Nickel-Catalyzed Hydrodeoxygenation of Aryl Sulfamates with Alcohols as Mild Reducing Agents

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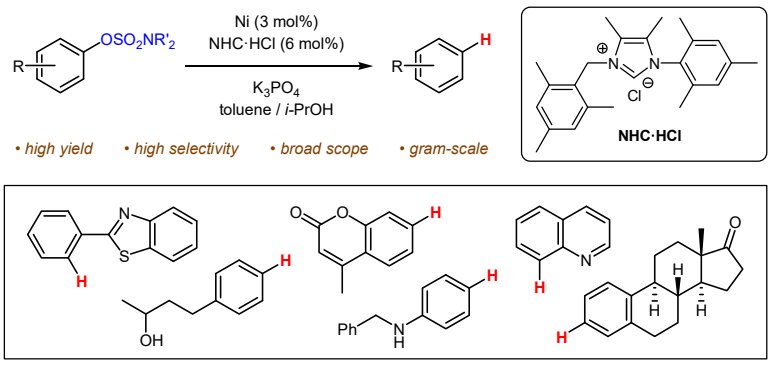


Abstract The nickel-catalyzed hydrodeoxygenation of aryl sulfamates has been developed with alcohols as mild reductants, and a variety of functional groups and heterocycles were tolerated in this reaction system to give desired products in high yields. In addition, the gram-scale process and stepwise *cine*-substitution were also achieved with high efficiency.

Key words nickel, reduction, hydrodeoxygenation, sulfamate, alcohol

The catalytic deoxygenation of hydroxyl groups is a fundamental transformation in organic chemistry.[1] Particularly, the catalytic reduction of phenols and their derivatives via the cleavage of $C_{(aryl)}$-O bond has attracted much interest because of its useful applications.[2] While phenolic compounds have positive features such as lower cost, easy availability, and high diversity, the ingenuity to improve the reactivity of phenols is often employed due to strong $C_{(aryl)}$-O bond with high bond dissociation energy.[2a] The reductive deoxygenation of phenols has been effectively conducted through the transformation of phenols into phenol derivatives, such as sulfonates, esters, and carbamates.[3-8] In a few cases, simple alcohols are used as an attractive reductant because of their lower cost, milder reactivity, and easy removability, but precious metal catalysts such as palladium and rhodium are required.[4a,6a] As practical examples, the catalytic removal of triflate groups has been applied to the synthesis of biologically active agents.[9] Carbamate moieties are utilized as a directed metalation group (DMG) and leaving group to prepare *cine*-substituted products in a stepwise manner.[6c] On the other hand, aryl sulfamates are known to be a useful class of phenol derivatives on the ground of their easy preparation and high stability, and sulfamoyloxy groups have been employed for a variety of transformations, such as *ortho*-functionalization via directed metalation and catalytic cross-coupling reactions,[10-12] in which nickel often serves as an effective and less expensive base metal catalyst. However, to our best knowledge, no hydrodeoxygenation process for aryl sulfamates has been developed. In this context, we envisaged that the combination use of a nickel catalyst and an alcohol as a reductant would give an attractive reduction system for sulfamoylated phenols. Herein, we report the nickel-catalyzed reductive deoxygenation of aryl sulfamates with simple alcohols as mild reductants. This method has noticeable features compared with our underlying deuteration,[13b] such as the milder conditions, broader scope, and useful application.

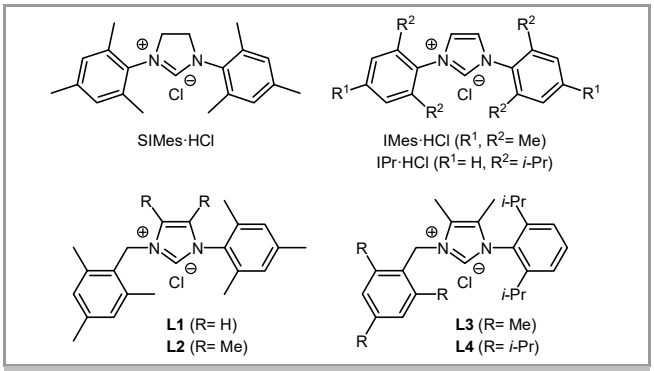
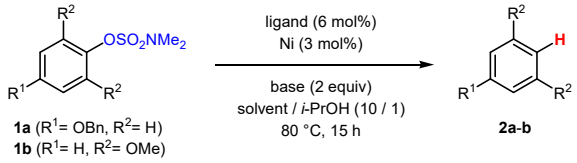


Figure 1 Precursors of *N*-heterocyclic carbene ligands

At the outset, a series of ligands were examined in the nickel-catalyzed hydrodeoxygenation of the aryl sulfamate **1a** in toluene/*i*-PrOH (10/1) under the presence of K_3PO_4 (Table 1). The reaction conditions with no addition of ligands gave no desired product (entry 1), and neither phosphine ligands nor nitrogen-containing ligands were suitable for this catalytic reduction (entries 2-5). In these cases, **1a** was recovered and the C-O coupling product was not detected. Whereas SIMes·HCl also led to no reaction (entry 6), the use of IMes·HCl afforded an excellent yield (entry 7). In the case of IPr·HCl, the significant decrease in yield was observed (entry 8). Besides, unsymmetrical NHC precursors (Figure 1) were tested because we found that this type of NHC ligand was effective in the transition metal-catalyzed deuteration reactions.[13] The NHC precursors **L1**-**4** proved to be promising to provide quite high yields (entries 9-12). Then, IMes·HCl and **L1**-**4** were evaluated in the catalytic hydrodeoxygenation of the bulkier substrate **1b** with the steric hindrance near a reaction site (entries 13-17). While

the catalytic reduction with IMes·HCl resulted in 5% yield (entry 13), the NHC precursor **L2** kept the similar efficiency to entry 10, leading to 91% yield (entry 15). This higher level of result relative to our related study[13b] was achieved at the lower catalyst loading and reaction temperature even with the use of the secondary alkyl alcohol with the lower reactivity than previously employed benzylic alcohols. The use of **L1**, **L3**, and **L4** caused the large decrease in yield (entries 14, 16, and 17). The methyl groups on the imidazolium ring were found to be important (entries 14 and 15), and the bulkier isopropyl groups were less suitable (entries 15-17). In the case of **L2**, the metal-arene interaction could be formed more effectively by the steric repulsion between the benzyl moiety and methyl group on the *N*-heterocycle and lead to the superior catalyst performance.[13] Subsequently, the examination of nickel sources was conducted (entries 15 and 18-21). Ni(1-naph)Cl(PPh_3)$_2$[14] showed high suitability for this reduction, although the other zero- and divalent nickel complexes were ineffective. In the screening of bases (entries 15 and 22-26), a set of inorganic bases such as trisodium phosphate, inorganic carbonates, and potassium fluoride gave no desired product except for tripotassium phosphate. Then, the influence of solvents was explored (entries 15 and 27-29). More highly polar solvents had a tendency to decrease yields, and toluene proved to be a solvent of choice. In all the reactions with NHCs, no C-O cross-coupling was observed.

