59%, 25 °C, 30 h ^b
 2cb , 48%, 10 °C, 8.5 h	 2da , 60%, 15 °C, 20 h	 2db , 72%, 0 °C, 5 h	 2ea , 75%, 70 °C, 4 h	 2eb , 59%, 0 °C, 5.5 h
 2fa , 68%, 70 °C, 26 h	 2fba , 11%, 0 °C, 4.5 h	 2fbb , 13%, 0 °C, 4.5 h	 2ga , 39%, 70 °C, 46 h	2gb , R ¹ = 4-CN, R ² = 4-OMe, 0 °C, 5 h, DP 2ha , R ¹ = 4-CF ₃ , R ² = 4-H, 70 °C, 48 h, NR 2hb , R ¹ = 4-CF ₃ , R ² = 4-OMe, 25 °C, 20 h, DP 2ia , R ¹ = 4-NO ₂ , R ² = 4-H, 70 °C, 40 h, DP 2ib , R ¹ = 4-NO ₂ , R ² = 4-OMe, 5 °C, 40 h, DP

^a Reaction conditions: **1** (1 mmol), PPA (0.6 mmol), DCM or toluene (2 mL); isolated yield. NR and DP mean not detectable, no reaction, deprotection of Bn or PMB group, respectively. Asterisk (*) denotes minor regioisomer. ^b The solvent is DCE except toluene.

(Scheme 1). It is noticed that the para to OH product **2ba** (*p*)^[13b] was a minor product of Bn ether compound **1ba**,^[13a] while PMB ether compound **1bb**^[14a] produced the para to OH product **2bb**^[14b] as the sole product, and compound **1ca**^[15a] (Table 2) proceeded the rearrangement in toluene to yield **2ca**^[15c] but no reaction happened in DCE.

The EDG may not be helpful for the formation of the negative ion of phenolic oxygen, but it makes phenolic moiety more nucleophilic and readily accept the electrophilic attack by benzyl cation to establish the rearrangement of benzyl moiety (Table 2). Instead, electron withdrawing group (EWG) speeds up the formation of the negative ion of phenolic oxygen while it prevents phenolic moiety from being attacked by benzyl cation (Table 2). Compound **1fa**^[18a] (Table 2) and compound **1fb**^[18c] (Table 2) with a carboxylate group at phenolic moiety underwent the rearrangement, but **1fa**^[18a] afforded much better yield of the rearranged product **2fa**^[18b] than **1fb** generated mono-rearranged product **2fba** and bi-rearranged product **2fbb**. Meanwhile, bearing cyano group at phenolic moiety, compound **1ga**^[19a] gave approximately 40% yield of the rearranged product **2ga** (Table 2) but compound **1gb**^[19b] did not produce any rearranged product (Table 2).

2.3 Influences of varied arenes and combined substitutions

The effects of combined substitutions of EWGs and EDGs, substitution positions or varied arenes on the rearrangement were further investigated. Compared to compounds **1ia**^[16] and **1ib**^[21] (Table 2), introduction of an EDG of methoxy group made compound **1ja**^[22a] undergo the rearrangement of benzyl group, but compound **1jb**^[22b] produced the mixture and no detectable rearranged product of PMB group (Table 3). The same results as **1ja** and **1jb** happened for compounds **1ka**^[23a] and **1kb**,^[23a] which **1ka** gave rearranged product **2ka**^[23b] but **1kb** generated the mixture (Table 3). Compounds **1la** (2'-methoxy),^[24a] **1ma** (3'-methoxy)^[11a] and **1na** (2'-methyl)^[26a] smoothly underwent the rearrangement of benzyl group to afford products **2la** (*o*)^[24b] (*ortho* to OH) and **2la** (*m*)^[24c] (*para* to OMe), **2ma** (*o*)^[25a] (*ortho* to OH and OMe) and **2ma** (*o'*)^[25b] (*para* to OMe), **2na** (*o*)^[26b] (*ortho* to OH) and **2na** (*p*)^[26c] (*para* to OH), respectively (Table 3). Product **2ma** (*o*) has the identical ¹H NMR signal pattern of 3 aromatic C—Hs of phenolic moiety to the literature,^[25a] in which **2ma** (*o*) was prepared by other route. The regio-chemistry observations suggested that the regio-selectivity of these products obeyed the substitution directing rule at the aromatic ring.

α -Naphtholate of Bn ether **1oa**^[16] (Table 3) or PMB ether **1ob**^[28a] (Table 3) displayed a good rearrangement reactivity to afford 2'-rearranged Bn product **2oa**^[27] (*ortho* to OH) or 2'- and 4'-rearranged PMB products **2ob** (*o*)^[27,28b] (*ortho* to OH) and **2ob** (*p*) (*para* to OH), respectively. Due to relatively lower reactivity of Bn, 56% unreacted **1oa** were isolated. Meanwhile, β -naphtholate of benzyl ether **1pa**^[29a] (Table 3) or PMB ether **1pb**^[29a] (Table 3) produced 1'-(*ortho* to OH) product **2pa**^[29b] or

1'-(*ortho* to OH) product **2pb**.^[29b] These results suggest that the scope of phenolic moiety for the rearrangement is adaptable.

