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Palladium on carbon-diethylamine-mediated hydrodeoxygenation of phenol derivatives under mild conditions

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Abstract—We have found that phenolic hydroxyl groups were readily deoxygenated via aryl sulfonate under the Pd/C-catalyzed hydrogenation conditions in the presence of diethylamine and the method could also be applicable to the hydrodeoxygenation of morphine to afford 3-deoxy-7,8-dihydromorphine. Diethylamine is not only a scavenger of the corresponding methanesulfonic acid derivative, which is produced during the reaction progress, but also a strong promoter of the Pd/C-catalyzed reduction of aryl sulfonates. This catalyst system could provide a general method for the deoxygenation of various phenol derivatives because of its mild reaction conditions, ease of handling, and no need of particular apparatus.

1. Introduction

Many natural products containing phenol moieties isolated from plants, animals, and bacteria are known as biologically active compounds, such as antimicrobial essential oils[1] and antiallergic,[2] antitumor,[3] and antioxidant polyphenols.[4] Medicinal chemists have been strongly attracted to such natural products with phenolic hydroxyl groups, which play an important role in the biological activities. Therefore, a number of structure activity relationship studies on phenolic hydroxyl groups of the bioactive compounds have been carried out.[5] Deoxygenated derivatives of such phenolic hydroxyl groups containing bioactive compounds have also been of great interest for the biological studies. For the preparation of such deoxygenated derivatives, the conventional methods in the literature are categorized into the following two types: (1) the multistep synthetic methods starting from small synthons without phenolic hydroxyl groups and (2) the deoxygenation of phenolic hydroxyl groups in a direct manner[6] or through an activation of the hydroxyl groups as a leaving group based upon chemical modifications.[7–14] While the former multistep synthetic methods (1) have some problems in terms of time- and cost-efficiencies, the latter methods (2) would be highly efficient and practical.

Although some methods for the deoxygenation of phenolic hydroxyl groups were reported, they have some drawbacks from the aspect of practical utility and environmental concerns. Direct deoxygenation methods previously reported in the literature could only be applied to quite restricted phenol derivatives, because of the drastic reaction conditions and low yields.[6] Reductive cleavage methods of a phenolic hydroxyl group after converting to the corresponding leaving group, such as sulfonate,[7–9] isourea,[7,10] dimethylthiocarbamate,[7] aryl ether,[11] 5-phenyltetrazolyl ether,[12] and phosphate ester,[13] are known as deoxygenation methods of phenol derivatives. Nevertheless, these conventional methods still have some disadvantages: the lack of stability of the activated intermediates; the requirement of an environmentally harmful phosphine ligand and/or a vast amount of catalysts or hydride reducing agents. A Pd-catalyzed hydrogenative removal of phenolic hydroxyl groups using aryl mesylates in the presence of triethylamine, which was carried out under comparatively mild reaction conditions, was reported by Jensen and Clauss in 1973.[8b] However, the communication did not clarify the scope and limitation of their method. Moreover, according to our preliminary results the cleavage of the methanesulfonyloxy group was incomplete using their conditions. Therefore, developing a general, practical, and environmentally benign method for the deoxygenation of phenolic hydroxyl groups is still a subject of great importance in synthetic organic chemistry. We recently developed a Pd/C-catalyzed deoxygenation method of phenolic hydroxyl groups via aryl triflates or mesylates using Mg metal in MeOH under an argon atmosphere.[14] Although various types of aryl triflates could undergo deoxygenation using this method, hydrolysis of triflates to phenol was observed when electron-deficient aryl triflates were employed as a substrate. We also reported a facile and effective Pd/C-catalyzed hydrodehalogenation

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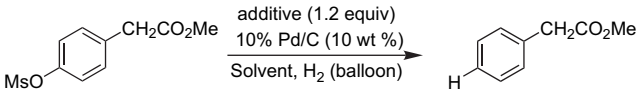
of aromatic halides in the presence of triethylamine,[15] and expected that the modification and optimization of the reaction conditions would make the dechlorination method applicable to the hydrodeoxygenation of aryl sulfonates. In this paper we describe a general method for the deoxygenation of phenolic hydroxyl groups by a simple and practical Pd/C-catalyzed hydrogenolysis of aryl sulfonates, together with the detailed mechanistic study.

2. Results and discussion

Initially, a Pd/C-catalyzed hydrogenolysis of methyl 4-methanesulfonyloxyphenylacetate (**1a**) was performed under an ordinary hydrogen pressure (balloon) using 10% Pd/C (10 wt % of **1a**) and 1.2 equiv of a nitrogen-containing base as an additive in a solvent at room temperature (Table 1). While the reductive cleavage of the methanesulfonyloxy group did not proceed without an additive (entry 1), the addition of ammonia or ethylamine completed the hydrogenolysis of **1a** in 21 or 22 h, respectively (entries 2 and 3). Furthermore, diethylamine dramatically affected the reactivity to complete the reduction within 4 h (entry 4). However, the addition of triethylamine was not effective as already mentioned in Section 1.[8b] The hydrogenolysis of mesylate (**1a**) could not be completed even after 48 h (entry 11). The addition of an aromatized heterocyclic base such as pyridine and quinoline did not lead to completion of the deoxygenation of **1a** (entries 12 and 13). According to these results, it was found that diethylamine was the most effective additive among the nitrogen-containing bases that we investigated. Further investigation using a variety of solvents revealed that the use of an alcoholic solvent, especially MeOH, was highly effective for the hydrogenolysis (entries 4–10). Based on these results, the optimum conditions for the deoxygenation of **1a** were determined as follows: treatment of **1a** with 10% Pd/C (10 wt % of **1a**) and 1.2 equiv of diethylamine at room temperature under an ordinary hydrogen pressure (balloon).

Table 1. Optimization of the reaction conditions[a]



1a **2a**

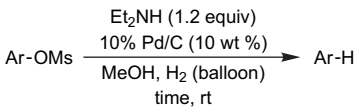
Entry	Additive	Solvent	Time (h)	**1a**:**2a**[b]
1	None	MeOH	48	100:0
2	NH_3	MeOH	21	0:100
3	$EtNH_2$	MeOH	22	0:100
4	*Et_2NH*	*MeOH*	*4*	*0:100*
5	Et_2NH	EtOH	32	3:97
6	Et_2NH	*i*-PrOH	24	0:100
7	Et_2NH	THF	48	32:68
8	Et_2NH	AcOEt	48	80:20
9	Et_2NH	DMF	48	19:81
10	Et_2NH	H_2O	48	68:32
11	Et_3N	MeOH	48	63:37
12	Pyridine	MeOH	48	23:77
13	Quinoline	MeOH	48	100:0

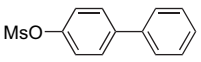
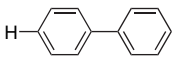
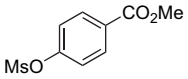
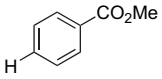
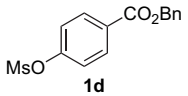
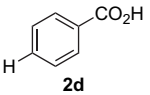
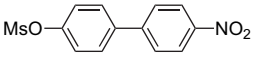
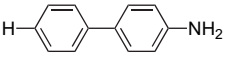
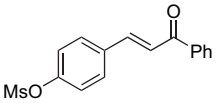
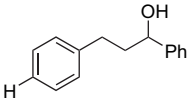
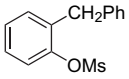
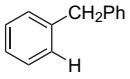
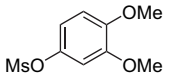
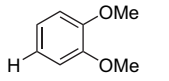
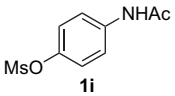
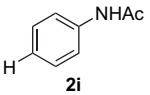
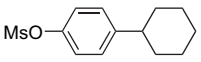
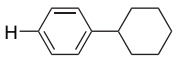
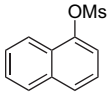
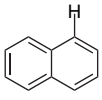
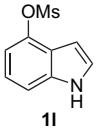
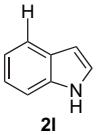
[a] The reaction was carried out using **1a** (244 mg, 1.00 mmol), 10% Pd/C (24.5 mg, 10 wt % of **1a**), and an additive (1.20 mmol) in a solvent (2 mL) under an ordinary hydrogen pressure (balloon) with vigorous stirring at room temperature (ca. 20 °C).