Table 1 Optimization of Reaction Conditions [a]



1a (R^1= OBn, R^2= H)
1b (R^1= H, R^2= OMe)

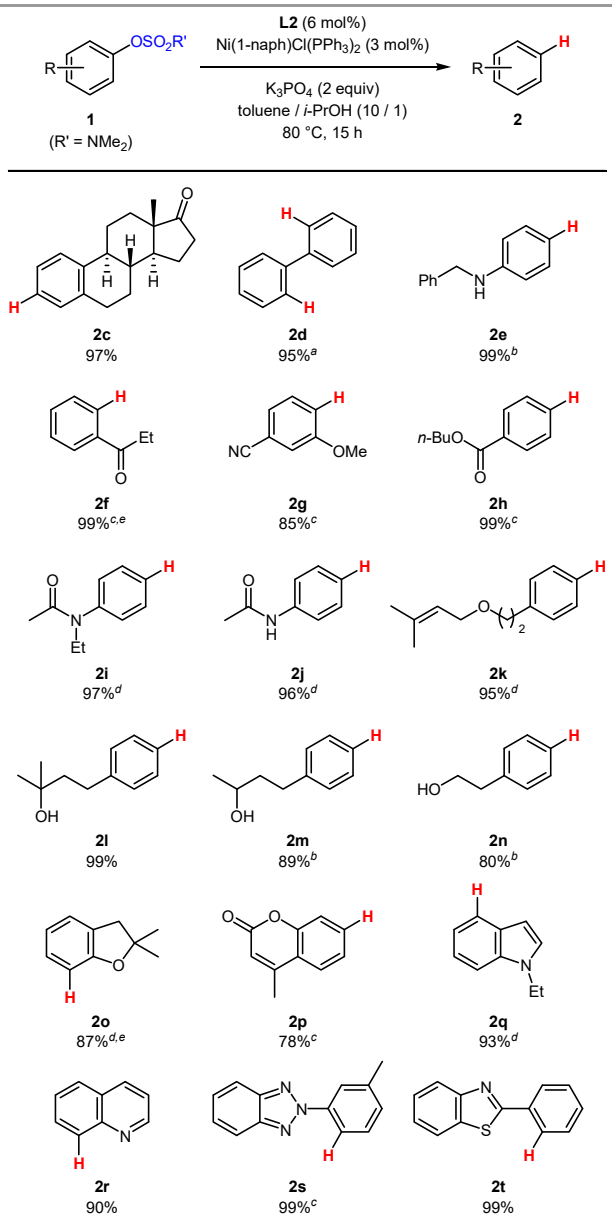
2a-b

Entry	1	Ligand	Ni	Base	Solvent	Yield (%) [b]
1	**1a**	None	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	0
2	**1a**	PCy_3·HBF_4	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	0
3	**1a**	BINAP [c]	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	0
4	**1a**	TMEDA [c]	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	0
5	**1a**	2,2′-bpy [c,d]	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	0
6	**1a**	SIMes·HCl	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	0
7	**1a**	IMes·HCl	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	95
8	**1a**	IPr·HCl	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	2
9	**1a**	**L1**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	93
10	**1a**	**L2**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	95
11	**1a**	**L3**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	93
12	**1a**	**L4**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	95
13	**1b**	IMes·HCl	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	5
14	**1b**	**L1**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	57
15	**1b**	**L2**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	91
16	**1b**	**L3**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	69
17	**1b**	**L4**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Toluene	45
18	**1b**	**L2**	$NiCl_2(PPh_3)_2$	K_3PO_4	Toluene	0
19	**1b**	**L2**	$NiCl_2$	K_3PO_4	Toluene	0
20	**1b**	**L2**	$Ni(OTf)_2$	K_3PO_4	Toluene	0
21	**1b**	**L2**	$Ni(COD)_2$	K_3PO_4	Toluene	11
22	**1b**	**L2**	Ni(1-naph)Cl(PPh_3)$_2$	Na_3PO_4	Toluene	0
23	**1b**	**L2**	Ni(1-naph)Cl(PPh_3)$_2$	Na_2CO_3	Toluene	0
24	**1b**	**L2**	Ni(1-naph)Cl(PPh_3)$_2$	K_2CO_3	Toluene	0
25	**1b**	**L2**	Ni(1-naph)Cl(PPh_3)$_2$	Cs_2CO_3	Toluene	0
26	**1b**	**L2**	Ni(1-naph)Cl(PPh_3)$_2$	KF	Toluene	0
27	**1b**	**L2**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	Dioxane	74
28	**1b**	**L2**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	DMA	4
29	**1b**	**L2**	Ni(1-naph)Cl(PPh_3)$_2$	K_3PO_4	DMSO	0

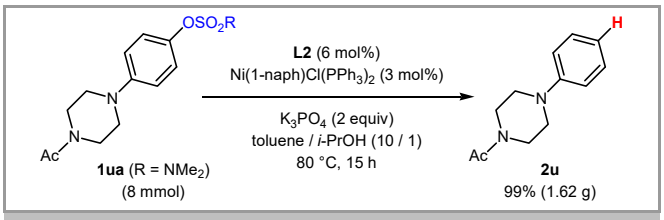
[a] Reaction conditions: **1** (0.5 mmol), ligand (6 mol%), Ni (3 mol%), base (1 mmol), solvent (1 mL), *i*-PrOH (0.1 mL), 80 °C, 15 h. [b] Isolated yield. [c] 3 mol%. [d] 2,2′-bipyridine.

The investigation of substrate scope in the nickel-catalyzed reductive deoxygenation of aryl sulfamates was conducted (Scheme 1). The catalytic reduction of the sulfamoylated estrone **1c** proceeded without problems to provide a high yield (**2c**). Both the two reaction sites in the aryl sulfamate **1d** were converted smoothly in spite of the steric hindrance (**2d**). The effective deoxygenation of the electron-rich substrate with a secondary amino group was achieved with 2-propanol as a solvent (**2e**). The electron-withdrawing groups such as propionyl and cyano groups were well tolerated without side products (**2f** and **2g**). The ester and amide-containing aryl sulfamates led to positive results (**2h** and **2i**), and a secondary amide group also proved to be suitable even with a free NH moiety (**2j**). In addition to a reducible alkenyl moiety, a tertiary alcohol group was acceptable, leading to high yields (**2k** and **2l**). In the presence of secondary and primary alcohol groups, desired products were obtained sufficiently using 2-propanol as a solvent (**2m** and **2n**). 4-Phenylbutan-2-one was obtained in only 5% yield (**2m**) and phenylacetaldehyde was not detected (**2n**). The successful results on **2e**, **2m**, and **2n** would indicate that reducing groups also can be tolerated with the conditions. Then, heterocycle-containing aryl sulfamates were explored. The sul-

famoyloxy moieties in dihydrobenzofuran and coumarin derivatives were removed with high yields (**2o** and **2p**). The *N*-heterocyclic substrates derived from hydroxyindole and quinolinol were found to be good reaction partners (**2q** and **2r**). The catalytic hydrodeoxygenation of aryl sulfamates with benzotriazole and benzothiazole moieties resulted in excellent yields (**2s** and **2t**). In addition to high selectivity, this reaction system showed the superior efficiency for sterically hindered and heterocyclic substrates to our previous process.[13b] Subsequently, the gram-scale reaction with a piperazine-containing substrate was carried out (Scheme 2), and the desired product **2u** was obtained in 99% yield (1.62 g).



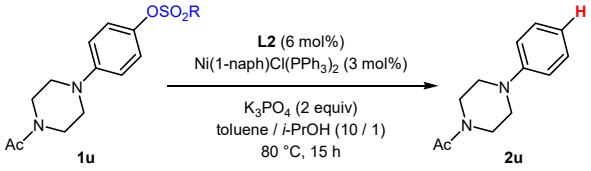
Scheme 1 Substrate scope of Ni-catalyzed hydrodeoxygenation for aryl sulfamates. *Reaction conditions*: **1** (0.5 mmol), **L2** (6 mol%), Ni(1-naph)Cl(PPh$_3$)$_2$ (3 mol%), K$_3$PO$_4$ (1 mmol), toluene (1 mL), *i*-PrOH (0.1 mL), 80 °C, 15 h. Isolated yields are shown. [a] *i*-PrOH (0.2 mL), K$_3$PO$_4$ (2 mmol). [b] *i*-PrOH (1 mL) was used instead of toluene / *i*-PrOH (1 mL / 0.1 mL). [c] 3-Pentanol (0.1 mL), 110 °C. [d] 100 °C. [e] Determined by ^{1}H NMR due to the product volatility.

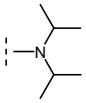


Scheme 2 Gram-scale reaction

The influence of varying sulfamoyl moieties in this catalytic hydrodeoxygenation was also investigated (Table 2). The diethylsulfamoyloxy group reacted readily to afford the desired product **2u** in a quite high yield (entry 1). The substrate including piperidine moiety was also suitable (entry 2). Even in the presence of bulkier substituents on nitrogen atom, no decrease in yield was observed, leading to excellent results (entries 3 and 4).

