Copper(II)-catalyzed O-phenylation of alcohols with organobismuth(V) reagents

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Dedicated to Professor Atta-ur-Rahman on the occasion of his 65th birthday

Abstract

A convenient method for the Cu(II)-catalyzed O-phenylation of tertiary alcohols with organobismuth(V) compounds under mild conditions is described. Functionalized tertiary alcohols such as α-hydroxy carbonyl compounds were phenylated by using either $Ph_3Bi(OAc)_2$ or tetraphenylbismuth compounds. In the cases of O-phenylation of simple tertiary alcohols, the use of tetraphenylbismuth fluoride (Ph_4BiF) was particularly effective and gave various *tert*-alkyl phenyl ethers in high yields. The synthesis of alkyl phenyl ethers from primary and secondary alcohols are also described.

Keywords: Organobismuth reagent, *O*-phenylation, tertiary alcohol, copper catalysis, ether synthesis

Introduction

Aryl ethers are quite useful compounds in organic synthesis, whose synthetic methods have therefore been studied by many groups. Transition metal-catalyzed (Cu or Pd) coupling reactions between aryl halides and alcohols are often used in the synthesis of alkyl aryl ether. The Ullmann ether synthesis,[1] for example, has now become a classical method for the Cu-mediated etherification.[2] However, this method was not convenient since it needed harsh reaction conditions such as high temperatures, uses of strong bases and stoichiometric amounts of copper or copper salts, long reaction times and so on, besides yields of the product were moderate. Recently, Buchwald reported a coupling reaction between aryl halides and alcohols in the presence of a catalytic amount of CuI and 1,10-phenanthroline.[3] Despite various aryl halides

employed, there still needed refluxing conditions and long reaction times, and no tertiary alcohols were employed under the above conditions. On the other hand, Pd-catalyzed arylation was intensively studied by Hartwig[4] and Buchwald[5], and a coupling reaction of aryl halides and alcohols in the presence of bulky phosphine ligands was reported. Although tertiary alcohols employed in this reaction, there needed to use strongly basic alkoxides as nucleophiles. Furthermore, hardly any reactions of aryl halides that have strongly electron-donating substituents in the *ortho* or *para* positions took place.[6] Then, a cross-coupling reaction of alcohols with organometalloid reagents such as organo-Bi and -B compounds was an alternative approach to the synthesis of alkyl aryl ethers. Recently, Batey reported that coupling reactions of alcohols with potassium aryltrifluoroborate salts proceeded in the presence of catalytic amounts of $Cu(OAc)_2$ and 4-(dimethylamino)pyridine under essentially neutral conditions,[7] which is a modified protocol of Chan-Evans's method for the arylation of phenols using aryl boronic acids.[8] Although these Cu(II)-catalyzed *O*-arylation reactions were carried out effectively with primary or secondary alcohols, a similar etherification of sterically-hindered secondary alcohols such as (−)-menthol and tertiary alcohols did not proceed at all.