Table 3 Influences of combined substitutions, substitution positions and varied arenes at phenolic moiety on the rearrangement^a

^a Reaction conditions: **1** (1 mmol), PPA (0.6 mmol), DCM or toluene (2 mL); isolated yield; ND represent that the reaction generated complicated mixture and target products were not detectable; asterisk (*) denotes minor regioisomer; ^b The yield is based on 44% conversion of compound **1oa** and the isolated yield is 29%. ^c The solvent is toluene.

2.4 Effects of benzyl groups on the rearrangement

As 4'-OMe of PMB affected on the balance between the rearrangement and the deprotection (Tables 2, 3), other EDGs at benzyl moiety or benzyl-like moiety were explored (Table 4). As reported, allyl phenyl ether **1ac**^[30a] (Table 4) underwent the rearrangement in PPA to yield an *ortho* to OH product **2ac**^[30b] in 39% yield. Interestingly,

2'-PMB ether **1ad** (Table 4) gave better yield of rearranged product **2ad** than 4'-PMB ether **1ab** did (Table 2).

Table 4 Effects of benzyl groups or benzyl-like groups on the rearrangement^a

^a Reaction conditions: **1** (1 mmol), PPA (0.6 mmol), DCM or toluene (2 mL); isolated yield; NR represent no reaction. Asterisk (*) denotes minor regioisomer.

Introduction of EWG to aromatic moiety of benzyl moiety resulted in reducing the reactivity of these ethers, e.g., 4'- or 3'-nitro-benzyl compound **1ae**^[31] or **1af**, 4'-cyano-benzyl compound **1ag**, and 4'-carboxylate benzyl compound **1ah**^[18c] showed no reaction for the rearrangement and the deprotection (Table 4). Compared to EWG substitutions at phenolic moiety (Table 2), it is suggested that EWG substitutions at benzyl moiety more strongly affect the reactivity both for the rearrangement and the deprotec-

tion.

The effects of menaphthyl group were also studied. Both of β -menaphthyl and α -menaphthyl phenyl ethers **1ai** and **1aj**^[32] smoothly underwent the rearrangement to produce *ortho* to OMe products **2ai** and **2aj**, respectively, which showed similar ¹H NMR patterns of phenolic C—H to product **2aa** (*m*) (Table 2). We next extended “ R^3 ” from H to methyl and phenyl. Compound **1ak**^[33a] ($R^3 = \text{Me}$, Table 4) afforded as normal two rearranged products **2ak** (*o*)^[33b] and **2ak** (*m*). The *ortho* to OH product **2ak** (*o*)^[33b], which ¹H NMR signal pattern of 3 aromatic C—Hs of phenolic moiety is identical to the literature^[33b] and similar to **2aa** (*o*) but not **2aa** (*m*), was a major product, and the *ortho* to OMe product **2ak** (*m*) was a minor product. Compound **1al**^[34a] ($R^3 = \text{Ph}$, Table 4) produced only 16% mono-rearranged product **2ala**^[34b] but 23% bi-rearranged product **2alb**, and both of **2ala**^[34b] and **2alb** are *ortho* to OMe products.

3 Conclusions

In summary, the rearrangement activity of benzyl aryl ether catalyzed by PPA has been systematically investigated. In general, EWG substitutions at phenolic moiety ($R^1 = \text{EWG}$) or benzyl moiety ($R^2, R^3 = \text{EWG}$) decelerate the rearrangement, and EDG substitutions at phenolic moiety ($R^1 = \text{EDG}$) exert a positive influence on the rearrangement. However, EDG substitutions at benzyl moiety ($R^2 = \text{EDG}$) exert a positive influence on both rearrangement and deprotection. Importantly, optimal tuning of the rearrangement activity by substitutions of EWG and EDG at phenolic moiety or benzyl moiety could be beneficial for the rearrangement, and the regio-selectivity of the rearrangement obeyed the substitution directing rule at the aromatic ring.

4 Experimental section

4.1 General information

¹H NMR and ¹³C NMR spectra were recorded on a Bruker AV-400 spectrometer at 400 and 100 MHz, respectively, in indicated deuterated solvents. The low or high resolution of ESIMS was recorded on an Agilent 1200 HPLC-MSD mass spectrometer or Applied Biosystems Q-STAR Elite ESI-LCMS/MS mass spectrometer, respectively. Melting points were measured using an YRT-3 melting point apparatus and were uncorrected.

4.2 General synthetic procedure for the unknown starting materials of ether compounds

Phenol (1.0 mmol) was dissolved in 10 mL of acetonitrile and then 1.2 mmol of allyl chloride, ethyl chloroacetate, benzyl chloride/bromide, PMB chloride/bromide or the related chloride/bromide analogues was added. The reaction mixture was monitored by TLC and generally refluxed for 2~10 h. Diluted with water, extracted by ethyl acetate, washed with brine, the organic phase was dried over anhydrous MgSO_4 and the filtrate was rotava-

pored *in vacuo*. The residue was further purified using flash column chromatography and eluting with petroleum ether and ethyl acetate or re-crystallized to afford the benzyl aryl ether product.

4-(4'-Methoxybenzyloxy)phenyl acetate (**1db**): From *p*-(*p*-methoxybenzyloxy)phenol and acetic anhydride, yield 95%. White solid, m.p. 104~106 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ: 7.41~7.35 (m, 2H), 7.05~6.98 (m, 4H), 6.97~6.92 (m, 2H), 5.00 (s, 2H), 3.75 (s, 3H), 2.23 (s, 3H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 169.42, 158.99, 155.92, 155.47, 143.94, 129.46, 129.26, 128.81, 128.67, 122.53, 115.28, 114.92, 113.80, 69.29, 55.05, 20.74.