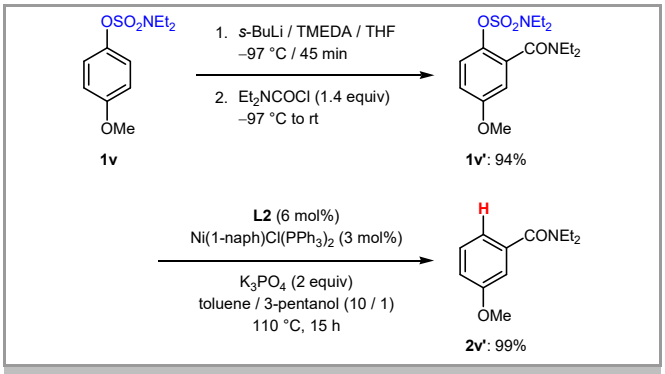
Table 2 Examination of sulfamoyl groups [a]



Entry	1u	R	Yield (%) [b]
1	**1ub**		99
2	**1uc**		98
3	**1ud**		99
4	**1ue**		99

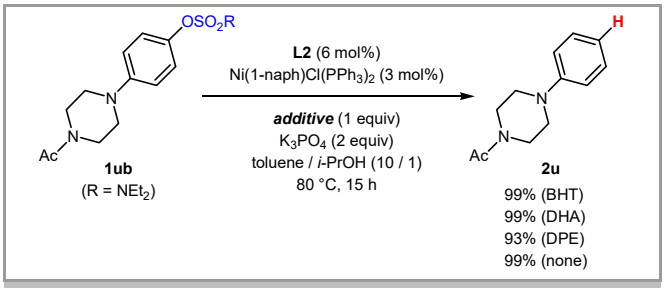
[a] Reaction conditions: **1** (0.5 mmol), **L2** (6 mol%), Ni(1-naph)Cl(PPh$_3$)$_2$ (3 mol%), K$_3$PO$_4$ (1 mmol), toluene (1 mL), *i*-PrOH (0.1 mL), 80 °C, 15 h. [b] Isolated yield.

Subsequently, this reductive deoxygenation was applied to the *cine*-substitution of the aryl sulfamate **1v** (Scheme 3). As the first transformation, the *ortho*-functionalization of **1v** with diethylcarbamoyl chloride was conducted via the directed metalation with *s*-BuLi, leading to the selective formation of **1v'** with 94% yield even in the presence of a methoxy group, which was consistent with the literature data.[10d] Then, the removal of diethylsulfamoyloxy group was achieved with the nickel-catalyzed hydrodeoxygenation process to provide the *meta*-substituted product **2v'** in 99% yield.

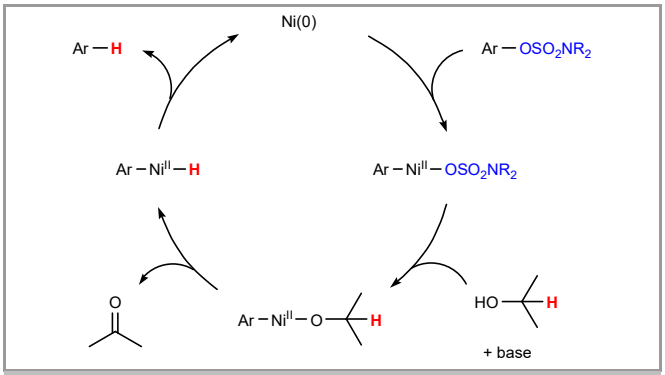


Scheme 3 *Cine*-substitution of aryl sulfamate **1v**

Radical scavengers such as 2,6-di-*tert*-butyl-4-methylphenol (BHT), 9,10-dihydroanthracene (DHA), and 1,1-diphenylethylene (DPE) were examined in the nickel-catalyzed hydrodeoxygenation of the aryl sulfamate **1ub**, and the high levels of yield were observed in all cases (Scheme 4), which suggested that single electron transfer processes might not be included in this catalytic transformation. On the basis of the results in this research as well as the findings in the literatures,[13] a plausible reaction mechanism is shown in Scheme 5. The formation of an aryl-nickel complex takes place through oxidative addition. This intermediate reacts with 2-propanol to give an alkoxy-nickel species. Then, β-hydrogen elimination leads to an aryl-nickel-hydride complex, and reductive elimination provides a desired product with the regeneration of Ni(0) catalyst.



Scheme 4 Hydrodeoxygenation in the presence of radical scavengers



Scheme 5 Plausible reaction mechanism

In summary, the hydrodeoxygenation of aryl sulfamates has been catalytically achieved with simple alcohols as mild reductants. The nickel/unsymmetrical NHC system showed the high catalyst performance, and a variety of substrates proved to be suitable. This method tolerated reducible functional groups as well as primary and secondary alcohol moieties. The heterocycle-containing substrates were found to be good reaction partners, and the gram-scale process was successfully carried out. The *cine*-substitution of an aryl sulfamate was also accomplished through the *ortho*-functionalization and catalytic C-O bond cleavage.

All melting points are not corrected. ^{1}H NMR spectra were taken at 300, 400, and 500 MHz, and ^{13}C{^{1}H} NMR spectra were taken at 100 and 125 MHz (Varian Gemini300, JEOL JNM-ECZ400R, and Varian NMR System 500PS SN). Chemical shift values are expressed in ppm relative to internal or external TMS (δ 0.00 ppm) for ^{1}H NMR data and $CDCl_3$ (δ 77.0 ppm) for ^{13}C{^{1}H} NMR data. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded using electron ionization (EI) and fast atom bombardment (FAB) mass spectrometry (JEOL JMS-700N). All reactions were performed under an argon atmosphere unless otherwise specified. The products were isolated by silica gel column chromatography. Commercially available chemicals were purchased from Sigma-Aldrich, Tokyo Chemical Industry Co., Ltd., and Fujifilm Wako Pure Chemical Corporation and used as received unless otherwise specified. Toluene was distilled from sodium benzophenone ketyl under an argon atmosphere. Alcohols such as 2-propanol and 3-pentanol were dried with 4Å MS before use. The NHC precursors **L1**-**4**[13c] and the aryl sulfamates **1a**-**c**[13b], **1g**[15a], **1h**[13b], **1j**[15b], **1o**[15c], **1r**[13b], **1ua**[13b], **1v**[10d] were prepared as previously reported.

Compound 2; General Procedure

A reaction tube was charged with **L2** (11.5 mg, 0.03 mmol), Ni(1-naph)Cl(PPh$_3$)$_2$ (11.2 mg, 0.015 mmol), and K_3PO_4 (212 mg, 1.0 mmol). After toluene (1.0 mL) was added, the mixture was stirred for 15 min at 80 °C. Then, aryl sulfamate **1** (0.5 mmol) and 2-propanol (0.1 mL) were added at room temperature. The reaction mixture was stirred at 80 °C for 15 h. After water (5 mL) was added at room temperature, the resulting mixture was extracted with AcOEt (10 mL x 3). The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography gave desired product **2**.

Benzyloxybenzene (2a)[16a]

For easier purification, triphenylphosphine in the crude product was oxidized as follows. After concentration of the combined organic layers, dioxane (1.0 mL) and 30% H_2O_2 (0.25 mL) were added at 0 °C, and the mixture was stirred for 15 min at 0 °C. The resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/*i*-Pr$_2$O = 100/1) gave 87.5 mg of the product (0.475 mmol, 95% yield).

White solid; mp 37-38 °C; R_f = 0.29 (hexane/*i*-Pr$_2$O = 100/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.07 (s, 2H), 6.95-7.00 (m, 3H), 7.28-7.35 (m, 3H), 7.39 (t, *J* = 7.3 Hz, 2H), 7.45 (d, *J* = 7.3 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 69.9 (CH_2), 114.8 (CH), 120.9 (CH), 127.5 (CH), 127.9 (CH), 128.6 (CH), 129.5 (CH), 137.0 (C), 158.7 (C).

IR (ATR): 680, 1030, 1050, 1210, 1150, 1490, 1590 cm^{-1}.

EIMS *m/z*: 184 (M$^+$).