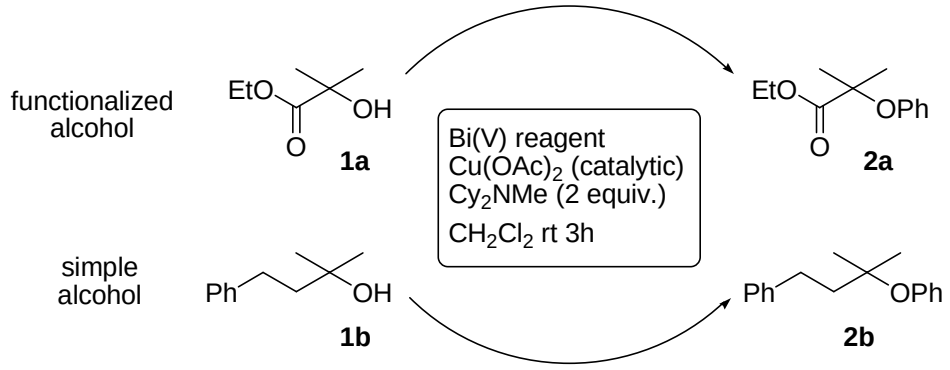
It is also known that organobismuth(V) reagents transfer their aryl groups to aliphatic alcohols in the presence of copper catalysts. Through the intensive studies on Bi-mediated arylation of alcohols during these decades,[9] Barton,[10] Finet,[11] and Dodonov[12] introduced useful methods for *O*-phenylation by using organobismuth compounds (1. combination with $Ph_3Bi(OAc)_2$ and catalytic amounts of $Cu(OAc)_2$, 2. Ph_3Bi and a stoichiometric amount of $Cu(OAc)_2$, 3. $Ph_4BiOCOCF_3$ in benzene or toluene under reflux.). Whereas the yields of primary and secondary alcohols were moderate, the yields of tertiary alcohols stayed low in these phenylation methods. Interestingly, it was reported that the reactivity of $Ph_4BiOCOCF_3$ and $Ph_3Bi(OAc)_2$ toward hydroxyl functions was greatly improved by the presence of a neighboring group such as hydroxyl, carbonyl, and sulfanyl.[13] It was reported that the chelating effect was utilized in *O*-arylation of hydroxyl groups of biologically-active natural products in Merck medicinal chemistry group.[14]

Very recently, *O*-phenylation of tertiary alcohols by using organobismuth(V) reagents was also reported from our laboratory.[15] Since effective C(aryl)−O bond formation of simple tertiary alcohols under mild conditions has not yet been developed, *O*-phenylation of simple tertiary alcohols using organobismuth(V) compounds under mild conditions was examined. Further, a reactivity difference between a functionalized alcohol and a simple alcohol was discussed.

Result and Discussion

The reactivity of the organobismuth(V) reagents was initially examined by using ethyl 2-hydroxy-2-methylpropionate (**1a**) as a model for a functionalized alcohol because of its chelating effect and 2-methyl-4-phenyl-butan-2-ol (**1b**) as a model for a simple alcohol. *O*-Phenylation of the alcohols was examined by using Bi reagents (1.6 equiv.) in the presence of catalytic amounts

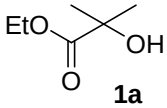
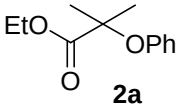
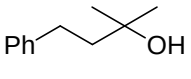
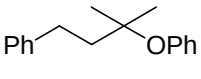
of copper salts and *N,N*-dicyclohexylmethylamine (Cy_2NMe) in CH_2Cl_2 at room temperature. The reactions were carried out without excluding moisture (Scheme 1), and the results are summarized in Table 1.



Scheme 1. *O*-phenylation of tertiary alcohol with organobismuth(V) compounds.

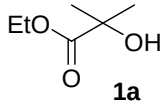
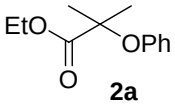
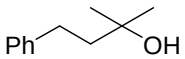
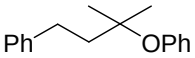
Concerning triphenyl bismuth reagents, functionalized alcohol **1a** was efficiently phenylated in 89 % yield when $Ph_3Bi(OAc)_2$ was used (Entry 1). This phenylation proceeded efficiently even when the $Cu(OAc)_2$ catalyst was reduced to 1 mol% (Entry 2). However, simple alcohol **1b** was not phenylated at all by using $Ph_3Bi(OAc)_2$ when the amount of $Cu(OAc)_2$ catalyst was increased even to 15 mol% and phenyl acetate was obtained as a major product under these conditions (Entries 15 and 16). Other triphenyl bismuth derivatives were less effective (Entries 3−8). On the other hand, most tetraphenyl bismuth reagents afforded **2a** in over 85% yield, yet the Ph_4BiOTs did not afford **2a** (Entries 9−13). Under these conditions, pentaphenylbisumuth gave mainly biphenyl (Entry 14). In the case of **1b**, the expected phenyl ether was not formed when tetraphenylbismuth complexes such as $[Ph_4Bi^+][BF_4^-]$ or $[Ph_4Bi^+][OTf^-]$ were employed (Entries 18 and 19). Instead, the desired phenyl ether was obtained in 6% or 54% yields, respectively, when the reaction was carried out in the presence of $Ph_4BiOCOCF_3$ or Ph_4BiF (Entries 17 and 20) though the reaction itself was sluggish by using 5 mol% of $Cu(OAc)_2$ (Entry 21). Although *O*-phenylation of both functionalized and simple alcohols took place efficiently when Ph_4BiF was used, other pentavalent bismuth(V) derivatives showed remarkable differences in their reactivity.