Ethyl 2-(4-(4'-methoxybenzyloxy)phenoxy)acetate (**1eb**): From *p*-(*p*-methoxybenzyloxy)phenol and ethyl chloroacetate, yield 81%. White solid, m.p. 84~86 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ: 7.37~7.33 (m, 2H), 6.95~6.89 (m, 4H), 6.87~6.82 (m, 2H), 4.94 (s, 2H), 4.68 (s, 2H), 4.15 (q, *J*=7.1 Hz, 2H), 3.75 (s, 3H), 1.20 (t, *J*=7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 169.19, 159.46, 153.83, 152.24, 129.20, 115.89, 114.00, 70.44, 66.40, 61.27, 55.30, 14.17.

1-Methoxy-4-((4'-(trifluoromethyl)phenoxy)methyl)benzene (**1hb**): From 4-(trifluoromethyl)phenol and *p*-methoxybenzyl chloride, yield 50%. White solid, m.p. 131~134 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ: 7.65 (d, *J*=8.7 Hz, 2H), 7.42~7.37 (m, 2H), 7.18 (d, *J*=8.6 Hz, 2H), 6.98~6.93 (m, 2H), 5.11 (s, 2H), 3.76 (s, 3H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 161.21, 159.12, 129.60, 128.21, 126.92, 126.88, 126.85, 126.81, 125.88, 123.19, 121.28, 120.96, 120.64, 115.27, 113.85, 69.31, 55.07.

1-(2'-Methoxybenzyloxy)-4-methoxybenzene (**1ad**): From 4-methoxyphenol and 2-methoxybenzyl bromide, yield 82%. Colorless liquid. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 7.39~7.29 (m, 2H), 7.04 (d, *J*=7.8 Hz, 1H), 6.97~6.89 (m, 3H), 6.87~6.83 (m, 2H), 4.98 (s, 2H), 3.82 (s, 3H), 3.69 (s, 3H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 156.79, 153.38, 152.50, 129.15, 128.85, 124.94, 120.22, 115.50, 114.57, 110.79, 64.94, 55.37, 55.30.

1-(3'-Nitrobenzyloxy)-4-methoxybenzene (**1af**): From 4-methoxyphenol and 3-nitrobenzyl bromide, yield 91%. Colorless liquid. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 8.30~8.28 (m, 1H), 8.22~8.15 (m, 1H), 7.92~7.87 (m, 1H), 7.69 (t, *J*=7.9 Hz, 1H), 7.00~6.95 (m, 2H), 6.90~6.85 (m, 2H), 5.20 (s, 2H), 3.69 (s, 3H).

4-((4'-Methoxyphenoxy)methyl)benzonitrile (**1ag**): From 4-(chloromethyl)benzonitrile and 4-methoxyphenol, yield 94%. White solid, m.p. 88~89 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ: 7.85 (d, *J*=8.1 Hz, 2H), 7.62 (d, *J*=8.1 Hz, 2H), 6.99~6.81 (m, 4H), 5.15 (s, 2H), 3.69 (s, 3H).

2-((4'-Methoxyphenoxy)methyl)naphthalene (**1ai**): From 2-(chloromethyl)naphthalene and 4-methoxyphenol, yield 84%. White solid, m.p. 127~128 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ: 7.97~7.90 (m, 4H), 7.57 (dd, *J*=8.4, 1.6 Hz, 1H), 7.55~7.49 (m, 2H), 7.01~6.96 (m, 2H), 6.89~6.83 (m, 2H), 5.21 (s, 2H), 3.68 (s, 3H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 153.50, 152.31, 135.01, 132.76,

132.48, 127.97, 127.73, 127.57, 126.26, 126.08, 126.03, 125.64, 115.83, 114.59, 69.81, 55.31.

4.3 General procedure for the rearrangement or deprotection

To the titled compound (1.0 mmol) in 2.0 mL of DCE or toluene, 200 mg of PPA was added at the indicated temperature. The reaction progress was monitored by TLC. After the reaction was completed, the reaction mixture was worked-up with saturated NaHCO₃ and extracted by ethyl acetate. The organic phase was dried over anhydrous Na₂SO₄ and then the filtrate was rotavapored *in vacuo*. The residue was further purified using flash column chromatography and eluting with petroleum ether and ethyl acetate to afford the titled product.

2-Benzyl-4-methoxyphenol (**2aa** (o)):^[11b,12b] Yield 62%. White solid, m.p. 104~105 °C; ¹H NMR (DMSO-*d*₆) δ: 8.91 (s, 1H), 7.27~7.20 (m, 4H), 7.17~7.12 (m, 1H), 6.71 (d, *J*=8.2 Hz, 1H), 6.63~6.58 (m, 2H), 3.83 (s, 2H), 3.61 (s, 3H); NOESY (DMSO-*d*₆): NOE between phenolic-OH and only one aromatic CH, NOE between CH₂ of PMB with one aromatic CH and weak NOE between phenolic-OH and CH₂ of PMB, NOE between OCH₃ with one or two aromatic CHs.