1,3-Dimethoxybenzene (2b)[16b]

Silica gel chromatography (hexane/benzene = 2/1) gave 62.8 mg of the product (0.455 mmol, 91% yield).

Colorless oil; R_f = 0.40 (hexane/benzene = 2/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.80 (s, 6H), 6.47-6.48 (m, 1H), 6.52 (dd, *J* = 2.2, 8.3 Hz, 2H), 7.19 (t, *J* = 8.3 Hz, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 55.2 (CH_3), 100.4 (CH), 106.1 (CH), 129.8 (CH), 160.8 (C).

IR (ATR): 690, 750, 1000, 1040, 1480, 3030 cm^{-1}.

EIMS *m/z*: 138 (M$^+$).

(8*R*,9*S*,13*S*,14*S*)-13-Methyl-7,8,9,11,12,13,15,16-octahydro-6*H*-cyclopenta[*a*]phenanthren-17(14*H*)-one (2c)[16c]

Silica gel chromatography (hexane/AcOEt = 10/1) gave 124 mg of the product (0.487 mmol, 97% yield).

White solid; mp 136-138 °C; R_f = 0.13 (hexane/AcOEt = 10/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (s, 3H), 1.42-1.68 (m, 6H), 1.96-2.19 (m, 4H), 2.33 (dt, *J* = 4.4, 11.5 Hz, 1H), 2.42-2.54 (m, 2H), 2.93 (dd, *J* = 4.2, 8.8 Hz, 2H), 7.10-7.18 (m, 3H), 7.30 (d, *J* = 7.3 Hz, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 13.8 (CH_3), 21.6 (CH_2), 25.6 (CH_2), 26.5 (CH_2), 29.3 (CH_2), 31.6 (CH_2), 35.8 (CH_2), 38.0 (CH), 44.4 (CH), 48.0 (C), 50.5 (CH), 125.3 (CH), 125.7 (CH), 125.8 (CH), 129.3 (CH), 136.4 (C), 139.6 (C), 220.9 (C).

IR (ATR): 750, 1000, 1490, 1730 cm^{-1}.

EIMS *m/z*: 254 (M^+).

Biphenyl (2d)[16d]

Silica gel chromatography (hexane/AcOEt = 5/1) gave 73.6 mg of the product (0.477 mmol, 95% yield).

White solid; mp 68-69 °C; R_f = 0.25 (hexane/AcOEt = 5/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (t, *J* = 7.3 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 4H), 7.60 (d, *J* = 7.3 Hz, 4H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 127.2 (CH), 127.3 (CH), 128.8 (CH) 141.3 (C).

IR (ATR): 690, 730, 1170, 1480, 3030 cm^{-1}.

EIMS *m/z*: 154 (M^+).

***N*-Benzylaniline (2e)**[16e]

Silica gel chromatography (hexane/*i*-Pr_2O = 100/1) gave 90.4 mg of the product (0.493 mmol, 99% yield).

Colorless oil; R_f = 0.29 (hexane/ *i*-Pr_2O = 100/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.03 (brs, 1H), 4.34 (s, 2H), 6.64 (d, *J* = 7.6 Hz, 2H), 6.72 (t, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 2H), 7.26-7.29 (m, 1H), 7.33-7.39 (m ,4H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 48.3 (CH_2), 112.8 (CH), 117.5 (CH), 127.2 (CH), 127.5 (CH), 128.6 (CH), 129.2 (CH), 139.4 (C), 148.1 (C).

IR (ATR): 750, 1250, 1500, 3420 cm^{-1}.

EIMS *m/z*: 183 (M^+).

Propiophenone (2f)[16f]

The yield was determined by ^{1}H NMR due to the product volatility (99% yield). Silica gel chromatography (hexane/AcOEt = 20/1) gave 49.7 mg of the product (0.370 mmol, 74% yield).

Colorless oil; R_f = 0.44 (hexane/AcOEt = 20/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, *J* =7.3 Hz, 3H), 3.02 (q, *J* = 7.3Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.97 (d, *J* = 7.6 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 8.2 (CH_3), 31.7 (CH_2), 127.9 (CH), 128.5 (CH), 132.8 (CH), 136.8 (C), 200.8 (C).

IR (ATR): 740, 1220, 1580, 1680 cm^{-1}.

EIMS *m/z*: 134 (M^+).

3-Methoxybenzonitrile (2g)[16g]

Silica gel chromatography (hexane/Et_2O = 10/1) gave 56.7 mg of the product (0.426 mmol, 85% yield).

Pale yellow oil; R_f = 0.12 (hexane/Et_2O = 10/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3H), 7.13-7.15 (m, 2H), 7.24-7.26 (m, 1H), 7.38 (t, *J* = 7.8 Hz, 1H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 55.4 (CH_3), 113.2 (C), 116.8 (CH) 118.7 (C), 119.3 (CH), 124.5 (CH), 130.3 (CH), 159.7 (C).

IR (ATR): 680, 790, 1260, 1480, 1580, 2230 cm^{-1}.

EIMS *m/z*: 133 (M^+).

Butyl benzoate (2h)[16h]

Silica gel chromatography (hexane/benzene = 2/1) gave 88.5 mg of the product (0.497 mmol, 99% yield).

Pale yellow oil; R_f = 0.44 (hexane/benzene = 2/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.3 Hz, 3H), 1.44-1.53 (m, 2H), 1.72-1.79 (m, 2H), 4.33 (t, *J* = 6.8 Hz, 2H), 7.44 (t, *J* = 7.3 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 8.05 (d, *J* = 7.3 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 13.8 (CH_3), 19.3 (CH_2), 30.8 (CH_2), 64.8 (CH_2) 128.3 (CH), 129.5 (CH), 130.5 (C), 132.8 (CH), 166.7 (C).

IR (ATR): 710, 1110, 1270, 1450, 1720 cm^{-1}.

EIMS *m/z*: 178 (M^+).

***N*-Ethyl-*N*-phenylacetamide (2i)**[16i]

Silica gel chromatography (hexane/AcOEt = 4/1) gave 79.5 mg of the product (0.487 mmol, 97% yield).

Pale yellow solid; mp 47-48 °C; R_f = 0.18 (hexane/AcOEt = 4/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11 (t, *J* = 7.3 Hz, 3H), 1.82 (s, 3H), 3.75 (q, *J* = 7.3 Hz, 2H), 7.17 (d, *J* = 7.3 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.43 (t, *J* = 7.3 Hz, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 12.9 (CH_3), 22.7 (CH_3), 43.7 (CH_2) 127.8 (CH), 128.1 (CH), 129.5 (CH), 142.7 (C), 169.9 (C).

IR (ATR): 710, 770, 1140, 1490, 1650 cm^{-1}.

EIMS *m/z*: 163 (M^+).

***N*-Phenylacetamide (2j)**[16j]

Silica gel chromatography (hexane/AcOEt = 1/1) gave 64.7 mg of the product (0.479 mmol, 96% yield).

White solid; mp 112-113 °C; R_f = 0.28 (hexane/AcOEt = 1/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.19 (s, 3H), 7.11 (t, *J* = 8.1 Hz, 1H), 7.15 (brs, 1H), 7.33 (t, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 24.6 (CH_3), 119.9 (CH), 124.3 (CH), 128.9 (CH), 137.8 (C), 168.4 (C).

IR (ATR): 750, 1490, 1660, 3290 cm^{-1}.

EIMS *m/z*: 135 (M^+).

(2-(3-Methylbut-2-enyloxy)ethyl)benzene (2k)

Silica gel chromatography (hexane/benzene = 1/5) gave 90.8 mg of the product (0.477 mmol, 95% yield).

Colorless oil; R_f = 0.43 (hexane/benzene = 1/5).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.66 (s, 3H), 1.74 (s, 3H), 2.90 (t, *J* = 7.3 Hz, 2H), 3.63 (t, *J* = 7.3 Hz, 2H), 3.98 (d, *J* = 6.9 Hz, 2H), 5.35 (t, *J* = 6.9 Hz, 1H), 7.19-7.24 (m, 3H), 7.29 (t, *J* = 7.6 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 18.0 (CH_3), 25.8 (CH_3), 36.4 (CH_2), 67.3 (CH_2), 71.1 (CH_2), 121.1 (CH), 126.1 (CH), 128.3 (CH), 128.8 (CH), 136.8 (C), 138.9 (C).