[b] The ratio was determined by ^1H NMR analysis.

To explore the scope and limitation of our method, the deoxygenation of a variety of phenol derivatives was examined (Table 2). Electron-deficient substrates were readily hydrogenolyzed under the conditions to obtain the corresponding arene products (entries 1–3 and 5). When a reducible

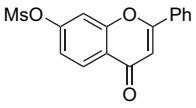
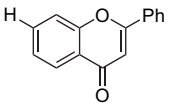
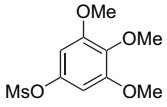
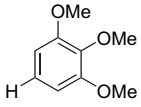
Table 2. Pd/C-catalyzed hydrogenolysis of various aryl mesylates[a]



Entry	Substrate	Product	Time (h)	Yield (%)[b]
1	 **1b**	 **2b**	18	92
2	 **1c**	 **2c**	20	95
3	 **1d**	 **2d**	19	91
4[c]	 **1e**	 **2e**	57	96
5	 **1f**	 **2f**	17	90
6[d]	 **1g**	 **2g**	24	94
7[e]	 **1h**	 **2h**	58	79
8[f]	 **1i**	 **2i**	129	82
9[g]	 **1j**	 **2j**	24	88[h]
10	 **1k**	 **2k**	31	91
11[e]	 **1l**	 **2l**	29	99

(*continued*)

Table 2. (*continued*)

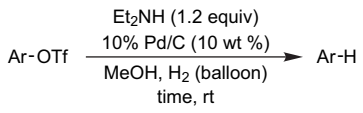
Entry	Substrate	Product	Time (h)	Yield (%)[b]
12[i]	 **1m**	 **2m**	24	71
13	 **1n**	 **2n**	48	Trace

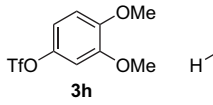
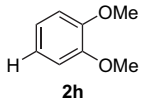
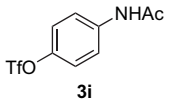
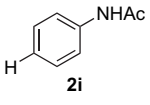
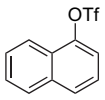
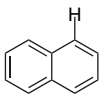
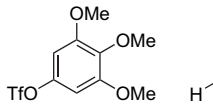
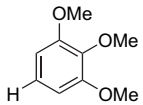
[a] Unless otherwise noted, the reaction was carried out using 1.0 mmol of the substrate in MeOH (2.0 mL) with 10% Pd/C (10 wt % of the substrate) and Et_2NH (1.2 mmol) with vigorous stirring at room temperature (ca. 20 °C) under an ordinary hydrogen pressure (balloon).
[b] Isolated yield.
[c] After 48 h, additional 10% Pd/C (10 wt % of the substrate) and 1.2 equiv of Et_2NH were added into the reaction mixture.
[d] The reaction was carried out in the presence of 15 wt % of 10% Pd/C and 1.5 equiv of Et_2NH.
[e] The reaction was carried out in the presence of 30 wt % of 10% Pd/C and 3.0 equiv of Et_2NH.
[f] The reaction was carried out in the presence of 15 wt % of 10% Pd/C and 1.5 equiv of Et_2NH and after 48 h, additional 10% Pd/C (10 wt % of the substrate) and 1.2 equiv of Et_2NH were added into the reaction mixture.
[g] The reaction was carried out in the presence of 10% Pd/C (20 wt % of the substrate) and 2.4 equiv of Et_2NH.
[h] Conversion yield determined by ^1H NMR.
[i] The reaction was carried out in the presence of 10% Pd/C (30 wt % of the substrate) and 3.6 equiv of Et_2NH.

functionality such as olefin, benzyl ester, nitro, or aromatic ketone was contained within the substrate, the reduction of such functionalities as well as hydrogenolysis of the mesyloxy group took place (entries 3–5). In the case of the substrate (**1e**) the reduction of the nitro group proceeded in preference to the mesyloxy group and the generated amine diminished the catalyst activity of Pd/C to prolong the reaction time since amines generally work as a catalyst poison for the Pd/C-catalyzed hydrogenolysis[16] (entry 4). While the introduction of electron-donating groups on the aromatic ring of the substrate decreased the reactivity, simple modification of the reaction conditions, such as increasing the amount of catalyst loading or an additive, achieved the complete deoxygenation of even electron sufficient substrates to obtain the desired arene products in good yields (entries 6–9). Moreover, naphthalene, indole, and flavone derivatives were also applicable (entries 10–12).

As a limitation, the introduction of three electron-donating methoxy groups on the benzene ring acutely reduced the reactivity of the substrate and no hydrogenolysis of the mesyloxy group of **1n** occurred even after any optimization of the reaction conditions (Table 2, entry 13). In order to apply our method to such highly electron sufficient phenol derivative, we examined the use of the corresponding aryl triflate (**3n**) in the place of aryl mesylate (**1n**). The Pd/C-catalyzed reductive cleavage of the trifluoromethanesulfonyloxy group of **3n** in the presence of diethylamine (1.2 equiv) under an ordinary hydrogen pressure gave the corresponding arene (**2n**) within 4 h in quantitative yield (Table 3, entry 4). It is noteworthy that the triflate was never hydrolyzed under the reaction conditions. The

Table 3. Pd/C-catalyzed hydrogenolysis of various aryl triflates[a]

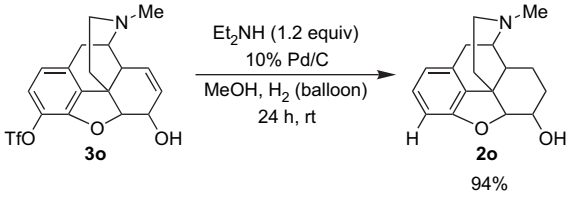


Entry	Substrate	Product	Time (h)	Yield (%)[b]
1	 **3h**	 **2h**	6	89
2	 **3i**	 **2i**	4.5	82
3	 **3k**	 **2k**	1	48[c]
4[c]	 **3n**	 **2n**	4	99

[a] Unless otherwise noted, the reaction was carried out using 1.0 mmol of the substrate in MeOH (2.0 mL) with 10% Pd/C (10 wt % of the substrate) and Et_2NH (1.2 mmol) with vigorous stirring at room temperature (ca. 20 °C) under an ordinary hydrogen pressure (balloon).
[b] Isolated yield.
[c] The low isolated yield of the product is due to the volatile nature.

hydrogenolyses of other aryl triflates were also proceeded smoothly (within 6 h) under these reaction conditions to give the corresponding arenes (Table 3).

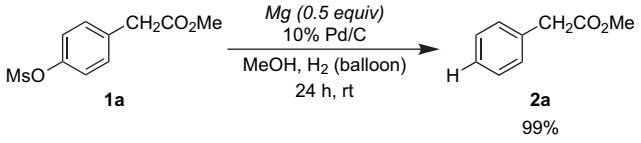
Further application of a triflate was investigated. The deoxygenation of a bioactive morphine derivative (**3o**) proceeded smoothly accompanying the hydrogenation of the olefin within the molecule of **3o** to afford 3-deoxy-7,8-dihydromorphine (**2o**) in excellent yield (Scheme 1). Eventually, it was revealed that our method is applicable to the deoxygenation of complicated biologically active substances.



Scheme 1. Hydrogenolysis of the morphine derivative (**3o**).

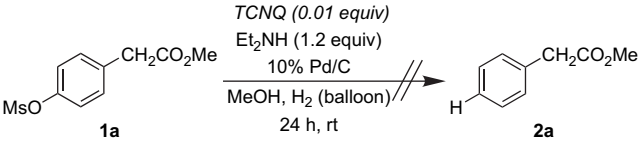
We next planned to clarify the reaction mechanism of the hydrogenolysis of aryl sulfonates. Since the reactivity significantly depended on the types of the amines used (Table 1), the additive may work not only as a scavenger of methanesulfonic or trifluoromethanesulfonic acid, which is generated as the reaction progresses, but also as a strong activator of the catalytic process. We assume that a single electron transfer (SET) from diethylamine as an additive

directly or indirectly (via Pd metal) to the substrate is the initial step in the catalytic cycle.[15a] The reaction also smoothly proceeded by the addition of Mg metal, which can be a single electron donor, in lieu of diethylamine (Scheme 2).