Table 1. Effect of organobismuth(V) reagents

Alcohol	Entry	Bi reagent	$Cu(OAc)_2$ (mol%)	Isolated yield (%)	
 **1a**	1	$Ph_3Bi(OAc)_2$	5	89	 **2a**
	2	$Ph_3Bi(OAc)_2$	1	79	
	3	$Ph_3Bi(OCOCF_3)_2$	5	5	
	4	$Ph_3Bi(OTs)_2$	5	ND	
	5	$Ph_3Bi(OMs)_2$	5	ND	
	6	Ph_3BiF_2	5	5	
	7	Ph_3BiCO_3	5	ND	
	8	Ph_3BiCl_2	5	ND	
	9	$Ph_4BiOCOCF_3$	5	85	
	10	Ph_4BiOTs	5	ND	
	11	$[Ph_4Bi^+][OTf^-]$	5	86	
	12	$[Ph_4Bi^+][BF_4^-]$	5	95	
	13	Ph_4BiF	5	93	
	14	Ph_5Bi	5	ND	
 **1b**	15	$Ph_3Bi(OAc)_2$	5	ND	 **2b**
	16	$Ph_3Bi(OAc)_2$	15	ND	
	17	$Ph_4BiOCOCF_3$	15	6	
	18	$[Ph_4Bi^+][OTf^-]$	15	ND	
	19	$[Ph_4Bi^+][BF_4^-]$	15	ND	
	20	Ph_4BiF	15	54	
	21	Ph_4BiF	5	3	

The effects of copper salts and solvents were examined next and the corresponding results are summarized in Table 2. Concerning **1a**, the reaction proceeded smoothly in methyl ethyl ketone (MEK), THF, CH_3CN and toluene while it proceeded sluggishly when DMF was used (Entries 1−5). With respect to copper salts, $Cu(OAc)_2$ was the most useful for the promotion of this reaction. On the other hand, CuOAc and other Cu(II) salts (CuF_2, $Cu(OCOCF_3)_2 \cdot xH_2O$ and $Cu(OTf)_2$) were less effective (Entries 6−9) and no reactions proceeded in the absence of a copper salt (Entry 10). In the case of **1b**, it was shown that the use of a non-polar solvent such as toluene gave the best result and **2b** was obtained in 84% yield (Entry 15) whereas the use of polar solvents such as MEK, THF, CH_3CN, DMF resulted in giving poor yields (Entries 11−14). When the amounts of Ph_4BiF and $Cu(OAc)_2$ increased to 2 equiv. and 20 mol%, respectively, **2b** was afforded in a quantitative yield (Entry 16). The effects of copper salts in toluene were then examined and $Cu(OCOCF_3)_2 \cdot xH_2O$ was found to give **2b** in 63 % yield (Entry 18) but CuOAc, $Cu(OTf)_2$ and CuF_2 were hardly effective (Entries 17, 19 and 20). Thus it was proved best to use of Ph_4BiF (2 equiv.), $Cu(OAc)_2$ (20 mol%) and Cy_2NMe (2 equiv.) in toluene for the phenylation of simple alcohol. Although *O*-phenylation of both functionalized and simple alcohols took place efficiently when $Cu(OAc)_2$ was used, remarkable reactivity differences were observed in the cases of using other copper salts.