3-Benzyl-4-methoxyphenol (**2aa** (m)):^[12b] Yield 7%, colorless liquid. ¹H NMR (DMSO-*d*₆) δ: 8.82 (s, 1H), 7.29~7.23 (m, 2H), 7.19~7.14 (m, 3H), 6.77 (d, *J*=8.7 Hz, 1H), 6.55 (dd, *J*=3.0, 8.7 Hz, 1H), 6.48 (d, *J*=3.0 Hz, 1H), 3.80 (s, 2H), 3.68 (s, 3H).

2-(4'-Methoxybenzyl)-4-methoxyphenol (**2ab**)^[12b] Yield 60%, colorless liquid. ¹H NMR (DMSO-*d*₆) δ: 8.86 (s, 1H), 7.15~7.11 (m, 2H), 6.84~6.79 (m, 2H), 6.72~6.67 (m, 1H), 6.61~6.55 (m, 2H), 3.75 (s, 2H), 3.70 (s, 3H), 3.61 (s, 3H). The signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (o) but not **2aa** (m).

2-Benzyl-phenol (**2ba** (o)):^[13b] Yield 60%, colorless liquid. ¹H NMR (DMSO-*d*₆) δ: 9.36 (s, 1H), 7.29~7.10 (m, 5H), 7.03~6.99 (m, 2H), 6.80 (dd, *J*=1.1, 7.3 Hz, 1H), 6.70 (td, *J*=1.1, 7.4 Hz, 1H), 3.85 (s, 2H).

4-Benzyl-phenol (**2ba** (p)):^[13b] Yield 17%, colorless liquid. ¹H NMR (DMSO-*d*₆) δ: 9.17 (s, 1H), 7.31~7.12 (m, 5H), 7.03~6.97 (m, 2H), 6.69~6.63 (m, 2H), 3.80 (s, 2H).

4-(4'-Methoxybenzyl)-phenol (**2bb**)^[14b] Yield 58%. White solid, m.p. 75~78 °C; ¹H NMR (DMSO-*d*₆) δ: 9.15 (s, 1H), 7.11~7.06 (m, 2H), 6.99~6.94 (m, 2H), 6.85~6.80 (m, 2H), 6.67~6.62 (m, 2H), 3.73 (s, 2H), 3.70 (s, 3H).

2-Benzyl-1,4-hydroquinone (**2ca**)^[15c] Yield 59%. White solid, m.p. 122~123 °C; ¹H NMR (DMSO-*d*₆) δ: 8.63 (s, 1H), 8.52 (s, 1H), 7.28~7.23 (m, 2H), 7.21~7.12 (m, 3H), 6.63~6.57 (m, 1H), 6.42~6.40 (m, 2H), 3.78 (s, 2H).

2-(4'-Methoxybenzyl)-1,4-hydroquinone (**2cb**)^[15c] Yield 48%. White solid, m.p. 133~135 °C; ¹H NMR (DMSO-*d*₆) δ: 8.60 (s, 1H), 8.50 (s, 1H), 7.12~7.08 (m, 2H), 6.84~6.79 (m, 2H), 6.57 (t, *J*=8 Hz, 1H), 6.40~6.34 (m,

2H), 3.70 (s, 5H).

2-Benzyl-4-acetoxyphenol (**2da**): Yield 60%. White solid, m.p. 100~102 °C; ¹H NMR (DMSO-*d*₆) δ: 9.51 (s, 1H), 7.29~7.19 (m, 4H), 7.19~7.13 (m, 1H), 6.80~6.74 (m, 3H), 3.84 (s, 2H), 2.18 (s, 3H). The signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (o) but not **2aa** (m). ¹³C NMR (DMSO-*d*₆) δ: 169.5, 152.5, 142.5, 140.7, 128.7, 128.2, 125.8, 123.0, 120.0, 115.1, 35.0, 20.7; ESI-HRMS calcd for C₁₅H₁₄NaO₃ [M+Na]⁺ 265.0841, found 265.0797.

2-(4'-Methoxybenzyl)-4-acetoxyphenol (**2db**): Yield 64%. White solid, m.p. 100~102 °C; ¹H NMR (DMSO-*d*₆) δ: 9.45 (s, 1H), 7.15~7.11 (m, 2H), 6.85~6.80 (m, 2H), 6.79~6.72 (m, 2H), 6.69 (d, *J*=2.6 Hz, 1H), 3.77 (s, 2H), 3.70 (s, 3H), 2.17 (s, 3H), the signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (o) but not **2aa** (m); ¹³C NMR (DMSO-*d*₆) δ: 169.5, 157.4, 152.4, 142.5, 132.5, 129.7, 128.8, 122.8, 119.9, 115.1, 113.7, 54.9, 34.1, 20.7; ESI-HRMS calcd for C₁₆H₁₆NaO₄ [M+Na]⁺ 295.0946, found 295.0953.

Ethyl 2-(3-benzyl-4-hydroxyphenoxy)acetate (**2ea**): Yield 75%. White solid, m.p. 89~90 °C; ¹H NMR (DMSO-*d*₆) δ: 8.99 (s, 1H), 7.30~7.10 (m, 5H), 6.70 (d, *J*=8.3 Hz, 1H), 6.65~6.55 (m, 2H), 4.57 (s, 2H), 4.11 (q, *J*=7.1 Hz, 2H), 3.82 (s, 2H), 1.17 (t, *J*=7.1 Hz, 3H), the signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (o) but not **2aa** (m); ¹³C NMR (DMSO-*d*₆) δ: 169.0, 150.4, 149.3, 140.9, 128.8, 128.7, 128.3, 128.1, 125.7, 116.8, 115.3, 112.7, 65.3, 60.4, 35.3, 14.0; ESI-HRMS calcd for C₁₇H₁₈NaO₄ [M+Na]⁺ 309.1103, found 309.1090.