IR (ATR): 750, 820, 1080, 1500 cm^{-1}.

HRMS (EI) *m/z* Calcd for $C_{13}H_{18}O$: 190.1358; Found: 190.1357.

2-Methyl-4-phenylbutan-2-ol (2l)[16k]

Silica gel chromatography (hexane/AcOEt = 5/1) gave 81.7 mg of the product (0.497 mmol, 99% yield).

Colorless oil; R_f = 0.35 (hexane/AcOEt = 5/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (brs, 1H), 1.30 (s, 6H), 1.78-1.82 (m, 2H), 2.69-2.73 (m, 2H), 7.17-7.22 (m, 3H), 7.29 (t, *J* = 7.6 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 29.3 (CH_3), 30.7 (CH_2), 45.7 (CH_2), 70.9 (C), 125.7 (CH), 128.3 (CH), 128.4 (CH), 142.5 (C).

IR (ATR): 740, 1120, 1210, 3380 cm^{-1}.

EIMS *m/z*: 164 (M^+).

4-Phenylbutan-2-ol (2m)[16l]

Silica gel chromatography (hexane/AcOEt = 5/1) gave 67.1 mg of the product (0.447 mmol, 89% yield).

Colorless oil; R_f = 0.39 (hexane/AcOEt = 5/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.23 (d, *J* = 6.4 Hz, 3H), 1.32 (brs, 1H), 1.72-1.83 (m, 2H), 2.65-2.71 (m, 1H), 2.74-2.79 (m, 1H), 3.81-3.86 (m, 1H), 7.18-7.21 (m, 3H), 7.29 (t, *J* = 7.6 Hz, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 23.6 (CH_3), 32.1 (CH_2), 40.8 (CH_2), 67.5 (CH), 125.8 (CH), 128.4 (CH), 142.0 (C).

IR (ATR): 740, 1080, 1490, 3340 cm^{-1}.

EIMS *m/z*: 150 (M^+).

2-Phenylethanol (2n)[16l]

Silica gel chromatography (hexane/AcOEt = 5/1) gave 48.7 mg of the product (0.399 mmol, 80% yield).

Colorless oil; R_f = 0.28 (hexane/AcOEt = 5/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35-1.38 (m, 1H), 2.88 (t, *J* = 6.6 Hz, 2H), 3.86-3.89 (m, 2H), 7.23-7.25 (m, 3H), 7.32 (t, *J* = 7.8 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 39.1 (CH_2), 63.6 (CH_2), 126.4 (CH), 128.5 (CH), 129.0 (CH), 138.4 (C).

IR (ATR): 740, 1040, 1490, 3340 cm^{-1}.

EIMS *m/z*: 122 (M^+).

2,2-Dimethyl-2,3-dihydrobenzofuran (2o)[16m]

The yield was determined by ^{1}H NMR due to the product volatility (87% yield). Silica gel chromatography (hexane/benzene = 20/1) gave 51.8 mg of the product (0.350 mmol, 70% yield).

Yellow oil; R_f = 0.16 (hexane/benzene = 20/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.48 (s, 6H), 3.01 (s, 2H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.82 (t, *J* = 7.3 Hz, 1H), 7.09-7.14 (m, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 28.1 (CH_3), 42.8 (CH_2), 86.4 (C) 109.5 (CH), 119.9 (CH), 125.2 (CH), 127.1 (C), 128.0 (CH), 158.9 (C).

IR (ATR): 740, 1080, 1140, 1220, 1480, 1600 cm^{-1}.

EIMS *m/z*: 148 (M^+).

4-Methyl-2*H*-chromen-2-one (2p)[16n]

Silica gel chromatography (hexane/AcOEt = 5/1) gave 62.4 mg of the product (0.390 mmol, 78% yield).

White solid; mp 78-79 °C; R_f = 0.28 (hexane/AcOEt = 5/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.46 (s, 3H), 6.31 (s, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.53-7.56 (m, 1H), 7.62 (dd, *J* = 1.0, 7.8 Hz, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 18.6 (CH_3), 115.1 (CH), 117.1 (CH), 119.9 (C), 124.2 (CH), 124.5 (CH), 131.7 (CH), 152.3 (C), 153.5 (C), 160.8 (C).

IR (ATR): 750, 850, 1490, 1720 cm^{-1}.

EIMS *m/z*: 160 (M^+).

1-Ethyl-1*H*-indole (2q)[16o]

Silica gel chromatography (hexane/AcOEt = 4/1) gave 67.5 mg of the product (0.465 mmol, 93% yield).

Pale yellow oil; R_f = 0.56 (hexane/AcOEt = 4/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.47 (t, *J* = 7.3 Hz, 3H), 4.19 (q, *J* = 7.3 Hz, 2H), 6.49 (d, *J* = 2.9 Hz, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 7.12 (d, *J* = 2.9 Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 15.4 (CH_3), 40.9 (CH_2), 100.9 (CH), 109.2 (CH), 119.1 (CH), 120.9 (CH), 121.3 (CH), 126.9 (CH), 128.6 (C), 135.6 (C).

IR (ATR): 730, 1220, 1510 cm^{-1}.

EIMS *m/z*: 145 (M^+).

Quinoline (2r)[16p]

Silica gel chromatography (hexane/AcOEt = 3/1) gave 58.0 mg of the product (0.449 mmol, 90% yield). Yellow oil; R_f = 0.17 (hexane/AcOEt = 3/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.54-7.57 (m, 1H), 7.71-7.74 (m, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 8.12 (d, *J* = 8.3 Hz, 1H), 8.16 (d, *J* = 8.1, 1H), 8.93 (d, *J* = 2.7 Hz, 1H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 121.1 (CH), 126.6 (CH), 127.8 (CH) 128.3 (C), 129.47 (CH), 129.50 (CH), 136.1 (CH), 148.4 (C), 150.5 (CH).

IR (ATR): 800, 1500 cm^{-1}.

EIMS *m/z*: 129 (M^+).

2-*m*-Tolyl-2*H*-benzo[*d*][1,2,3]triazole (2s)[16q]

Silica gel chromatography (hexane/AcOEt = 10/1) gave 104 mg of the product (0.497 mmol, 99% yield).

White solid; mp 90-91°C; R_f = 0.45 (hexane/AcOEt = 10/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.50 (s, 3H), 7.27-7.29 (m, 1H), 7.42-7.46 (m, 3H), 7.93-7.95 (m, 2H), 8.15 (d, *J* = 8.1 Hz, 1H), 8.20 (s, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.5 (CH_3), 117.8 (CH), 118.3 (CH), 121.1 (CH), 127.1 (CH), 129.3 (CH), 129.8 (CH), 139.6 (C), 140.3 (C), 144.9 (C).

IR (ATR): 680, 740, 870, 1500, 1590, 3070 cm^{-1}.

EIMS *m/z*: 209 (M^+).

2-Phenylbenzo[*d*]thiazole (2t)[16r]

Silica gal chromatography (hexane/benzene = 20/1) gave 105 mg of the product (0.497 mmol, 99% yield).

White solid; mp 112-113 °C; R_f = 0.17 (hexane/benzene = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (t, *J* = 7.8 Hz, 1H), 7.49-7.51 (m, 4H), 7.92 (d, *J* = 7.8 Hz, 1H), 8.08-8.12 (m, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 121.7 (CH), 123.3 (CH), 125.2 (CH) 126.4 (CH), 127.6 (CH), 129.1 (CH), 131.0 (CH), 133.7 (C), 135.1 (C), 154.2 (C), 168.2 (C).

IR (ATR): 680, 760, 1220, 1480 cm^{-1}.

EIMS *m/z*: 211 (M^+).

1-(4-Phenylpiperazin-1-yl)ethanone (2u)[16s]

The reaction was conducted on 8.0 mmol scale. Silica gel chromatography (AcOEt/benzene = 1/1) gave 1.62 g of the product (7.93 mmol, 99% yield).