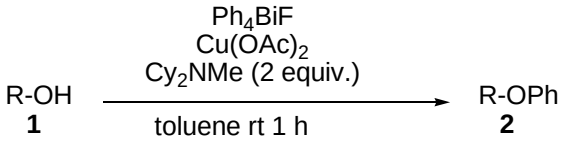
Table 2. Effect of copper salts and solvents

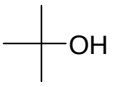
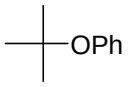
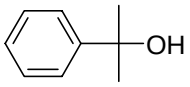
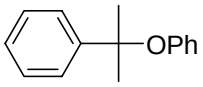
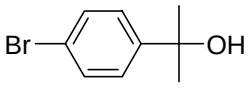
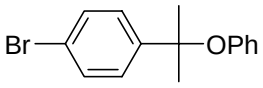
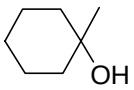
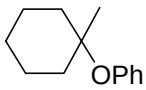
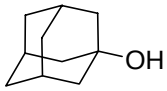
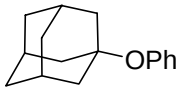
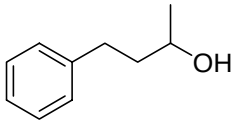
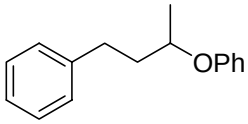
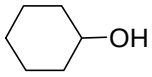
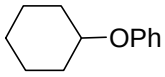
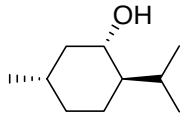
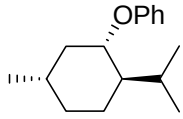
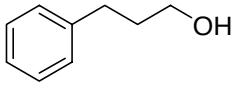
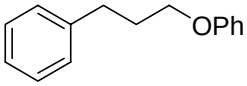
	Entry	Condition	Copper salt	Solvent	Isolated yield (%)	
 **1a**	1	A	$Cu(OAc)_2$	MEK	93	 **2a**
	2	A	$Cu(OAc)_2$	THF	91	
	3	A	$Cu(OAc)_2$	CH_3CN	82	
	4	A	$Cu(OAc)_2$	DMF	12	
	5	A	$Cu(OAc)_2$	toluene	94	
	6	A	CuOAc	CH_2Cl_2	71	
	7	A	$Cu(OCOCF_3)_2{\cdot}xH_2O$	CH_2Cl_2	60	
	8	A	$Cu(OTf)_2$	CH_2Cl_2	77	
	9	A	CuF_2	CH_2Cl_2	73	
	10	A	none	CH_2Cl_2	N.D.	
 **1b**	11	B	$Cu(OAc)_2$	MEK	59	 **2b**
	12	B	$Cu(OAc)_2$	THF	49	
	13	B	$Cu(OAc)_2$	CH_3CN	43	
	14	B	$Cu(OAc)_2$	DMF	22	
	15	B	$Cu(OAc)_2$	toluene	84	
	16	C	$Cu(OAc)_2$	toluene	quant.	
	17	B	CuOAc	toluene	trace	
	18	B	$Cu(OCOCF_3)_2{\cdot}xH_2O$	toluene	63	
	19	B	$Cu(OTf)_2$	toluene	N.R.	
	20	B	CuF_2	toluene	N.R.	

condition A: $[Ph_4Bi^+][BF_4^-]$ (1.6 equiv.) and Cu salts (5 mol%) were used.
condition B: Ph_4BiF (1.6 equiv.) and Cu salts (15 mol%) were used.
condition C: Ph_4BiF (2.0 equiv.) and Cu salts (20 mol%) were used.
ND: Not Detected

The *O*-phenylation reactions of simple tertiary alcohols (**1c**−**1k**) with Ph_4BiF under the above optimized conditions are shown in Table 3. The reactions of tertiary alcohols by using 2.0 equiv. of Ph_4BiF such as *t*-butanol (**1c**), 2-phenylpropan-2-ol (**1d**), 2-(4-bromophenyl)propan-2-ol (**1e**), 1-methylcyclohexanol (**1f**) and adamanthan-1-ol (**1g**) gave the corresponding phenyl ethers (**2c**−**2g**) in more than 86% yields. It is noted that the reaction of **1e** gave the phenyl ether **2e** in 86 % yield without affecting the *p*-bromophenyl moiety that was not used for the previously reported Pd- or Cu-catalyzed *O*-arylation. Additionally, secondary alcohols such as 4-phenylbutan-2-ol (**1h**), cyclohexanol (**1i**), (−)-menthol (**1j**) and a primary alcohol such as 4-phenylbutan-1-ol (**1k**) were phenylated efficiently to give the corresponding phenyl ethers in excellent yields without accompanying ketones or aldehydes formed by oxidation of alcohols with organobismuth(V) species.