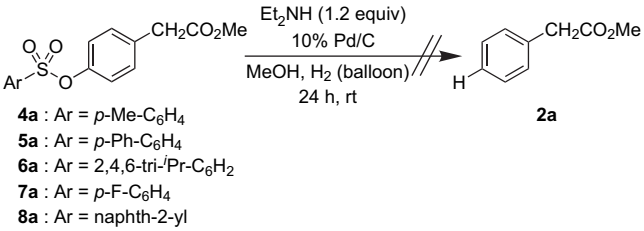
Scheme 2. Pd/C-catalyzed hydrogenolysis of **1a** promoted by Mg metal in lieu of Et_2NH.

On the other hand, the diethylamine-promoted hydrogenolysis of aryl mesylates was thoroughly suppressed by the addition of 0.01 equiv of TCNQ (7,7,8,8-tetracyanoquinodimethane) as a single electron capture to the reaction mixture (Scheme 3).



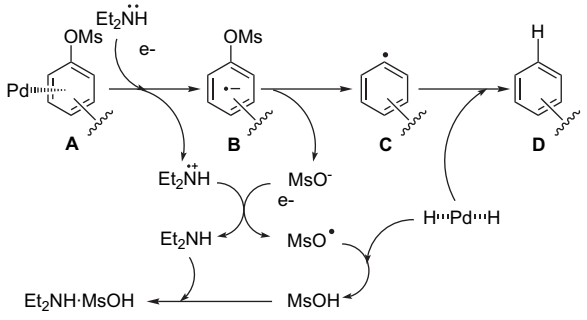
Scheme 3. Additive effect of a single electron capture.

Furthermore, when the arylsulfonyloxy derivatives (**4a**–**8a**) were used as substrates, the reductive cleavage of the arylsulfonyloxy groups did not proceed and the starting materials were entirely recovered (Scheme 4).



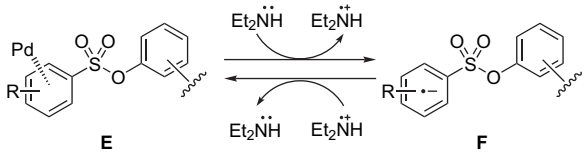
Scheme 4. Investigation of a variety of sulfonates under the hydrodeoxygenation conditions.

On the basis of these results, we speculated the reaction mechanism of this reaction as illustrated in Scheme 5. The reaction is initiated via an SET from diethylamine to the benzene ring of **A**, which is activated by coordination of Pd, to form an anion radical **B**. The subsequent elimination of the methanesulfonyl anion of **B** affords the corresponding phenyl radical **C** and then, the deoxygenated product **D** and a stoichiometric amount of diethylamine methanesulfonate is generated.[17]



Scheme 5. Plausible reaction mechanism of the reductive cleavage of aryl mesylates.

In the case of arylsulfonyloxy derivatives used as substrates, the hydrodeoxygenation would not proceed since an initial SET from diethylamine takes place exclusively toward the benzene ring of the arylsulfonyl group rather than of the phenolic moiety because of lower electron density of the former benzene ring (Scheme 6).



Scheme 6. Reaction mechanism in the case of aryl sulfonates.

3. Conclusion

We have developed a mild and an efficient method for the hydrodeoxygenation of phenolic hydroxyl groups via a methanesulfonyloxy or trifluoromethanesulfonyloxy functionality under the Pd/C-catalyzed hydrogenation conditions in the presence of diethylamine. The reaction is likely to involve an SET mechanism from diethylamine to the aromatic ring of aryl mesylates or aryl triflates. All reagents for the hydrogenation are commercially available and this method is very simple, widely applicable, and environmentally benign (e.g., heterogeneous catalyst and ligandless). Present efforts would contribute to a wide variety of synthetic organic chemistry fields including process chemistry as well as medicinal chemistry.

4. Experimental

4.1. General

10% Pd/C was purchased from Aldrich (catalog no. 205699). MeOH, *i*-PrOH, and distilled water for HPLC, dehydrated AcOEt and dehydrated DMF were purchased from Wako Pure Chemical Industries, Ltd. and used without purification. THF and CH_2Cl_2 were distilled from sodium benzophenone ketyl and calcium hydride, respectively. All other reagents were purchased from commercial sources and used without further purification. Flash column chromatography was performed with silica gel Merck 60 (230–400 mesh ASTM), or Kanto Chemical Co., Inc. 60N (63–210 μm spherical, neutral). ^1H NMR and ^{13}C NMR spectra were recorded on a JEOL AL 400 spectrometer or JEOL EX 400 spectrometer (400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR). Chemical shifts (δ) are expressed in parts per million and are internally referenced (0.00 ppm for TMS and $CDCl_3$ and 2.49 ppm for DMSO-d_6 for ^1H NMR and 77.0 ppm for $CDCl_3$ and 39.5 ppm for DMSO-d_6 for ^{13}C NMR). Elemental analyses were performed by a YANAKO CHN CORDER MT-5 instrument. EI and FAB mass spectra were taken on a JEOL JMS-SX102A instrument.

4.2. General procedure for the synthesis of aryl mesylates

To a solution of a phenol (10.0 mmol) and triethylamine (1.67 mL, 12.0 mmol) in dichloromethane, THF or DMF (20 mL) was added dropwise methanesulfonyl chloride (0.929 mL, 12.0 mmol) and the mixture was stirred at ambient temperature. After a certain reaction time the volatile was concentrated under reduced pressure. The residue was extracted with ethyl acetate (20 mL) and water (20 mL). The organic layer was washed with saturated aqueous sodium hydrogen carbonate solution (20 mL), 10% aqueous sodium hydrogen sulfonate solution (20 mL), and brine (20 mL), dried over $MgSO_4$, and concentrated under reduced pressure. If necessary, the residue was purified by flash column chromatography on silica gel or recrystallization.

4.2.1. Methyl 4-methanesulfonyloxyphenylacetate (1a). Obtained from methyl 4-hydroxyphenylacetate (1.66 g, 10.0 mmol), triethylamine (1.67 mL, 12.0 mmol), and methanesulfonyl chloride (0.929 mL, 12.0 mmol) according to the general procedure for the synthesis of aryl mesylates after 1 h of the reaction without any purification, in 94% yield (2.29 g) as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.32 (d, 2H, J=8.6 Hz), 7.23 (d, 2H, J=8.6 Hz), 3.69 (s, 3H), 3.62 (s, 2H), 3.12 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.4, 148.3, 133.4, 131.0, 122.1, 52.2, 40.4, 37.3; MS (EI) m/z 244 (M^+, 85), 185 (75), 166 (42), 107 (100), 78 (34), 44 (30); HRMS (EI) Calcd for $C_{10}H_{12}O_5S$ (M^+): 244.0405. Found: 244.0396. Anal. Calcd for $C_{10}H_{12}O_5S$: C, 49.17; H, 4.95. Found: C, 49.08; H, 4.99.

4.2.2. 4-Methanesulfonyloxybiphenyl (1b). Obtained from 4-hydroxybiphenyl (1.70 g, 10.0 mmol), triethylamine (1.67 mL, 12.0 mmol), and methanesulfonyl chloride (0.929 mL, 12.0 mmol) according to the general procedure for the synthesis of aryl mesylates after 19 h of the reaction followed by recrystallization (ethyl acetate/n-hexane) in 63% yield (1.57 g) as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.62 (d, 2H, J=8.8 Hz), 7.55 (d, 2H, J=7.3 Hz), 7.45 (d, 2H, J=7.3 Hz), 7.39–7.35 (m, 3H), 2.97 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 148.5, 140.6, 139.7, 128.9, 128.7, 127.7, 127.1, 122.3, 37.3; MS (EI) m/z 248 (M^+, 43), 169 (100), 141 (45), 115 (28); HRMS (EI) Calcd for $C_{13}H_{12}O_3S$ (M^+): 248.0507. Found: 248.0500. Anal. Calcd for $C_{13}H_{12}O_3S$: C, 62.88; H, 4.87. Found: C, 62.79; H, 4.93.