White solid; mp 87-88 °C; R_f = 0.27 (AcOEt/benzene = 1/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.15 (s, 3H), 3.15 (t, *J* = 5.0 Hz, 2H), 3.19 (t, *J* = 5.0 Hz, 2H), 3.63 (t, *J* = 5.0 Hz, 2H), 3.78 (t, *J* = 5.0 Hz, 2H) 6.89-6.95 (m, 3H), 7.27-7.31 (m, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.4 (CH_3), 41.3 (CH_2), 46.2 (CH_2), 49.4 (CH_2), 49.7 (CH_2), 116.6 (CH), 120.5 (CH), 129.2 (CH), 150.9 (C), 169.0 (C).

IR (ATR): 700, 770, 1160, 1220, 1600, 1620, 3060 cm^{-1}.

EIMS *m/z*: 204 (M^+).

***N*,*N*-Diethyl-3-methoxybenzamide (2v')**[16t]

Silica gel chromatography (hexane/AcOEt = 2/1) gave 103 mg of the product (0.497 mmol, 99% yield).

Yellow oil; R_f = 0.19 (hexane/AcOEt = 2/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11-1.25 (m, 6H), 3.22-3.29 (m, 2H), 3.51-3.58 (m, 2H), 3.82 (s, 3H), 6.91-6.94 (m, 3H), 7.30 (t, *J* = 7.8 Hz, 1H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 12.7 (CH_3), 14.1 (CH_3), 39.1 (CH_2), 43.1 (CH_2), 55.2 (CH_3), 111.6 (CH), 115.0 (CH), 118.4 (CH), 129.5 (CH),138.6 (C), 159.6 (C), 171.0 (C).

IR (ATR): 750, 790, 1040, 1240, 1580, 1630 cm^{-1}.

EIMS *m/z*: 207 (M^+).

Compound 1; General Procedure

A round-bottom flask was charged with NaH (60% in mineral oil, 480 mg, 12.0 mmol), and a phenol (10.0 mmol) in dry DME (12 mL) was added at 0 °C. The reaction mixture was stirred at room temperature for 10 min. Dimethylsulfamoyl chroride (1.72 g, 12.0 mmol) in dry DME (3 mL) was added at 0 °C, and the reaction was allowed to stir at room temperature for 15 h. After water (10 mL) was added, the solvent was removed. The residue was dissolved in Et_2O (10 mL) and washed with 1M KOH (15 mL) and water (10 mL). After the aqueous layers were extracted with Et_2O (30mL x 3), the organic layers were washed with brine (10 mL) and dried over Na_2SO_4. Concentration and purification through silica gel column chromatography gave desired product **1**.

Biphenyl-2,2'-diyl bis(dimethylsulfamate) (1d)

This compound was prepared from 2,2'-dihydroxybiphenyl (559 mg, 3.0 mmol). Silica gel chromatography (hexane/AcOEt = 3/1) gave 1.17 g of the product (2.92 mmol, 97% yield).

White solid; 137-139 °C; R_f = 0.11 (hexane/AcOEt = 3/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.59 (s, 12H), 7.33 (t, *J* = 8.1 Hz, 2H), 7.40-7.43 (m, 4H), 7.56 (d, *J* = 8.1 Hz, 2H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 38.1 (CH_3), 120.8 (CH), 126.1 (CH), 129.5 (CH) 130.0 (C), 132.1 (CH), 147.8 (C).

IR (ATR): 750, 840, 1190, 1360, 1500, 3070 cm^{-1}.

HRMS (FAB) *m/z* $[M+H]^+$ Calcd for $C_{16}H_{21}N_2O_6S_2$: 401.0841; Found: 401.0841.

4-(Benzylamino)phenyl dimethylsulfamate (1e)

This compound was prepared from 4-(benzylamino)phenol[18] (1.40 g, 7.0 mmol). Silica gel chromatography (benzene) gave 2.05 g of the product (6.69 mmol, 96% yield).

White solid; mp 113-114 °C; R_f = 0.32 (benzene).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.94 (s, 6H), 4.11 (brs, 1H), 4.31 (d, *J* = 5.4 Hz, 2H), 6.59 (d, *J* = 8.8 Hz, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 7.28-7.31 (m, 1H), 7.35-7.36 (m, 4H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 38.7 (CH_3), 48.4 (CH_2), 113.1 (CH), 122.7 (CH), 127.38 (CH), 127.44 (CH), 128.7 (CH), 138.8 (C), 141.3 (C), 146.8 (C).

IR (ATR): 790, 830, 1340, 1610, 3420 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{15}H_{18}N_2O_3S$: 306.1038; Found: 306.1038.

2-Propionylphenyl dimethylsulfamate (1f)

This compound was prepared from 1-(2-hydroxyphenyl)propan-1-one (3.00 g, 20 mmol). Silica gel chromatography (hexane/AcOEt = 4/1) gave 3.18 g of the product (12.4 mmol, 62% yield).

Colorless oil; R_f = 0.26 (hexane/AcOEt = 4/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.1 Hz, 3H), 2.97 (q, *J* = 7.1 Hz, 2H), 2.98 (s, 6H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.45-7.52 (m, 2H), 7.59 (d, *J* = 7.6 Hz, 1H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 8.0 (CH_3), 35.9 (CH_2), 38.6 (CH_3), 123.2 (CH), 126.7 (CH), 129.1 (CH), 132.2 (CH), 133.9 (C), 146.9 (C), 202.1 (C).

IR (ATR): 750, 1370, 1480, 1700 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{11}H_{15}NO_4S$: 257.0722; Found: 257.0722.

4-(*N*-Ethylacetamido)phenyl dimethylsulfamate (1i)

A round-bottom flask was charged with NaH (60% in mineral oil, 120 mg, 3.0 mmol). After 4-acetamidophenyl dimethylsulfamate (**1j**)[15b] (645 mg, 2.5 mmol) in dry DMF (3.25 mL) was added at 0 °C, the reaction mixture was stirred at 0 °C for 30 min. Ethyl iodide (437 mg, 2.8 mmol) was added, and the mixture was stirred at room temperature for 1 h. After water was added, the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/AcOEt = 1/1) gave 549 mg of the product (1.92 mmol, 77% yield).

White solid; mp 62-64 °C; R_f = 0.15 (hexane/AcOEt = 1/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11 (t, *J* = 6.8 Hz, 3H), 1.83 (s, 3H), 3.03 (s, 6H), 3.74 (q, *J* = 6.8 Hz, 2H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 12.9 (CH_3), 22.7 (CH_3), 38.6 (CH_3), 43.8 (CH_2) 122.9 (CH), 129.6 (CH), 141.3 (C), 149.4 (C), 169.8 (C).

IR (ATR): 770, 1150, 1370, 1500, 1650, 3060 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{12}H_{18}N_2O_4S$: 286.0987; Found: 286.0987.

4-(2-(3-Methylbut-2-enyloxy)ethyl)phenyl dimethylsulfamate (1k)

A round-bottom flask was charged with NaH (60% in mineral oil, 300 mg, 7.5 mmol), and then dry THF (15 mL) was added. After 4-(2-hydroxyethyl)phenyl dimethylsulfamate (**1n**) (1.23 g, 5.0 mmol) in dry THF (5.0 mL) was added at 0 °C, the mixture was stirred at room temperature for 1 h. 1-Bromo-3-methyl-2-butene (745 mg, 5.0 mmol) was added, and the reaction mixture was stirred at room temperature for 16 h. After water was added, the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/AcOEt = 5/1) to give 684 mg of the product (2.18 mmol, 44% yield).

Colorless oil; R_f = 0.25 (hexane/AcOEt = 5/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.66 (s, 3H), 1.74 (s, 3H), 2.89 (t, *J* = 7.1 Hz, 2H), 2.97 (s, 6H), 3.61 (t, *J* = 7.1 Hz, 2H), 3.96 (d, *J* = 6.9 Hz, 2H), 5.31-5.35 (m, 1H), 7.18-7.26 (m, 4H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 18.0 (CH_3), 25.8 (CH_3), 35.7 (CH_2), 38.7 (CH_3), 67.3 (CH_2), 70.7 (CH_2), 120.9 (CH), 121.5 (CH), 130.1 (CH), 137.1 (C), 137.8 (C), 148.5 (C).