Table 3. Phenylation of simple alcohols



Entry	Alcohol		Product		Isolated yield **2** (%)
1[a]	**1c**		**2c**		87
2[a]	**1d**		**2d**		86
3[a]	**1e**		**2e**		86
4[a]	**1f**		**2f**		87
5[a]	**1g**		**2g**		quant.
6[b]	**1h**		**2h**		93
7[b]	**1i**		**2i**		97
8[b]	**1j**		**2j**		91
9[b]	**1k**		**2k**		94

[a] Ph_4BiF (2 equiv.), $Cu(OAc)_2$ (20 mol%), and Cy_2NMe (2 equiv.) were used.
[b] Ph_4BiF (1.5 equiv.), $Cu(OAc)_2$ (15 mol%), and Cy_2NMe (2 equiv.) were used.

In conclusion, it is noted that a convenient method for the *O*-phenylation of simple tertiary alcohols by using a combination of Ph_4BiF and catalytic amounts of $Cu(OAc)_2$ under mild conditions was established. This method can be applied to the phenylation of various alcohols including primary and secondary alcohols. Further, remarkable reactivity differences were observed between the functionalized alcohol **1a** and the simple alcohol **1b** under the same phenylation conditions: that is, the alcohol **1a** was effectively phenylated by the use of

$Ph_3Bi(OAc)_2$, $[Ph_4Bi^+][BF_4^-]$, $[Ph_4Bi^+][OTf^-]$, $Ph_4BiOCOCF_3$, and Ph_4BiF. On the other hand, the simple alcohol **1b** was effectively phenylated only when Ph_4BiF was used as a phenyl donor. Thus, Ph_4BiF can be the reagent of choice for the formation of C(aryl)−O bond under mild conditions.

Experimental Section

General Procedures. Melting points were measured on a micro melting point apparatus (Yanaco MP-S3) and remain uncorrected. IR spectra were recorded on a Shimadzu IR-440 spectrophotometer (KBr or neat) or a Thermo Electron Nicolet Avatar 370 spectrometer (ATR). ^{1}H NMR spectra were recorded on a JEOL JNM-EX270 (270 MHz) spectrometer. Chemical shifts (δ_H) in $CDCl_3$ are reported in parts per million (ppm) relative to tetramethylsilane (TMS). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; m, multiplet; br, broad. ^{13}C NMR spectra were recorded on a JEOL JNM-EX270 (68 MHz) spectrometer with complete proton decoupling. Chemical shifts (δ_C) in $CDCl_3$ are reported in ppm relative to TMS using the solvent resonance ($CDCl_3$: δ_C 77.0 ppm) as an internal standard. HRMS spectra were recorded on a JEOL JMS-700V (EI positive) and Agilent 6890 series GC system. Analytical TLC was performed on Merck TLC plates coated with silica gel (60 F_{254}, 0.25 mm). Silica gel column chromatography was performed on Merck Silica gel 60 (0.063−0.200 mm). Preparative TLC was carried out on glass plates coated with silica gel (Wakogel B-5F). Anhydrous THF, DMF and CH_3CN were purchased from Kanto Chemical Co., Inc.. Other solvents were distilled after dehydrated by using appropriate drying agents. Alcohols and Cy_2NMe were purchased from Tokyo Kasei Kogyo. Copper(II) acetate was purchased from Kanto Chemical Co., Inc.. All reagents were purchased from Tokyo Kasei Kogyo, Kanto Chemical Co., Inc., Wako Pure Chemical Industry or Aldrich, and commercially-available reagents were used without purification.