4.2.3. Methyl 4-methanesulfonyloxybenzoate (1c).[18] Obtained from methyl 4-hydroxybenzoate (1.52 g, 10.0 mmol), triethylamine (1.67 mL, 12.0 mmol), and methanesulfonyl chloride (0.929 mL, 12.0 mmol) according to the general procedure for the synthesis of aryl mesylates after 20 h of the reaction followed by flash column chromatography on silica gel (n-hexane) in 94% yield (2.17 g) as a colorless solid. ^{1}H NMR spectrum of **1c** was identical with that in the literature.[18]

4.2.4. Benzyl 4-methanesulfonyloxybenzoate (1d). Obtained from benzyl 4-hydroxybenzoate (2.28 g, 10.0 mmol), triethylamine (1.67 mL, 12.0 mmol), and methanesulfonyl chloride (0.929 mL, 12.0 mmol) according to the general procedure for the synthesis of aryl mesylates after 1.5 h of the reaction without any purification, in 99% yield (3.05 g) as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 8.14 (d, 2H, J=8.8 Hz), 7.44–7.34 (m, 7H), 5.37 (s, 2H), 3.17 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.4, 152.4, 135.6, 131.7, 129.1, 128.6, 128.3, 128.1, 121.8, 66.9, 37.7; MS (EI) m/z 306 (M^+, 27), 199 (100), 121 (25), 91 (53); HRMS (EI) Calcd for $C_{15}H_{14}O_5S$ (M^+): 306.0562. Found: 306.0552. Anal. Calcd for $C_{15}H_{14}O_5S$: C, 58.81; H, 4.61. Found: C, 58.79; H, 4.54.

4.2.5. 4-Methanesulfonyloxy-4′-nitrobiphenyl (1e). Obtained from 4-hydroxy-4′-nitrobiphenyl (645 mg, 3.00 mmol), triethylamine (0.502 mL, 3.60 mmol), and methanesulfonyl chloride (0.279 mL, 3.60 mmol) according to the general procedure for the synthesis of aryl mesylates after 1.5 h of the reaction without any purification, in 100% yield (879 mg) as a yellow solid. ^{1}H NMR ($CDCl_3$) δ 8.32 (dd, 2H, J=2.0 and 6.7 Hz), 7.72–7.66 (m, 4H), 7.43 (dd, 2H, J=2.0 and 6.7 Hz), 3.21 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 149.5, 147.3, 146.0, 138.1, 129.1, 127.8, 124.2, 122.8, 37.6; MS (EI) m/z 293 (M^+, 70), 214 (100), 184 (17), 156 (29), 139 (59), 128 (23); HRMS (EI) Calcd for $C_{13}H_{11}NO_5S$ (M^+): 293.0358. Found: 293.0364. Anal. Calcd for $C_{13}H_{11}NO_5S$: C, 53.24; H, 3.78; N, 4.78. Found: C, 53.17; H, 3.79; N, 4.65.

4.2.6. (*E*)-3-(4-Methanesulfonyloxyphenyl)-1-phenyl-2-propen-1-one (1f). Obtained from 4-hydroxychalcone (2.25 g, 10.0 mmol), triethylamine (1.67 mL, 12.0 mmol), and methanesulfonyl chloride (0.929 mL, 12.0 mmol) according to the general procedure for the synthesis of aryl mesylates after 1 h of the reaction followed by recrystallization (ethyl acetate–/n-hexane) in 71% yield (2.10 g) as a yellow solid. ^{1}H NMR ($CDCl_3$) δ 8.01 (d, 2H, J=8.8 Hz), 7.79 (d, 1H, J=15.6 Hz), 7.70 (d, 2H, J=8.3 Hz), 7.61 (t, 1H, J=7.3 Hz), 7.54–7.49 (m, 3H), 7.35 (d, 2H, J=8.8 Hz), 3.19 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 190.1, 150.3, 142.8, 137.9, 134.1, 133.0, 130.0, 129.0, 128.8, 128.7, 128.5, 123.1, 122.6, 37.6; MS (EI) m/z 302 (M^+, 32), 223 (100), 195 (23), 167 (24); HRMS (EI) Calcd for $C_{16}H_{14}O_4S$ (M^+): 302.0613. Found: 302.0603. Anal. Calcd for $C_{16}H_{14}O_4S$: C, 63.56; H, 4.67. Found: C, 63.42; H, 4.63.

4.2.7. 2-Benzylphenyl methanesulfonate (1g). Obtained from 2-benzylphenol (1.84 g, 10.0 mmol), triethylamine (1.67 mL, 12.0 mmol), and methanesulfonyl chloride (0.929 mL, 12.0 mmol) according to the general procedure for the synthesis of aryl mesylates after 2 h of the reaction followed by flash column chromatography on silica gel (n-hexane/Et_2O=10/1) in 96% yield (2.51 g) as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.39 (d, 1H, J=7.8 Hz), 7.31–7.18 (m, 8H), 4.08 (s, 2H), 2.97 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 147.6, 139.5, 133.8, 131.6, 128.9, 128.5, 127.8, 127.2, 126.3, 121.7, 37.7, 36.2; MS (EI) m/z 262 (M^+, 52), 183 (100), 181 (85), 165 (50); HRMS (EI) Calcd for $C_{14}H_{14}O_3S$ (M^+): 262.0664. Found: 262.0670; Anal. Calcd for $C_{14}H_{14}O_3S$: C, 64.10; H, 5.38. Found: C, 64.00; H, 5.49.

4.2.8. 3,4-Dimethoxyphenyl methanesulfonate (1h). Obtained from 3,4-dimethoxyphenol (771 mg, 5.00 mmol), triethylamine (0.836 mL, 6.00 mmol), and methanesulfonyl chloride (0.465 mL, 6.00 mmol) according to the general procedure for the synthesis of aryl mesylates after 1.5 h of

the reaction followed by flash column chromatography on silica gel (*n*-hexane/Et_2O=10/1→2/1) in 77% yield (892 mg) as a colorless solid. ^1H NMR ($CDCl_3$) δ 6.84 (m, 3H), 3.89 (s, 3H), 3.14 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 149.6, 148.1, 142.7, 113.3, 111.1, 106.2, 56.2, 37.0; MS (EI) *m/z* 232 (M^+, 28), 153 (100), 125 (32), 110 (15); HRMS (EI) Calcd for $C_9H_{12}O_5S$ (M^+): 232.0405. Found: 232.0400. Anal. Calcd for $C_9H_{12}O_5S$: C, 46.54; H, 5.21. Found: C, 46.40; H, 5.24.

4.2.9. 4-Acetamidophenyl methanesulfonate (1i). Obtained from 4-acetamidophenol (1.51 g, 10.0 mmol), triethylamine (1.67 mL, 12.0 mmol), and methanesulfonyl chloride (0.929 mL, 12.0 mmol) according to the general procedure for the synthesis of aryl mesylates after 72 h of the reaction followed by flash column chromatography on silica gel ($CHCl_3$ only →$CHCl_3$/MeOH=100/1) in 69% yield (1.59 g) as a colorless solid. ^1H NMR (DMSO-d_6) δ 10.09 (br s, 1H), 7.64 (d, 2H, *J*=9.3 Hz), 7.27 (d, 2H, *J*=9.3 Hz), 3.33 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 168.6, 144.3, 138.6, 122.7, 120.3, 37.3, 24.1; MS (EI) *m/z* 229 (M^+, 24), 150 (18), 108 (100), 80 (10); HRMS (EI) Calcd for $C_9H_{11}NO_4S$ (M^+): 229.0409. Found: 229.0412. Anal. Calcd for $C_9H_{11}NO_4S$: C, 47.15; H, 4.84; N, 6.11. Found: C, 46.98; H, 6.05; N, 6.05.