IR (ATR): 740, 810, 1150, 1370, 1500 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{15}H_{23}NO_4S$: 313.1348; Found: 313.1348.

4-(3-Hydroxy-3-methylbutyl)phenyl dimethylsulfamate (1l)

4-(3-Oxobutyl)phenyl dimethylsulfamate (**1l'**) was prepared from 4-(4-hydroxyphenyl)-2-butanone (3.28 g, 20 mmol) according to the typical procedure for sulfamate preparation. Silica gel chromatography (benzene) gave 3.49 g of 4-(3-oxobutyl)phenyl dimethylsulfamate (**1l'**) (12.9 mmol, 64% yield).

White solid; mp 60-61 °C; R_f = 0.24 (benzene).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.15 (s, 3H), 2.75 (t, *J* = 7.3 Hz, 2H), 2.89 (t, *J* = 7.3 Hz, 2H), 2.97 (s, 6H), 7.18-7.21 (m, 4H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 28.9 (CH_2), 30.1 (CH_3), 38.7 (CH_3), 44.9 (CH_2), 121.7 (CH), 129.6 (CH), 139.7 (C), 148.4 (C), 207.5 (C).

IR (ATR): 790, 850, 1360, 1500, 1710 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{12}H_{17}NO_4S$: 271.0878; Found: 271.0878.

A round-bottom flask was charged with 4-(3-oxobutyl)phenyl dimethylsulfamate (**1l'**) (1.09 g, 4.0 mmol), and then dry Et_2O (12 mL) was added. CH_3MgBr (3.0 M in Et_2O, 8.0 mL, 24 mmol) was added dropwise at 0 °C, and the reaction mixture was stirred at room temperature for 1.5 h. After brine was added, the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/AcOEt = 1/1) to give 1.14 g of the product **1l** (3.97 mmol, 99% yield).

White solid; mp 69-70 °C; R_f = 0.26 (hexane/AcOEt = 1/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.23 (s, 1H), 1.29 (s, 6H), 1.75-1.79 (m, 2H), 2.69-2.73 (m, 2H), 2.97 (s. 6H), 7.18-7.22 (m, 4H).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 29.4 (CH_3), 30.1 (CH_2), 38.7 (CH_3), 45.6 (CH_2), 70.8 (C), 121.6 (CH), 129.5 (CH), 141.2 (C), 148.2 (C).

IR (ATR): 770, 1370, 1500, 3300 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{13}H_{21}NO_4S$: 287.1191; Found: 287.1191.

4-(3-Hydroxybutyl)phenyl dimethylsulfamate (1m)

To 4-(3-oxobutyl)phenyl dimethylsulfamate (**1l'**) (814 mg, 3.0 mmol) in H_2O/dioxane (3.0 mL/3.0 mL), $NaBH_4$ (1.70 g, 45 mmol) was added. The reaction mixture was stirred for 13 h at room temperature. The resulting mixture was diluted with 25% HCl to acidify to pH 7.0 at 0 °C and extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography (benzene/AcOEt = 2/1) to give 802 mg of the product (2.93 mmol, 98% yield).

White solid; mp 48-49 °C; R_f = 0.28 (hexane/AcOEt = 2/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.24 (d, *J* = 6.1 Hz, 3H), 1.31 (d, *J* = 4.7 Hz, 1H), 1.72-1.78 (m, 2H), 2.64-2.71 (m, 1H), 2.74-2.80 (m, 1H), 2.97 (s, 6H), 3.80-3.84 (m, 1H), 7.18-7.22 (m, 4H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 23.7 (CH_3), 31.5 (CH_2), 38.7 (CH_3), 40.7 (CH_2), 67.3 (CH), 121.6 (CH), 129.6 (CH), 140.8 (C), 148.2 (C).

IR (ATR): 740, 970, 1170, 1500, 3240 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{12}H_{19}NO_4S$: 273.1035; Found: 273.1035.

4-(2-Hydroxyethyl)phenyl dimethylsulfamate (1n)

This compound was prepared from 4-hydroxyphenylethanol (2.07 g, 15 mmol). Silica gel chromatography (hexane/AcOEt = 1/2) gave 3.21 g of the product (13.1 mmol, 87% yield).

Colorless oil; R_f = 0.39 (hexane/AcOEt = 1/2).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 5.6 Hz, 1H), 2.88 (t, *J* = 6.4 Hz, 2H), 2.98 (s, 6H), 3.85-3.88 (m, 2H), 7.22-7.26 (m, 4H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 38.5 (CH_2), 38.7 (CH_3), 63.5 (CH_2), 121.8 (CH), 130.3 (CH), 137.3 (C), 148.7 (C).

IR (ATR): 780, 1360, 1500, 3340 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{10}H_{15}NO_4S$: 245.0722; Found: 245.0722.

4-Methyl-2-oxo-2*H*-chromen-7-yl dimethylsulfamate (1p)

A round-bottom flask was charged with 4-methylumbelliferone (881 mg, 5.0 mmol) and DMAP (30.5 mg, 0.25 mmol), and then dry CH_2Cl_2 (17.5 mL) was added. After triethylamine (607 mg, 6.0 mmol) was added, the mixture was stirred at room temperature for 10 min. Dimethylsulfamoyl chloride (862 mg, 6.0 mmol) was added and the reaction mixture was stirred at room temperature for 16 h. After water was added, the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/AcOEt = 1/1) to give 1.10 g of the product (3.88 mmol, 78% yield).

White solid; mp 144-145 °C; R_f = 0.27 (hexane/AcOEt = 1/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.45 (s, 3H), 3.03 (s, 6H), 6.30 (s, 1H), 7.25-7.29 (m, 2H), 7.63 (d, *J* = 8.8 Hz, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 18.8 (CH_3), 38.8 (CH_3), 110.3 (CH), 114.9 (CH), 117.8 (CH), 118.4 (C), 125.8 (CH), 151.7 (C), 152.4 (C), 154.2 (C), 160.2 (C).

IR (ATR): 770, 820, 1360, 1610, 1720 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{12}H_{13}NO_5S$: 283.0514; Found: 283.0514.

1-Ethyl-1*H*-indol-4-yl dimethylsulfamate (1q)

1*H*-Indol-4-yl dimethylsulfamate was prepared from 4-hydroxyindole (1.07 g, 8.0 mmol) according to the typical procedure for sulfamate synthesis. Silica gel chromatography (hexane/AcOEt = 4/1) gave 1.51 g of 1*H*-indol-4-yl dimethylsulfamate (6.28 mmol, 79% yield).

White solid; mp 116-117 °C; R_f = 0.27 (hexane/AcOEt = 4/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.00 (s, 6H), 6.71-6.72 (m, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.24 (t, *J* = 2.7 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 8.29 (brs, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 38.8 (CH_3), 99.7 (CH), 109.9 (CH), 112.2 (CH), 121.6 (C), 122.1 (CH), 124.8 (CH), 137.9 (C), 143.0 (C).

IR (ATR): 780, 1340, 1500, 3410 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{10}H_{12}N_2O_3S$: 240.0569; Found: 240.0570.

A round-bottom flask was charged with NaH (60% in mineral oil, 90.0 mg, 2.25 mmol), and then 1*H*-indol-4-yl dimethylsulfamate (360 mg, 1.5 mmol) in dry THF (2.25 mL) was added at 0 °C. The mixture was stirred at room temperature for 30 min. Ethyl iodide (281 mg, 1.8 mmol) was added dropwise at 0 °C, and the reaction mixture was stirred at room temperature for 3 h. After water was added, the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/AcOEt = 4/1) to give 260 mg of the product (0.969 mmol, 65% yield).