Preparation of organobismuth(V) reagents

All organobismuth(V) derivatives such as triphenylbismuth diacetate ($Ph_3Bi(OAc)_2$),[16] triphenylbismuth bis(trifluoroacetate) ($Ph_3Bi(OCOCF_3)_2$),[16,17] triphenylbismuth di-*p*-toluenesulfonate ($Ph_3Bi(OTs)_2$),[17] triphenylbismuth dimesylate ($Ph_3Bi(OMs)_2$),[16,17] triphenylbismuth difluoride (Ph_3BiF_2),[18] triphenylbismuth carbonate (Ph_3BiCO_3),[17] triphenylbismuth dichloride (Ph_3BiCl_2),[18] tetraphenylbismuth trifluoroacetate ($Ph_4BiOCOCF_3$),[19] tetraphenylbismuth toluene-*p*-sulfonate (Ph_4BiOTs),[19] tetraphenylbismuthonium tetrafluoroborate ($[Ph_4Bi^+][BF_4^-]$,[20] tetraphenylbismuthonium trifluoromethansulfonate ($[Ph_4Bi^+][OTf^-]$),[17] tetraphenylbismuth fluoride (Ph_4BiF)[21] and pentaphenylbismuth (Ph_5Bi),[22] were prepared from triphenylbismuthane (Ph_3Bi) according to literature methods.[23]

Typical procedure for the *O*-phenylation of functionalized tertiary alcohol, ethyl 2-hydroxy-2-methylpropionate (1a). To a solution of the alcohol **1a** (39.6 mg, 0.30 mmol) and

$Cu(OAc)_2$ (2.7 mg, 0.015 mmol) in anhydrous CH_2Cl_2 (1.5 mL) was added Cy_2NMe (0.127 mL, 0.60 mmol) and the mixture was stirred at rt for 10 min. Tetraphenylbisumuth(V) bismuth trifluoroacetate ($(Ph_4BiOCOCF_3)$ 303 mg, 0.48 mmol) was then added and the resulted solution was allowed to react at rt for 3 h under air without excluding moisture. The reaction was quenched by the addition of 5% aq NH_3. The mixture was extracted with CH_2Cl_2 (3 times), and the combined organic layer was washed with brine and dried over Na_2SO_4. After concentration in vacuo, the residue was purified by preparative TLC on silica gel (hexane/AcOEt = 4/1) to afford the desired phenyl ether **2a** (53.0 mg, 0.25 mmol) in 85% yield.

Typical procedure for the *O*-phenylation of simple tertiary alcohol, 2-methyl-4-phenylbutan-2-ol (1b). To a solution of the alcohol **1b** (49.3 mg, 0.3 mmol) and Cy_2NMe (0.127 mL, 0.6 mmol) in toluene (1.5 mL) was added $Cu(OAc)_2$ (10.9 mg, 20 mol%) and the mixture was stirred at room temperature for 20 min. Then, Ph_4BiF (321.8 mg, 0.6 mmol) was added and the resulted solution was kept stirring at rt for 1 h. The reaction was carried out under air without excluding moisture. The reaction mixture was quenched with 5% aq. NH_3 and the resulted mixture was extracted with CH_2Cl_2 (3 times), and the combined organic layer was washed with brine and dried over Na_2SO_4. After concentration in vacuo, the residue was purified by preparative TLC on silica gel (hexane/CH_2Cl_2 = 1/1) to afford the desired phenyl ether **2b** (72.8 mg, 0.3 mmol) quantatively.

If a phenyl ether was not purified completely by using preparative TLC owing to difficulty of separation from Ph_3Bi generated by the above reaction, triphenylbismuthane contained in the residue should be decomposed selectively before the second purification by preparative TLC. In the case of **2e**, ca. 40 uL of SO_2Cl_2 was added dropwise to a CH_2Cl_2 solution of Ph_3Bi and **2e** at 0□ until residual Ph_3Bi disappeared, and then, **2e** was purified again by preparative TLC. In the case of **2i**, ca. 120 uL of trifluoroacetic acid was added dropwise to a CH_2Cl_2 solution of Ph_3Bi and **2i** until Ph_3Bi disappeared, and then, insoluble white precipitate was filtered off, and **2i** was purified again by preparative TLC.