4.2.10. 4-Cyclohexylphenylmethanesulfonate (1j). Obtained from 4-cyclohexylphenol (881 mg, 5.00 mmol), triethylamine (0.836 mL, 6.00 mmol), and methanesulfonyl chloride (0.465 mL, 6.00 mmol) according to the general procedure for the synthesis of aryl mesylates after 1 h of the reaction followed by flash column chromatography on silica gel (*n*-hexane) in 99% yield (1.26 g) as a colorless solid. ^1H NMR ($CDCl_3$) δ 7.24 (d, 2H, *J*=8.5 Hz), 7.19 (d, 2H, *J*=8.5 Hz), 3.12 (s, 3H), 2.55–2.48 (m, 1H), 1.90–1.85 (m, 4H), 1.79–1.73 (m, 1H), 1.45–1.32 (m, 4H), 1.30–1.22 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 147.5, 147.2, 128.3, 121.7, 44.0, 37.2, 34.4, 26.8, 26.0; MS (EI) *m/z* 254 (M^+, 100), 198 (20), 175 (32), 131 (20), 119 (38), 107 (33), 84 (23); HRMS (EI) Calcd for $C_{13}H_{18}O_3S$ (M^+): 254.0977. Found: 254.0986. Anal. Calcd for $C_{13}H_{18}O_3S$: C, 61.39; H, 7.13. Found: C, 61.22; H, 7.07.

4.2.11. 1-Naphthyl methanesulfonate (1k). Obtained from 1-naphthol (1.44 g, 10.0 mmol), triethylamine (1.67 mL, 12.0 mmol), and methanesulfonyl chloride (0.929 mL, 12.0 mmol) according to the general procedure for the synthesis of aryl mesylates after 2 h of the reaction followed by flash column chromatography on silica gel (*n*-hexane/Et_2O=5/1) in 97% yield (2.16 g) as a colorless oil. ^1H NMR ($CDCl_3$) δ 8.14 (d, 1H, *J*=8.8 Hz), 7.90 (d, 1H, *J*=7.3 Hz), 7.82 (d, 1H, *J*=8.3 Hz), 7.62–7.46 (m, 4H), 6.21 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 145.2, 134.8, 128.0, 127.3, 127.2, 126.9, 125.3, 121.4, 118.3, 37.8; MS (EI) *m/z* 222 (M^+, 30), 143 (75), 115 (100); HRMS (EI) Calcd for $C_{11}H_{10}O_3S$ (M^+): 222.0351. Found: 222.0358.

4.2.12. 4-Methanesulfonyloxyindole (1l). Obtained from 4-hydroxyindole (1.33 g, 10.0 mmol), triethylamine (1.67 mL, 12.0 mmol), and methanesulfonyl chloride (0.929 mL, 12.0 mmol) according to the general procedure for the synthesis of aryl mesylates after 1 h of the reaction followed by flash column chromatography on silica gel (*n*-hexane/Et_2O=20/1→1/1) in 49% yield (1.04 g) as a colorless solid. ^1H NMR ($CDCl_3$) δ 8.35 (br s, 1H), 7.36 (d, 1H, *J*=8.3 Hz), 7.25 (d, 1H, *J*=2.9 Hz), 7.19 (t, 1H, *J*=8.1 Hz), 7.10 (d, 1H, *J*=7.8 Hz), 6.68 (br s, 1H), 3.17 (s, 3H), 2.04 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 142.1, 138.0, 125.4, 122.2, 121.6, 112.7, 110.6, 99.5, 37.5; MS (EI) *m/z* 211 (M^+, 39), 132 (100), 104 (43), 84 (15); HRMS (EI) Calcd for $C_9H_9NO_3S$ (M^+): 211.0303. Found: 211.0294. Anal. Calcd for $C_9H_9NO_3S$: C, 51.17; H, 4.29; N, 6.63. Found: C, 51.39; H, 4.36; N, 6.53.

4.2.13. 7-Methanesulfonyloxyflavone (1m). Obtained from 7-hydroxyflavone (1.20 g, 5.00 mmol), triethylamine (0.836 mL, 6.00 mmol), and methanesulfonyl chloride (0.465 mL, 6.00 mmol) according to the general procedure for the synthesis of aryl mesylates after 24 h of the reaction followed by flash column chromatography on silica gel ($CHCl_3$/MeOH=100/1) in 65% yield (1.02 g) as a colorless solid. ^1H NMR ($CDCl_3$) δ 8.30 (d, 1H, *J*=8.8 Hz), 7.92 (dd, 2H, *J*=2.0 and 8.4 Hz), 7.60–7.53 (m, 4H), 7.32 (dd, 1H, *J*=2.0 and 8.4 Hz), 6.84 (s, 1H), 3.27 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 177.2, 164.0, 156.6, 131.9, 131.2, 129.1, 127.9, 126.3, 122.8, 119.2, 111.7, 107.8, 38.1; MS (EI) *m/z* 316 (M^+, 100), 238 (33), 209 (90); HRMS (EI) Calcd for $C_{16}H_{12}O_5S$ (M^+): 316.0405. Found: 316.0413.

4.2.14. 3,4,5-Trimethoxyphenyl methanesulfonate (1n). Obtained from 3,4,5-trimethoxyphenol (1.84 g, 10.0 mmol), triethylamine (1.67 mL, 12.0 mmol), and methanesulfonyl chloride (0.929 mL, 12.0 mmol) according to the general procedure for the synthesis of aryl mesylates after 19 h of the reaction followed by recrystallization (ethyl acetate/*n*-hexane) in 96% yield (2.52 g) as a colorless solid. ^1H NMR ($CDCl_3$) δ 6.53 (s, 2H), 3.86 (s, 6H), 3.83 (s, 3H), 3.16 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 153.6, 144.9, 136.9, 99.4, 60.8, 56.2, 37.2; MS (EI) *m/z* 262 (M^+, 32), 183 (100), 168 (27), 155 (16), 125 (11), 69 (13); HRMS (EI) Calcd for $C_{10}H_{14}O_5S$ (M^+): 262.0511. Found: 262.0516. Anal. Calcd for $C_{10}H_{14}O_5S$: C, 45.79; H, 5.38. Found: C, 45.63; H, 5.39.

4.3. General procedure of the hydrodeoxygenation of 1a (Table 1)

After two vacuum/H_2 cycles to replace air inside the reaction tube with hydrogen, a mixture of **1a** (244 mg, 1.00 mmol), 10% Pd/C (24.5 mg, 10 wt % of **1a**), and an additive (1.20 mmol) in a solvent (2.0 mL) was vigorously stirred at room temperature (ca. 20 °C) under an ordinary hydrogen pressure (balloon). After a certain reaction time the reaction mixture was filtered using a membrane filter (Millipore, Millex®-LH, 0.45 μm) and the filtrate was partitioned between Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (10 mL×3) and the combined organic layers were washed with brine (10 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford a mixture of **1a** and **2a**. The ratio of **1a** and **2a** was determined by ^1H NMR analysis.

4.3.1. Methyl phenylacetate (2a). Obtained from **1a** (244 mg, 1.00 mmol), 10% Pd/C (24.5 mg, 10 wt % of **1a**), and diethylamine (0.124 mL, 1.20 mmol) according to the general procedure of the hydrodeoxygenation after 4 h of the reaction without any purification, in 89% yield (134 mg) as a colorless oil. ^1H NMR spectrum of **2a** was

identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.4. General procedure for the hydrodeoxygenation of aryl mesylates (Table 2)

After two vacuum/H_2 cycles to replace air inside the reaction tube with hydrogen, a mixture of the substrate (500 μmol), 10% Pd/C (10 wt % of the substrate) and diethylamine (62.1 μL, 600 μmol) in MeOH (1.0 mL) was vigorously stirred at room temperature (ca. 20 °C) under an ordinary hydrogen pressure (balloon). After a certain reaction time the reaction mixture was filtered using a membrane filter (Millipore, Millex®-LH, 0.45 μm) and the filtrate was partitioned between Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (10 mL×3) and the combined organic layers were washed with brine (10 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford the corresponding deoxygenated product (**2a**–**2m**).