Ethyl 2-(3-(4'-methoxybenzyl)-4-hydroxyphenoxy)acetate (**2eb**): Reaction temperature: 0 °C, reaction time: 5.5 h; yield 59%. White solid, m.p. 123~125 °C; ¹H NMR (DMSO-*d*₆) δ: 8.98 (s, 1H), 7.16~7.10 (m, 2H), 6.85~6.80 (m, 2H), 6.72~6.66 (m, 1H), 6.61~6.55 (m, 2H), 4.57 (s, 2H), 4.12 (q, *J*=7.1 Hz, 2H), 3.75 (s, 2H), 3.71 (s, 3H), 1.18 (t, *J*=7.1 Hz, 3H), the signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (o) but not **2aa** (m); ¹³C NMR (DMSO-*d*₆) δ: 169.0, 157.4, 150.3, 149.2, 132.8, 129.6, 129.4, 128.8, 116.6, 115.3, 113.6, 112.5, 65.3, 60.4, 55.3, 54.9, 34.4, 14.0; HRMS (ESI) calcd for C₁₈H₂₀NaO₅ [M+Na]⁺ 339.1208, found 339.1202.

Ethyl 3-benzyl-4-hydroxybenzoate (**2fa**):^[18b] Reaction temperature: 70 °C, reaction time: 26 h; yield 68%. White solid, m.p. 137~139 °C; ¹H NMR (DMSO-*d*₆) δ: 10.41 (s, 1H), 7.69~7.66 (m, 2H), 7.30~7.13 (m, 5H), 6.89 (d, *J*=8.2 Hz, 1H), 4.21 (q, *J*=7.1 Hz, 2H), 3.90 (s, 2H), 1.25 (t, *J*=7.1 Hz, 3H); ¹³C NMR (DMSO-*d*₆) δ: 165.6, 159.6, 140.6, 131.7, 129.2, 128.6, 128.3, 127.7, 125.8, 120.5, 114.9, 60.0, 34.9, 14.2.

Ethyl 3-(4'-methoxybenzyl)-4-hydroxybenzoate (**2fba**): Reaction temperature: 0 °C, reaction time: 5 h; yield 11%. White solid, m.p. 120~122 °C; ¹H NMR (DMSO-*d*₆) δ: 9.36 (s, 1H), 7.29~7.10 (m, 5H), 7.03~6.99 (m, 2H), 6.81~6.79 (m, 1H), 6.70 (td, *J*=1.1, 7.4 Hz, 1H), 3.85 (s,

2H); ¹³C NMR (DMSO-*d*₆) δ: 165.6, 159.5, 157.4, 132.4, 131.5, 129.6, 129.1, 128.2, 120.4, 114.8, 113.7, 60.0, 54.9, 34.0, 14.2; ESI-HRMS calcd for C₁₇H₁₈NaO₄ [M+Na]⁺ 309.1103, found 309.1053.

Ethyl 3,5-bis(4'-methoxybenzyl)-4-hydroxybenzoate (**2fbb**): Reaction temperature: 0 °C, reaction time: 5 h; yield 13%. White solid, m.p. 117~119 °C; ¹H NMR (DMSO-*d*₆) δ: 9.17 (s, 1H), 7.31~7.12 (m, 5H), 7.03~6.97 (m, 2H), 6.69~6.63 (m, 2H), 3.80 (s, 2H); ¹³C NMR (DMSO-*d*₆) δ: 165.6, 159.5, 157.3, 155.1, 132.7, 132.1, 131.5, 130.5, 129.4, 129.1, 129.0, 128.1, 127.4, 120.4, 114.8, 113.5, 110.7, 60.0, 55.3, 54.9, 14.2; HRMS (ESI) calcd for C₂₅H₂₆O₅Na [M+Na]⁺ 429.1678, found 429.1674.

2-Benzyl-4-cyano-phenol (**2ga**): Reaction temperature: 70 °C, reaction time: 46 h; yield 39%. White solid, m.p. 126~127 °C; ¹H NMR (DMSO-*d*₆) δ: 10.74 (s, 1H), 7.52~7.49 (m, 2H), 7.30~7.15 (m, 5H), 6.96~6.91 (m, 1H), 3.87 (s, 2H); ¹³C NMR (DMSO-*d*₆) δ: 159.4, 140.0, 134.2, 132.1, 129.2, 128.6, 128.3, 126.0, 119.6, 115.9, 100.9, 34.7; HRMS (ESI) calcd for C₁₄H₁₁NNaO [M+Na]⁺ 232.0738, found 232.0731.