2-(4-Bromophenyl)propan-2-ol (1e).[24] A solution of methylmagnesium bromide (1 mol/l in THF, 2.4 mL, 2.4 mmol) was added at 0□ to a solution of 4-bromo acetophenone (400 mg, 2 mmol) in Et_2O (4 mL). The resulting mixture was stirred at rt for 10 h. The reaction mixture was quenched with sat aq. NH_4Cl and the resulted mixture was extracted with Et_2O (3 times), and the combined organic layer was washed with brine and dried over $MgSO_4$ and concentrated under *vacuo*. The crude product was purified by column chromatography (silica gel, hexane/AcOEt = 5/1) to afford **1e** (264 mg, 61 %) as a pale yellow oil.: IR (ATR, cm^{-1}) 3372, 2975, 1483, 1395, 1364, 1167, 1093, 1008, 954, 859, 822, 731, 718; ^1H NMR (270 MHz, $CDCl_3$) δ = 7.45 (d, J = 8.6 Hz, 2H), 7.36 (d, 8.9 Hz, 2H), 1.57 (s, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 148.0, 131.1, 126.2, 120.4, 72.2, 31.7.

Ethyl 2-methyl-2-phenoxypropionate (2a).[15a] Colorless oil; IR (ATR, cm^{-1}) 1731, 1174, 1135, 751; ^1H NMR (270 MHz, $CDCl_3$) δ = 7.28−7.18 (m, 2H), 7.02−6.93 (m, 1H), 6.88−6.80 (m, 2H), 4.23 (q, J = 7.1 Hz, 2H), 1.59 (s, 6H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 174.1, 155.2, 129.0, 121.9, 118.9, 78.9, 61.4, 25.4, 14.1.

1,1-Dimethyl-3-phenylpropyl phenyl ether (2b). Colorless oil; IR (ATR, cm^{-1}) 2977, 1592, 1487, 1229, 1197, 1160, 887, 748, 695; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.31−7.15 (m, 7H), 7.09−6.99 (m, 3H), 2.86−2.80 (m, 2H), 2.00−1.93 (m, 2H), 1.35 (s, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 155.3, 142.4, 128.8, 128.3, 128.3, 125.6, 123.8, 123.1, 80.0, 44.2, 30.7, 26.8; Anal. Calcd for $C_{17}H_{20}O$: C, 84.95; H, 8.39. Found: C, 85.04; H, 8.19.

***tert*-Butyl phenyl ether (2c).**[6b] Colorless oil; IR (ATR, cm^{-1}) 2977, 1593, 1487, 1365, 1233, 1159, 925, 913, 887, 779, 695; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.29−7.23 (m, 2H), 7.10−7.04 (m, 1H), 7.01−6.97 (m, 2H), 1.35 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 155.3, 128.7, 124.1, 123.2, 78.3, 29.0.

1-Methyl-1-phenylethyl phenyl ether (2d).[25] Colorless oil; IR (ATR, cm^{-1}) 2982, 1597, 1489, 1228, 1144, 753, 695; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.50−7.46 (m, 2H), 7.38−7.25 (m, 3H), 7.13−7.07 (m, 2H), 6.90−6.84 (m, 1H), 6.68−6.64 (m, 2H), 1.70 (s, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 155.9, 146.6, 128.7, 128.3, 126.9, 125.2, 121.2, 120.2, 80.1, 29.5; Anal. Calcd for $C_{15}H_{20}O$: C, 84.87; H, 7.60. Found: C, 84.87; H, 7.74.

1-(4-Bromophenyl)-1-methylethyl phenyl ether (2e). Colorless oil; IR (ATR, cm^{-1}) 2980, 1593, 1486, 1226, 1145, 1093 1008, 822, 753, 693; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.47 (d, J = 8.9 Hz, 2H), 7.35 (d, 8.9 Hz, 2H), 7.15−7.09 (m, 2H), 6.92−6.87 (m, 1H), 6.67−6.63 (m, 2H), 1.67 (s, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 155.5, 145.7, 131.4, 128.7, 127.1, 121.5, 120.9, 120.2, 79.6, 29.4; HRMS (EI positive) Calcd for $C_{15}H_{15}{}^{79}BrO$: $[M+H]^+$ 290.0306. Found: *m*/*z* 290.0300.