4.4.1. Biphenyl (2b). Obtained from **1b** (248 mg, 1.00 mmol), 10% Pd/C (24.8 mg, 10 wt % of **1b**), and diethylamine (0.124 mL, 1.20 mmol) according to the general procedure of the hydrodeoxygenation after 18 h of the reaction without any purification, in 92% yield (141 mg) as a colorless solid. ^{1}H NMR spectrum of **2b** was identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.4.2. Methyl benzoate (2c). Obtained from **1c** (115 mg, 500 μmol), 10% Pd/C (11.6 mg, 10 wt % of **1c**), and diethylamine (62.1 μL, 600 μmol) according to the general procedure of the hydrodeoxygenation after 20 h of the reaction without any purification, in 95% yield (64.5 mg) as a colorless oil. ^{1}H NMR spectrum of **2c** was identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.4.3. Benzoic acid (2d). Obtained from **1d** (306 mg, 1.00 mmol), 10% Pd/C (30.6 mg, 10 wt % of **1d**), and diethylamine (0.124 mL, 1.20 mmol) according to the general procedure of the hydrodeoxygenation after 19 h of the reaction without any purification, in 91% yield (111 mg) as a colorless solid. ^{1}H NMR spectrum of **2d** was identical with that of the commercial authentic sample from Aldrich.

4.4.4. 4-Phenylaniline (2e).[19] Obtained from **1e** (147 mg, 500 μmol), 10% Pd/C (14.7 mg, 10 wt % of **1e**), and diethylamine (62.1 μL, 600 μmol) according to the general procedure of the hydrodeoxygenation after 48 h of the reaction, followed by another 9 h of the reaction after the addition of additional 10% Pd/C (14.7 mg, 10 wt % of **1e**) and diethylamine (62.1 μL, 600 μmol), without any purification, in 96% yield (81.1 mg) as a colorless solid. ^{1}H NMR spectrum of **2e** was identical with that in the literature.[19]

4.4.5. 1,3-Diphenylpropan-1-ol (2f).[20] Obtained from **1f** (302 mg, 1.00 mmol), 10% Pd/C (30.2 mg, 10 wt % of **1f**), and diethylamine (0.124 mL, 1.20 mmol) according to the general procedure of the hydrodeoxygenation after 17 h of the reaction without any purification, in 90% yield (190 mg) as a colorless oil. ^{1}H NMR spectrum of **2f** was identical with that in the literature.[20]

4.4.6. Diphenylmethane (2g). Obtained from **1g** (131 mg, 500 μmol), 10% Pd/C (26.3 mg, 20 wt % of **1g**), and diethylamine (0.103 mL, 1.00 mmol) according to the general procedure of the hydrodeoxygenation after 24 h of the reaction without any purification, in 94% yield (79.8 mg) as a colorless oil. ^{1}H NMR spectrum of **2g** was identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.4.7. 1,2-Dimethoxybenzene (2h). Obtained from **1h** (101 mg, 500 μmol), 10% Pd/C (30.5 mg, 30 wt % of **1h**), and diethylamine (0.155 mL, 1.50 mmol) according to the general procedure of the hydrodeoxygenation after 58 h of the reaction without any purification, in 79% yield (54.6 mg) as a colorless oil. ^{1}H NMR spectrum of **2h** was identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.4.8. Acetanilide (2i). Obtained from **1i** (110 mg, 500 μmol), 10% Pd/C (27.5 mg, 25 wt % of **1i**), and diethylamine (0.130 mL, 1.25 mmol) according to the general procedure of the hydrodeoxygenation after 129 h of the reaction without any purification, in 82% yield (55.4 mg) as a colorless solid. ^{1}H NMR spectrum of **2i** was identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.4.9. Cyclohexylbenzene (2j).[21] Obtained from **1j** (127 mg, 500 μmol), 10% Pd/C (25.6 mg, 20 wt % of **1j**), and diethylamine (0.124 mL, 1.20 mmol) according to the general procedure of the hydrodeoxygenation after 24 h of the reaction in 82% conversion yield. ^{1}H NMR spectrum of **2j** was identical with that in the literature.[21]

4.4.10. Naphthalene (2k). Obtained from **1k** (220 mg, 1.00 mmol), 10% Pd/C (22.2 mg, 10 wt % of **1k**), and diethylamine (0.124 mL, 1.20 mmol) according to the general procedure of the hydrodeoxygenation after 31 h of the reaction without any purification, in 91% yield (116 mg) as a colorless solid. ^{1}H NMR spectrum of **2k** was identical with that of the commercial authentic sample from Aldrich.

4.4.11. Indole (2l). Obtained from **1l** (105 mg, 500 μmol), 10% Pd/C (21.2 mg, 20 wt % of **1l**), and diethylamine (0.124 mL, 1.20 mmol) according to the general procedure of the hydrodeoxygenation after 29 h of the reaction without any purification, in 99% yield (58.5 mg) as a colorless solid. ^{1}H NMR spectrum of **2l** was identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.4.12. Flavone (2m). Obtained from **1m** (79.1 mg, 250 μmol), 10% Pd/C (23.7 mg, 30 wt % of **1m**), and diethylamine (93.1 μL, 900 μmol) according to the general procedure of the hydrodeoxygenation after 24 h of the reaction followed by flash column chromatography on silica gel ($CHCl_3$) in 71% yield (39.2 mg) as a colorless solid. ^{1}H NMR spectrum of **2m** was identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.5. General procedure for the synthesis of aryl triflates (Table 3)[22]

To a cooled (0 °C) biphasic mixture of toluene (10 mL), 30% (w/v) aqueous K_3PO_4 (10 mL), and phenol (5.00 mmol) was added dropwise trifluoromethanesulfonic anhydride (1.02 mL, 6.00 mmol) at a rate to maintain the reaction temperature below 10 °C. The reaction was allowed to warm to ambient temperature and the mixture was stirred for 30 min. The layers were separated and the toluene layer was washed with water (10 mL), dried over $MgSO_4$, and then concentrated under reduced pressure. If necessary, the residue was purified by flash column chromatography on silica gel.

4.5.1. 3,4,5-Trimethoxyphenyl trifluoromethanesulfonate (3n).[23] Obtained from 3,4,5-trimethoxyphenol (921 mg, 5.00 mmol), according to the general procedure for the synthesis of aryl triflates after 0.5 h of the reaction without any purification, in 97% yield (1.54 g) as a colorless solid. ^{1}H NMR spectrum of **3n** was identical with that in the literature.[23]

4.5.2. 3,4-Dimethoxyphenyl trifluoromethanesulfonate (3h). Obtained from 3,4-dimethoxyphenol (771 mg, 5.00 mmol), according to the general procedure for the synthesis of aryl triflates after 2 h of the reaction followed by flash column chromatography on silica gel (*n*-hexane/Et_2O=10/1) in 94% yield (1.34 g) as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 6.85 (d, 2H, J=2.4 Hz), 6.78 (d, 1H, J=2.2 Hz), 3.90 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 148.6, 142.7, 118.5 (q, J=321 Hz), 112.7, 111.0, 105.1, 55.9, 49.7; MS (EI) m/z 286 (M^+, 28), 153 (100), 125 (30). HRMS (EI) Calcd for $C_9H_9O_5F_3S$ (M^+): 286.0123. Found: 286.0116.