2-Methoxy-4-nitro-6-benzyl-phenol (**2ja**): Reaction temperature: 70 °C, reaction time: 10 h; yield 20%. Yellow semi-solid; ¹H NMR (DMSO-*d*₆) δ: 10.39 (s, 1H), 7.71 (d, *J*=2.6 Hz, 1H), 7.67 (d, *J*=2.7 Hz, 1H), 7.31~7.16 (m, 5H), 3.97 (s, 2H), 3.92 (s, 3H); ¹³C NMR (DMSO-*d*₆) δ: 151.0, 147.1, 139.8, 139.0, 128.7, 128.4, 128.0, 126.1, 118.7, 105.1, 56.3, 34.8; HRMS (ESI) calcd for C₁₄H₁₄NO₄ [M+H]⁺ 260.0923, found 260.0918.

2-Methoxy-4-formyl-6-benzyl-phenol (**2ka**):^[23b] Reaction temperature: 25 °C, reaction time: 14 h; yield 45%, m.p. 89~91 °C; ¹H NMR (DMSO-*d*₆) δ: 10.50~9.70 (br s, 1H), 9.73 (s, 1H), 7.33~7.32 (m, 2H), 7.30~7.13 (m, 5H), 3.94 (s, 2H), 3.87 (s, 3H).

2-Methoxy-6-benzyl-phenol (**2la** (o)):^[24b] Reaction temperature: 70 °C, reaction time: 6 h; yield 22%. Colorless liquid. ¹H NMR (DMSO-*d*₆) δ: 9.26 (s, 1H), 7.27~7.13 (m, 5H), 6.81 (t, *J*=8.0 Hz, 1H), 6.71 (dd, *J*=2.0, 8.0 Hz, 1H), 6.58 (dd, *J*=2.0, 8.0 Hz, 1H), 3.87 (s, 2H), 3.62 (s, 3H).

2-Methoxy-5-benzyl-phenol (**2la** (m)):^[24c] Reaction temperature: 70 °C, reaction time: 6 h; yield 47%. Colorless liquid. ¹H NMR (DMSO-*d*₆) δ: 8.53 (s, 1H), 7.26~7.19 (m, 5H), 6.81 (dd, *J*=2.0, 4.0 Hz, 1H), 6.70~6.64 (m, 2H), 3.87 (s, 2H), 3.77 (s, 3H).

2-Benzyl-3-methoxy-phenol (**2ma** (o)):^[25a] Reaction temperature: 50 °C, reaction time: 22 h; yield 20%. Colorless liquid. ¹H NMR (DMSO-*d*₆) δ: 9.36 (s, 1H), 7.22~7.16 (m, 4H), 7.13~7.06 (m, 1H), 6.98 (t, *J*=8.2 Hz, 1H), 6.48 (d, *J*=10.1 Hz, 1H), 6.45 (d, *J*=10.1 Hz, 1H), 3.85 (s, 2H), 3.72 (s, 3H). Product **2ma** (o) has the identical ¹H NMR signal pattern of 3 aromatic C—Hs of phenolic moiety to the literature^[25a].

3-Methoxy-6-benzyl-phenol (**2ma** (o')):^[25b] Reaction temperature: 50 °C, reaction time: 22 h; yield 35%. Semi-solid. ¹H NMR (DMSO-*d*₆) δ: 9.40 (s, 1H), 7.26~

7.10 (m, 5H), 6.92 (d, $J=8.3$ Hz, 1H), 6.38 (s, 1H), 6.31 (dd, $J=2.5, 8.3$ Hz, 1H), 3.78 (s, 2H), 3.65 (s, 3H).

2-Benzyl-6-methyl-phenol (**2na** (o)).^[26b] Reaction temperature: 15 °C, reaction time: 15 h; yield 60%. Colorless liquid. ¹H NMR (DMSO- d_6) δ : 8.33 (s, 1H), 7.27~7.12 (m, 5H), 6.92 (d, $J=7.4$ Hz, 1H), 6.89~6.84 (m, 1H), 6.66 (t, $J=7.4$ Hz, 1H), 3.90 (s, 2H), 2.16 (s, 3H).

4-Benzyl-6-methyl-phenol (**2na** (p)).^[26c] Reaction temperature: 50 °C, reaction time: 15 h; yield 23%. Colorless liquid. ¹H NMR (DMSO- d_6) δ : 9.02 (s, 1H), 7.32~7.22 (m, 2H), 7.21~7.09 (m, 3H), 6.89 (s, 1H), 6.82 (d, $J=8.1$ Hz, 1H), 6.67 (d, $J=8.1$ Hz, 1H), 3.77 (s, 2H), 2.06 (s, 3H).

2-Benzyl-1-naphthol (**2oa**).^[27] Reaction temperature: 25 °C, reaction time: 19 h; yield 65% (based on 44% reacted compound **1oa**). White solid, m.p. 71~73 °C; ¹H NMR (DMSO- d_6) δ : 9.28 (s, 1H), 8.24~8.19 (m, 1H), 7.81~7.76 (m, 1H), 7.47~7.40 (m, 2H), 7.35 (d, $J=8.3$ Hz, 1H), 7.27~7.22 (m, 5H), 7.19~7.12 (m, 1H), 4.13 (s, 2H).

2-(4'-Methoxybenzyl)-1-naphthol (**2ob** (o)).^[27,28b] Reaction temperature: 25 °C, reaction time: 8 h; yield 38%. White solid, m.p. 80~82 °C; ¹H NMR (DMSO- d_6) δ : 9.25 (s, 1H), 8.22 (dd, $J=1.2, 7.9$ Hz, 1H), 7.77 (dd, $J=2.0, 7.3$ Hz, 1H), 7.47~7.39 (m, 2H), 7.34 (d, $J=8.3$ Hz, 1H), 7.21 (d, $J=8.4$ Hz, 1H), 7.19~7.14 (m, 2H), 6.85~6.80 (m, 2H), 4.07 (s, 2H), 3.69 (s, 3H).