1-Methylcyclohexyl phenyl ether (2f). Colorless oil; IR (ATR, cm^{-1}) 2930, 2858, 1592, 1491, 1221, 1154, 694; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.27−7.21 (m, 2H), 7.06−6.98 (m,3H), 1.92−1.71 (m, 4H), 1.53−1.34 (m, 6H), 1.25 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 155.3, 128.7, 123.7, 122.7, 79.6, 37.7, 26.2, 25.8, 22.7; HRMS (EI positive) Calcd for $C_{13}H_{18}O$: $[M+H]^+$ 190.1358. Found: *m*/*z* 190.1359.

1-Adamantyl phenyl ether (2g).[26] White solid; IR (ATR, cm^{-1}) 2906, 2854, 1486, 1213, 1055, 922, 904, 782, 700; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.28−7.22 (m, 2H), 7.11−7.05 (m,1H), 7.00−6.97 (m, 2H), 2.17 (bs, 3H), 1.87 (bs, 6H), 1.61 (bs, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 154.0, 128.5, 124.9, 123.5, 77.6, 42.9, 36.2, 31.0; HRMS (EI positive) Calcd for $C_{16}H_{20}O$: $[M+H]^+$ 228.1514. Found: *m*/*z* 228.1522.

1-Methyl-3-phenylpropyl phenyl ether (2h).[27] Colorless oil; IR (ATR, cm^{-1}) 2932, 1597, 1587, 1238, 748,692; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.29−7.15 (m, 7H), 6.94−6.84 (m, 3H), 4.41−4.30 (m, 1H), 2.86−2.66 (m, 2H), 2.14−2.01 (m, 1H), 1.94−1.81 (m, 1H), 1.32 (d, J = 6.2 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 158.0, 141.7, 129.3, 128.4, 128.3, 125.7, 120.5, 115.9, 72.8, 38.3, 31.9, 19.8.

Cyclohexyl phenyl ether (2i).[7] Colorless oil; IR (ATR, cm^{-1}) 2933, 2857, 1598, 1587, 1492, 1234, 1048, 963, 750, 690; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.28−7.22 (m, 2H), 6.92−6.87 (m, 3H), 4.27−4.18 (m, 1H), 2.00−1.75 (m, 4H), 1.58−1.26 (m, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 157.7, 129.3, 120.4, 116.0, 75.4, 32.0, 25.7, 23.9.

(1*S*, 2*R*, 5*S*)-2-Isopropyl-5-methylcyclohexyl phenyl ether (2j).[28] Colorless oil; IR (ATR, cm^{-1}) 2954, 2924, 2869, 1597, 1587, 1492, 1240, 1013, 750, 690; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.30−7.24 (m, 2H), 6.93−6.88 (m, 3H), 4.07−3.98 (m, 1H), 2.28−2.12 (m, 2H), 1.76−1.68 (m, 2H), 1.56−1.38 (m, 2H), 1.13−0.90 (m, 9H), 0.77 (d, J = 6.2 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 158.3, 129.4, 120.3, 115.8, 77.5, 48.2, 40.5, 34.7, 31.5, 26.2, 23.9, 22.2, 20.9, 16.7; HRMS (EI positive) Calcd for $C_{16}H_{24}O$: $[M+H]^+$ 232.1827. Found: m/z 232.1825.

Phenyl 3-phenylpropyl ether (2k).[7] Colorless oil; IR (ATR, cm^{-1}) 2942, 1599, 1587, 1495, 1470, 1242, 1037, 747, 691; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.32−7.16 (m, 7H), 6.96−6.87 (m, 3H), 3.96 (t, J = 6.5 Hz, 2H), 2.81 (t, J = 7.3 Hz, 2H), 2.16−2.05 (m, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ = 158.9, 141.4, 129.3, 128.4, 128.3, 125.8, 120.5, 114.5, 66.8, 32.2, 30.9.

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