4.5.3. 4-Acetamidophenyl trifluoromethanesulfonate (3i).[24] Obtained from 4-acetamidophenol (756 mg, 5.00 mmol), according to the general procedure for the preparation of aryl triflates after 0.5 h of the reaction followed by flash column chromatography on silica gel ($CHCl_3$/MeOH=100/1) in 53% yield (747 mg) as a colorless solid. ^{1}H NMR spectrum of **3i** was identical with that in the literature.[24]

4.5.4. 1-Naphthalenyl trifluoromethanesulfonate (3k).[8h] Obtained from 1-naphthol (721 mg, 5.00 mmol), according to the general procedure of the preparation for aryl triflates after 0.5 h of the reaction followed by flash column chromatography on silica gel (*n*-hexane) in 84% yield (1.16 g) as a colorless oil. ^{1}H NMR spectrum of **3k** was identical with that in the literature.[8h]

4.6. General procedure for the hydrodeoxygenation of aryl triflates (Table 3)

After two vacuum/H_2 cycles to replace air inside the reaction tube with hydrogen, a mixture of the substrate (500 μmol), 10% Pd/C (10 wt % of the substrate) and diethylamine (62.1 μL, 600 μmol) in MeOH (1.0 mL) was vigorously stirred at room temperature (ca. 20 °C) under an ordinary hydrogen pressure (balloon). After a certain reaction time the reaction mixture was filtered using a membrane filter (Millipore, Millex®-LH, 0.45 μm) and the filtrate was partitioned between Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (10 mL×3) and the combined organic layers were washed with brine (10 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford the corresponding deoxygenated product.

4.6.1. 1,2-Dimethoxybenzene (2h). Obtained from **3h** (143 mg, 500 μmol), 10% Pd/C (14.4 mg, 10 wt % of **3h**), and diethylamine (62.1 μL, 600 μmol) according to the general procedure of the hydrodeoxygenation of aryl triflates after 6 h of the reaction without any purification, in 89% yield (61.3 mg) as a colorless oil. ^{1}H NMR spectrum of **2h** was identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.6.2. Acetanilide (2i). Obtained from **3i** (115 mg, 500 μmol), 10% Pd/C (11.5 mg, 10 wt % of **3i**), and diethylamine (62.1 μL, 600 μmol) according to the general procedure of the hydrodeoxygenation of aryl triflates after 4.5 h of the reaction without any purification, in 82% yield (55.5 mg) as a colorless solid. ^{1}H NMR spectrum of **2i** was identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.6.3. Naphthalene (2k). Obtained from **3k** (111 mg, 500 μmol), 10% Pd/C (11.2 mg, 10 wt % of **3k**), and diethylamine (62.1 μL, 600 μmol) according to the general procedure of the hydrodeoxygenation of the aryl triflates after 1 h of the reaction without any purification, in 48% yield (30.9 mg) as a colorless solid. ^{1}H NMR spectrum of **2k** was identical with that of the commercial authentic sample from Aldrich.

4.6.4. 1,2,3-Trimethoxybenzene (2n). After two vacuum/H_2 cycles to replace air inside the reaction tube with hydrogen, a mixture of **3n** (79.1 mg, 250 μmol), 10% Pd/C (8.0 mg, 10 wt % of **3n**) and diethylamine (31.0 μL, 300 μmol) in MeOH (1.0 mL) was vigorously stirred at room temperature (ca. 20 °C) at an ordinary hydrogen pressure (balloon) for 4 h. The reaction mixture was filtered using a membrane filter (Millipore, Millex®-LH, 0.45 μm) and the filtrate was partitioned between Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (10 mL×3) and the combined organic layers were washed with brine (10 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford **2n** in 99% yield (84.1 mg) as a colorless oil. ^{1}H NMR spectrum of **2n** was identical with that of the commercial authentic sample from Tokyo Chemical Industry Co., Ltd.

4.6.5. 3-Deoxy-7,8-dihydromorphine (2o) (Scheme 1). After two vacuum/H_2 cycles to replace air inside the reaction tube with hydrogen, a mixture of **3o** (20.9 mg, 50.0 μmol), 10% Pd/C (2.1 mg, 10 wt % of **3o**), and diethylamine (6.20 μL, 60.0 μmol) in MeOH (0.5 mL) was vigorously stirred at room hydrogen pressure (balloon) and temperature (ca. 20 °C) for 24 h. The reaction mixture was filtered using a membrane filter (Millipore, Millex®-LH, 0.45 μm) and the filtrate was partitioned between $CHCl_3$ (10 mL) and water (10 mL). The aqueous layer was extracted with $CHCl_3$ (10 mL×3) and the combined organic layers were washed with brine (10 mL), dried with anhydrous $MgSO_4$, filtered,

and concentrated under reduced pressure to afford **2o** in 94% yield (12.7 mg) as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.10 (t, 1H, J=7.7 Hz), 6.71 (d, 2H, J=7.7 Hz), 6.67 (d, 2H, J=7.7 Hz), 4.58 (d, 1H, J=5.3 Hz), 4.09–4.05 (m, 1H), 3.34 (s, 1H), 3.06 (d, 1H, J=18.8 Hz), 2.79 (d, 1H, J=8.2 Hz), 2.61–2.49 (m, 6H), 2.15–2.12 (m, 1H), 1.75–1.72 (m, 1H), 1.58–1.45 (m, 3H), 1.22–1.16 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 168.1, 158.9, 128.7, 118.6, 106.0, 90.0, 67.4, 60.0, 46.8, 42.8, 39.9, 36.9, 29.7, 26.9, 20.8, 19.1; MS (EI) m/z 271 (M^+, 100), 254 (14), 227 (14), 164 (15), 84 (54); HRMS (EI) Calcd for $C_{17}H_{21}NO_2$ (M^+): 271.1572. Found: 271.1558.

4.6.6. 3-Trifluoromethanesulfonyloxymorphine (3o).[25] To a slurry of morphine hydrochloride (100 mg, 311 μmol) in dichloromethane (5.0 mL) was added triethylamine (108 μL, 777 μmol). The mixture was stirred for 2 h and then *N*-phenylbis(trifluoromethanesulfonimide) (133 mg, 0.373 mmol) was added. After being stirred for 48 h, 10% aqueous sodium hydrogen carbonate (10 mL) was added and the layers were separated. The organic layer was dried over $MgSO_4$ and then concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel ($CHCl_3$/MeOH=100/1→10/1) to afford **3o** in 62% yield (80.2 mg) as a colorless solid. ^{1}H NMR spectrum of **3o** was identical with that in the literature.[25]

4.6.7. Additive effect of Mg metal in place of Et_2NH (Scheme 2). After two vacuum/H_2 cycles to replace air inside the reaction tube with hydrogen, a mixture of **1a** (244 mg, 1.00 mmol), 10% Pd/C (24.5 mg, 10 wt % of **1a**), and Mg metal (12.2 mg, 500 μmol) in MeOH (2.0 mL) was vigorously stirred at room temperature (ca. 20 °C) under an ordinary hydrogen pressure (balloon) for 24 h. The reaction mixture was filtered using a membrane filter (Millipore, Millex®-LH, 0.45 μm) and the filtrate was partitioned between Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (10 mL×3) and the combined organic layers were washed with brine (10 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford **2a** (99% conversion yield) in 60% isolated yield (89.1 mg).

4.6.8. Additive effect of single electron capture (Scheme 3). After two vacuum/H_2 cycles to replace air inside the reaction tube with hydrogen, a mixture of **1a** (244 mg, 1.00 mmol), 10% Pd/C (24.5 mg, 10 wt % of **1a**), diethylamine (0.124 mL, 1.20 mmol), and TCNQ (7,7,8,8-tetracyanoquinodimethane) (2.1 mg, 10.0 μmol) in MeOH (2.0 mL) was vigorously stirred at room temperature (ca. 20 °C) under an ordinary hydrogen pressure (balloon) and for 24 h. The reaction mixture was filtered using a membrane filter (Millipore, Millex®-LH, 0.45 μm) and the filtrate was partitioned between Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (10 mL×3) and the combined organic layers were washed with brine (10 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure.