4-(4'-Methoxybenzyl)-1-naphthol (**2ob** (p)). Reaction temperature: 25 °C, reaction time: 8 h; yield 30%, Yellow liquid. ¹H NMR (DMSO- d_6) δ : 9.98 (s, 1H), 8.18~8.11 (m, 1H), 7.90 (dd, $J=2.1, 7.2$ Hz, 1H), 7.45~7.38 (m, 2H), 7.17~7.08 (m, 3H), 6.82~6.78 (m, 3H), 4.21 (s, 2H), 3.68 (s, 3H); ¹³C NMR (DMSO- d_6) δ : 157.3, 152.0, 133.2, 132.4, 129.3, 127.4, 127.2, 126.0, 125.0, 124.2, 124.1, 122.5, 113.6, 107.4, 54.9, 36.9; ESI-HRMS calcd for C₁₈H₁₅O₂ [M-H]⁻ 263.1072, found 263.1079.

2-Benzyl-1-naphthol (**2pa**).^[29b] Reaction temperature: 100 °C (in toluene); reaction time: 48 h; yield 47%. White solid, m.p. 92~94 °C; ¹H NMR (DMSO- d_6) δ : 9.60 (br s, 1H), 7.85 (d, $J=8.0$ Hz, 1H), 7.78 (d, $J=8.0$ Hz, 1H), 7.70 (d, $J=8.0$ Hz, 1H), 7.50~7.30 (m, 1H), 7.15~7.30 (m, 6H), 7.12~7.05 (m, 1H), 4.35 (s, 2H).

2-(4'-Methoxybenzyl)-1-naphthol (**2pb**).^[29b] Reaction temperature: 15 °C, reaction time: 8 h; yield 58%. White solid, m.p. 118~119 °C; ¹H NMR (DMSO- d_6) δ : 9.71 (s, 1H), 7.84 (d, $J=8.5$ Hz, 1H), 7.76 (d, $J=8.0$ Hz, 1H), 7.68 (d, $J=8.8$ Hz, 1H), 7.39~7.33 (m, 1H), 7.25~7.21 (m, 2H), 7.12 (d, $J=8.6$ Hz, 2H), 6.76 (d, $J=8.6$ Hz, 2H), 4.26 (s, 2H), 3.65 (s, 3H).

2-Allyl-4-methoxyphenol (**2ac**).^[30b] Reaction temperature: 20 °C, reaction time: 17 h; yield 39%. Colorless liquid. ¹H NMR (DMSO- d_6) δ : 8.82 (s, 1H), 6.72~6.67 (m, 1H), 6.62~6.56 (m, 2H), 5.98~5.88 (m, 1H), 5.07~4.96 (m, 2H), 3.64 (s, 3H), 3.25~3.24 (m, 2H), the signal pattern of 3 aromatic C—Hs of phenolic moiety is identical to the reference^[37b] and similar to **2aa** (o) but not **2aa** (m).

3-(2'-Methoxybenzyl)-4-methoxyphenol (**2ad**): Reaction

temperature: 20 °C, reaction time: 8 h; yield 76%. Colorless liquid. ¹H NMR (DMSO- d_6) δ : 8.84 (s, 1H), 7.18 (td, $J=8.2, 1.7$ Hz, 1H), 6.98~6.93 (m, 2H), 6.83 (td, $J=0.8, 7.3$ Hz, 1H), 6.71 (d, $J=8.7$ Hz, 1H), 6.59 (dd, $J=8.7, 3.1$ Hz, 1H), 6.45 (d, $J=3.1$ Hz, 1H), 3.78 (s, 3H), 3.77 (s, 2H), 3.58 (s, 3H), the signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (m) but not **2aa** (o); ¹³C NMR (DMSO- d_6) δ : 157.0, 152.0, 149.0, 129.7, 128.4, 127.5, 127.1, 120.1, 116.0, 115.2, 111.4, 110.5, 55.2, 55.10, 29.4; ESI-HRMS calcd for C₁₅H₁₇O₃ [M+H]⁺ 245.1178, found 245.1166.

4-Methoxy-3-(naphthalen-2'-ylmethyl)phenol (**2ai**): Reaction temperature: 25 °C, reaction time: 12 h; yield 59%. White solid, m.p. 89~90 °C; ¹H NMR (DMSO- d_6) δ : 8.95 (s, 1H), 7.86~7.78 (m, 3H), 7.69 (s, 1H), 7.48~7.39 (m, 3H), 6.73 (d, $J=8.7$ Hz, 1H), 6.68 (d, $J=3.0$ Hz, 1H), 6.62 (dd, $J=8.7, 3.1$ Hz, 1H), 4.00 (s, 2H), 3.61 (s, 3H), the signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (m) but not **2aa** (o); ¹³C NMR (DMSO- d_6) δ : 152.1, 148.8, 138.8, 133.1, 131.5, 128.1, 127.7, 127.6, 127.4, 127.3, 126.4, 125.9, 125.2, 116.2, 115.5, 111.9, 55.2, 35.6; ESI-HRMS calcd for C₁₈H₁₆NaO₂ [M+Na]⁺ 287.1048, found 287.1060.