4.7. General procedure for the synthesis of aryl sulfonates

To a solution of methyl 4-hydroxyphenylacetate (500 mg, 3.01 mmol) and triethylamine (0.510 mL, 3.61 mmol) in dichloromethane (10 mL) was added arenesulfonyl chloride (3.61 mmol) and the mixture was stirred at ambient temperature (ca. 20 °C). After a certain reaction time the solvent was concentrated under reduced pressure. The residue was extracted with ethyl acetate (10 mL) and water (10 mL). The organic layer was washed with saturated aqueous sodium carbonate solution (10 mL), 10% aqueous sodium hydrogen sulfonate solution (10 mL), and brine (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford the corresponding arenesulfonates (**4a–8a**).

4.7.1. Methyl 4-(4-toluenesulfonyloxy)phenylacetate (4a). Obtained from methyl 4-hydroxyphenylacetate (3.32 g, 20.0 mmol), triethylamine (3.07 mL, 22.0 mmol), and 4-toluenesulfonyl chloride (4.19 g, 22.0 mmol) according to the general procedure for the synthesis of arenesulfonates after 10 h of the reaction followed by flash column chromatography on silica gel (*n*-hexane/ethyl acetate=10/1→5/1) in 90% yield (5.77 g) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.71 (d, 2H, J=8.3 Hz), 7.31 (d, 2H, J=8.3 Hz), 7.20 (d, 2H, J=8.3 Hz), 6.93 (d, 2H, J=8.3 Hz), 3.61 (s, 3H), 3.58 (s, 2H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.5, 148.7, 145.3, 132.5, 130.5, 129.7, 128.5, 122.4, 52.1, 40.4, 21.7; MS (EI) m/z 320 (M^+, 75), 261 (14), 155 (100), 91 (84); HRMS (EI) Calcd for $C_{16}H_{16}O_5S$ (M^+): 320.0718. Found: 320.0721.

4.7.2. Methyl 4-(4-biphenylsulfonyloxy)phenylacetate (5a). Obtained from methyl 4-hydroxyphenylacetate (500 mg, 3.01 mmol), triethylamine (0.510 mL, 3.61 mmol), and 4-biphenylsulfonyl chloride (913 mg, 3.61 mmol) according to the general procedure for the synthesis of arenesulfonates after 66 h of the reaction followed by flash column chromatography on silica gel (*n*-hexane/Et_2O=20/1→0/100) in 47% yield (537 mg) as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.90 (d, 2H, J=8.6 Hz), 7.73 (d, 2H, J=8.6 Hz), 7.62 (d, 2H, J=6.8 Hz), 7.52–7.42 (m, 3H), 7.22 (d, 2H, J=8.8 Hz), 6.99 (d, 2H, J=8.8 Hz), 3.69 (s, 3H), 3.59 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 171.5, 148.7, 147.1, 133.9, 133.1, 130.6, 129.1, 128.9, 127.7, 127.4, 122.5, 52.2, 40.4; MS (EI) m/z 382 (M^+, 46), 217 (80), 153 (100); HRMS (EI) Calcd for $C_{21}H_{18}O_5S$ (M^+): 382.0875. Found: 382.0865. Anal. Calcd for $C_{21}H_{18}O_5S$: C, 65.95; H, 4.74. Found: C, 65.91; H, 4.74.

4.7.3. Methyl 4-(2,4,6-triisopropylbenzenesulfonyloxy)-phenylacetate (6a). Obtained from methyl 4-hydroxyphenylacetate (500 mg, 3.01 mmol), triethylamine (0.510 mL, 3.61 mmol), and 2,4,6-triisopropylphenylsulfonyl chloride (911 mg, 3.61 mmol) according to the general procedure for the synthesis of arenesulfonates after 19 h of the reaction followed by flash column chromatography on silica gel (*n*-hexane/Et_2O=10/1) in 88% yield (1.15 g) as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.21 (d, 2H, J=8.6 Hz), 7.19 (s, 2H), 6.96 (d, 2H, J=8.6 Hz), 4.08–4.01 (m, 2H), 3.66 (s, 3H), 3.58 (s, 2H), 2.95–2.91 (m, 1H), 1.27 (d, 6H, J=6.8 Hz), 1.17 (d, 12H, J=6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 171.4, 154.2, 151.2, 148.5, 132.8, 130.4, 129.6, 123.9, 122.6, 52.1, 40.4, 34.2, 29.7, 24.5, 23.5; MS (EI) m/z 432 (M^+, 13), 267 (100), 203 (14), 175 (16), 149 (8), 119 (10), 91 (12); HRMS (EI) Calcd for $C_{24}H_{32}O_5S$ (M^+): 432.1970. Found: 432.1978. Anal. Calcd for $C_{24}H_{32}O_5S$: C, 66.64; H, 7.46. Found: C, 66.57; H, 7.51.

4.7.4. Methyl 4-(4-fluorobenzenesulfonyloxy)phenylacetate (7a). Obtained from methyl 4-hydroxyphenylacetate (500 mg, 3.01 mmol), triethylamine (0.510 mL, 3.61 mmol), and 4-fluorobenzenesulfonyl chloride (586 mg, 3.61 mmol) according to the general procedure for the synthesis of arenesulfonates after 2 h of the reaction followed by flash column chromatography on silica gel (*n*-hexane/Et_2O=100/0→0/100) in 91% yield (909 mg) as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.96–7.93 (m, 2H), 7.35–7.28 (m, 4H), 7.03 (dd, 2H, J=2.0 and 6.8 Hz), 3.79 (s, 3H), 3.69 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 171.4, 167.2, 164.7, 148.5, 133.2, 131.4, 131.3, 130.6, 122.3, 116.7, 116.4, 52.1, 40.3; MS (EI) *m*/*z* 324 (M^+, 100), 265 (43), 159 (97), 121 (48), 95 (64), 78 (20), 91 (12); HRMS (EI) Calcd for $C_{15}H_{13}O_5FS$ (M^+): 324.0468. Found: 324.0460. Anal. Calcd for $C_{15}H_{13}O_5FS$: C, 55.55; H, 4.04. Found: C, 55.39; H, 4.04.

4.7.5. Methyl 4-(2-naphthalenesulfonyloxy)phenylacetate (8a). Obtained from methyl 4-hydroxyphenylacetate (831 mg, 5.00 mmol), triethylamine (0.836 mL, 6.00 mmol), and 2-naphthalenesulfonyl chloride (1.36 g, 6.00 mmol) according to the general procedure for the synthesis of arenesulfonates after 65 h of the reaction followed by flash column chromatography on silica gel (*n*-hexane/Et_2O=10/1) in 83% yield (1.48 g) as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 8.38 (s, 1H), 7.99 (d, 1H, J=8.8 Hz), 7.95–7.92 (m, 2H), 7.85 (dd, 1H, J=1.7 and 8.6 Hz), 7.7 (t, 1H, J=6.8 Hz), 7.63 (t, 1H, J=6.8 Hz), 7.17 (d, 2H, J=8.6 Hz), 6.95 (d, 2H, J=8.6 Hz), 3.67 (s, 3H), 3.56 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 171.4, 148.7, 135.4, 133.0, 132.2, 131.8, 130.6, 130.4, 129.6, 129.5, 128.0, 127.8, 122.8, 122.4, 122.4, 52.1, 40.4; MS (EI) *m*/*z* 356 (M^+, 33), 191 (53), 127 (100); HRMS (EI) Calcd for $C_{19}H_{16}O_5S$ (M^+): 356.0718. Found: 356.0726. Anal. Calcd for $C_{19}H_{16}O_5S$: C, 64.03; H, 4.53. Found: C, 64.01; H, 4.50.

4.8. Investigation of the leaving group (Scheme 4)

After two vacuum/H_2 cycles to replace air inside the reaction tube with hydrogen, a mixture of the substrates (**4a**–**8a**) (1.00 mmol), 10% Pd/C (10 wt % of the substrate), diethylamine (0.124 mL, 1.20 mmol) in MeOH (2.0 mL) was vigorously stirred at room temperature (ca. 20 °C) under an ordinary hydrogen pressure (balloon) for 24 h. The reaction mixture was filtered using a membrane filter (Millipore, Millex®-LH, 0.45 μm) and the filtrate was partitioned between Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (10 mL×3) and the combined organic layers were washed with brine (10 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure.

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