4-Methoxy-3-(naphthalen-1'-ylmethyl)phenol (**2aj**): Reaction temperature: 70 °C, reaction time: 6 h; yield 70%. Colorless liquid. ¹H NMR (DMSO- d_6) δ : 9.12 (s, 1H), 8.09~8.03 (m, 1H), 7.94~7.90 (m, 1H), 7.80 (d, $J=8.1$ Hz, 1H), 7.52~7.47 (m, 2H), 7.46~7.42 (m, 1H), 7.29 (d, $J=6.8$ Hz, 1H), 6.78 (d, $J=8.7$ Hz, 1H), 6.61 (dd, $J=3.1, 8.7$ Hz, 1H), 6.36 (d, $J=3.1$ Hz, 1H), 4.28 (s, 2H), 3.51 (s, 3H), the signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (m) but not **2aa** (o); ¹³C NMR (DMSO- d_6) δ : 152.0, 148.6, 136.8, 133.4, 131.6, 128.4, 127.5, 126.7, 126.6, 125.9, 125.6, 125.6, 124.1, 116.0, 115.4, 111.4, 55.0, 31.9; HRMS (ESI) calcd for C₁₈H₁₆NaO₂ [M+Na]⁺ 287.1048, found 287.1041.

4-Methoxy-2-(1'-phenylethyl)phenol (**2ak** (o)).^[33b] Reaction temperature: 25 °C, reaction time: 22 h; yield 25%. Colorless liquid. ¹H NMR (DMSO- d_6) δ : 8.80 (s, 1H), 7.29~7.12 (m, 5H), 6.76~6.74 (m, 1H), 6.54~6.52 (m, 2H), 4.42 (q, $J=7.2$ Hz, 1H), 3.65 (s, 3H), 1.46 (d, $J=7.3$ Hz, 3H), the signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (o) but not **2aa** (m). Product **2ak** (o) has the identical ¹H NMR signal pattern of 3 aromatic C—Hs of phenolic moiety to the literature^[33b].

4-Methoxy-3-(1'-phenylethyl)phenol (**2ak** (m)). Reaction temperature: 25 °C, reaction time: 22 h; yield 45%. Colorless liquid. ¹H NMR (DMSO- d_6) δ : 8.87 (s, 1H), 7.28~7.22 (m, 4H), 7.17~7.13 (m, 1H), 6.68 (d, $J=8.6$ Hz, 1H), 6.64 (d, $J=3.0$ Hz, 1H), 6.58 (dd, $J=3.1, 8.6$ Hz, 1H), 4.42 (q, $J=7.3$ Hz, 1H), 3.62 (s, 3H), 1.49 (d, $J=7.3$ Hz, 3H), the signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (m) but not **2aa** (o); ¹³C NMR (DMSO- d_6) δ : 152.1, 148.2, 146.1, 133.3, 128.0, 127.4, 125.6, 115.3, 113.6, 111.0, 55.2, 37.0, 20.5; HRMS (ESI) calcd for C₁₅H₁₆NaO₂ [M+Na]⁺ 251.1048, found 251.1041.

3-Benzhydryl-4-methoxyphenol (**2a**):^[34b] Reaction temperature: 15 °C, reaction time: 24 h; yield 16%. Colorless liquid. ¹H NMR (DMSO-*d*₆) δ: 8.99 (s, 1H), 7.30~7.26 (m, 4H), 7.21~7.17 (m, 2H), 7.10~6.96 (m, 4H), 6.73 (d, *J*=8.0 Hz, 1H), 6.65 (dd, *J*=4.0, 8.0 Hz, 1H), 6.25 (d, *J*=4.0 Hz, 1H), 5.77 (s, 1H), 3.55 (s, 3H), the signal pattern of 3 aromatic C—Hs of phenolic moiety is similar to **2aa** (m) but not **2aa** (o).

3,5-Dibenzhydryl-4-methoxyphenol (**2alb**): Reaction temperature: 15 °C, reaction time: 24 h; yield 23%. White solid, m.p. 146~148 °C; ¹H NMR (DMSO-*d*₆) δ: 8.88 (s, 1H), 7.31~7.27 (m, 8H), 7.21~7.17 (m, 4H), 7.10~7.08 (m, 4H), 7.04~7.02 (m, 4H), 6.38 (d, *J*=4.0 Hz, 2H), 5.74 (s, 2H); ¹³C NMR (DMSO-*d*₆) δ: 149.1, 148.1, 143.6, 143.6, 130.7, 129.0, 129.0, 128.4, 128.2, 128.2, 126.0, 126.0, 116.9, 113.4, 56.0, 49.3, 48.7; HRMS (ESI) calcd for C₃₃H₂₈NaO₂ [M+Na]⁺ 479.1987, found 479.1980.

Supporting Information Structures of bioactive diaryl-methanes; Structures of bioactive benzylated phenols; Structures of NOE effect in compound **1aa** (o); ¹H NMR and ¹³C NMR spectra of benzyl aryl ether compounds **1db**, **1eb**, **1hb**, **1ad**, **1af**, **1ag**, **1ai**; ¹H NMR and ¹³C NMR spectra of the rearranged products. The Supporting Information is available free of charge via the Internet at <http://sioc-journal.cn/>.

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