White solid; mp 77-79 °C; R_f = 0.33 (hexane/AcOEt = 4/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.48 (t, *J* = 7.3 Hz, 3H), 3.00 (s, 6H), 4.18 (q, *J* = 7.3 Hz, 2H), 6.64 (d, *J* = 2.9 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 7.15-7.19 (m, 2H), 7.26-7.27 (m, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 15.3 (CH_3), 38.8 (CH_3), 41.3 (CH_2), 98.1 (CH), 108.1 (CH), 111.6 (CH), 121.4 (CH), 122.1 (C), 127.6 (CH), 137.8 (C), 143.1 (C).

IR (ATR): 780, 1350, 1500 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{12}H_{16}N_2O_3S$: 268.0882; Found: 268.0881.

2-(2*H*-Benzo[*d*][1,2,3]triazol-2-yl)-4-methylphenyl dimethylsulfamate (1s)

This compound was prepared from 2-(2-hydroxy-5-methylphenyl)benzotriazole (676 mg, 3.0 mmol). Silica gel chromatography (hexane/AcOEt = 4/1) gave 713 mg of the product (2.15 mmol, 72% yield).

White solid; mp 144-146 °C; R_f = 0.32 (hexane/AcOEt = 4/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.46 (s, 3H), 2.73 (s, 6H), 7.35 (dd, *J* = 1.5, 8.3 Hz, 1H), 7.44-7.46 (m, 2H), 7.59 (d, *J* = 8.6 Hz, 1H), 7.75 (d, *J* = 1.2 Hz, 1H), 7.94-7.96 (m, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 20.7 (CH_3), 38.4 (CH_3), 118.4 (CH), 123.8 (CH), 127.4 (CH), 127.5 (CH), 131.3 (CH), 133.1 (C), 137.6 (C), 141.0 (C), 145.0 (C).

IR (ATR): 750, 830, 970, 1170, 1360, 1600, 3060 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{15}H_{16}N_4O_3S$: 332.0943; Found: 332.0944.

2-(Benzo[*d*]thiazol-2-yl)phenyl dimethylsulfamate (1t)

This compound was prepared from 2-(2-hydroxyphenyl)benzothiazole (682 mg, 3.0 mmol). Silica gel chromatography (hexane/AcOEt = 5/1) gave 477 mg of the product (1.43 mmol, 48% yield).

White solid; mp 77-78 °C; R_f = 0.15 (hexane/AcOEt = 5/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.91 (s, 6H), 7.40-7.45 (m, 2H), 7.51-7.55 (m, 2H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 8.12 (d, *J* = 8.1 Hz, 1H), 8.26 (dd, *J* = 1.7, 7.8 Hz, 1H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 38.6 (CH_3), 121.5 (CH), 122.1 (CH), 123.4 (CH), 125.5 (CH), 126.3 (C), 126.4 (CH), 126.7 (CH), 131.1 (CH), 131.7 (CH), 135.9 (C), 148.2 (C), 152.8 (C), 162.3 (C).

IR (ATR):730, 750, 970, 1150, 1370 cm^{-1}.

HRMS (FAB) *m/z* $[M+H]^+$ Calcd for $C_{15}H_{15}N_2O_3S_2$: 335.0524; Found: 335.0523.

4-(4-Acetylpiperazin-1-yl)phenyl diethylsulfamate (1ub)

Diethylsulfamoyl chloride was prepared according to the literature.[19] To a solution of Et_2NH (16.1 g, 220 mmol) in dry Et_2O (55 mL), sulfuryl chloride (13.5 g, 100 mmol) was added dropwise at -15 °C. The mixture was stirred at -15 °C for 80 min and at room temperature for 2.5 h. The resulting mixture was filtered. Concentration and purification through silica gel chromatography (hexane/AcOEt = 3/1) to give 12.3 g of diethylsulfamoyl chloride (71.7 mmol, 72% yield).

Colorless oil; R_f = 0.68 (hexane/AcOEt = 3/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.1 Hz, 6H), 3.43 (q, *J* = 7.1 Hz, 4H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 12.6 (CH_3), 45.0 (CH_2).

IR (ATR): 1170, 1200, 1380, 1450 cm^{-1}.

MS data was not obtained due to the instability.

The compound **1ub** was prepared from 1-acetyl-4-(4-hydroxyphenyl)-piperazine (1.10 g, 5.0 mmol) with diethylsulfamoyl chloride. Silica gel chromatography (AcOEt/benzene = 5/1) gave 1.39 g of the product (3.91 mmol, 78% yield).

White solid; mp 110-112 °C; R_f = 0.17 (AcOEt/benzene = 5/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.1 Hz, 6H), 2.14 (s, 3H), 3.12 (t, *J* = 4.9 Hz, 2H), 3.16 (t, *J* = 4.9 Hz, 2H), 3.36 (q, *J* = 7.1 Hz, 4H), 3.62 (t, *J* = 4.9 Hz, 2H), 3.77 (t, *J* = 4.9 Hz, 2H), 6.89 (d, *J* = 9.1 Hz, 2H), 7.18 (d, *J* = 9.1 Hz, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 13.6 (CH_3), 21.3 (CH_3), 41.2 (CH_2), 43.4 (CH_2), 46.1 (CH_2), 49.4 (CH_2), 49.8 (CH_2), 117.3 (CH), 122.7 (CH), 143.6 (C), 149.5 (C), 169.0 (C).

IR (ATR): 750, 1360, 1500, 1630 cm^{-1}.

HRMS (EI) *m/z* (M$^+$) Calcd for $C_{16}H_{25}N_3O_4S$: 355.1566; Found: 355.1566.

4-(4-Acetylpiperazin-1-yl)phenyl piperidine-1-sulfonate (1uc)

Piperidinesulfonyl chloride was prepared according to the literature.[19] To a solution of piperidine (3.75 g, 44 mmol) in dry Et_2O (11 mL), sulfuryl chloride (2.70 g, 20 mmol) was added dropwise at -15 °C. The mixture was stirred at -15 °C for 80 min and at room temperature for 2.5 h. The resulting mixture was filtered. Concentration and purification through silica gel chromatography (benzene) to give 1.65 g of piperidinesulfonyl chloride (8.98 mmol, 45% yield).

Colorless oil; R_f = 0.50 (benzene).

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60-1.61 (m, 2H), 1.76-1.82 (m, 4H), 3.18-3.44 (m, 4H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 22.8 (CH_2), 24.3 (CH_2), 48.7 (CH_2).

IR (ATR): 1180, 1390, 1450 cm^{-1}.

MS data was not obtained due to the instability.

The compound **1uc** was prepared from 1-acetyl-4-(4-hydroxyphenyl)-piperazine (1.10 g, 5.0 mmol) with piperidinesulfonyl chloride. Silica gel chromatography (AcOEt/benzene = 5/1) gave 563 mg of the product (1.53 mmol, 31% yield).

White solid; mp 151-153 °C; R_f = 0.17 (AcOEt/benzene = 5/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.57-1.60 (m, 2H), 1.65-1.69 (m, 4H), 2.14 (s, 3H), 3.13 (t, *J* = 5.1 Hz, 2H), 3.16 (t, *J* = 5.1 Hz, 2H), 3.36 (t, *J* = 5.1 Hz, 4H), 3.62 (t, *J* = 5.1 Hz, 2H), 3.77 (t, *J* = 5.1 Hz, 2H), 6.90 (d, *J* = 9.1 Hz, 2H), 7.19 (d, *J* = 9.1 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.3 (CH_3), 23.4 (CH_2), 25.0 (CH_2), 41.2 (CH_2), 46.1 (CH_2), 47.9 (CH_2), 49.4 (CH_2), 49.8 (CH_2), 117.3 (CH), 122.6 (CH), 143.5 (C), 149.5 (C), 168.9 (C).

IR (ATR): 760, 1350, 1500, 1640 cm^{-1}.

HRMS (EI) *m/z* (M$^+$) Calcd for $C_{17}H_{25}N_3O_4S$: 367.1566; Found: 367.1567.

4-(4-Acetylpiperazin-1-yl)phenyl 2-methylpiperidine-1-sulfonate (1ud)

2-Methylpiperidine-1-sulfonyl chloride was prepared according to the literature.[19] To a solution of 2-methylpiperidine (10.9 g, 110 mmol) in dry Et_2O (27.5 mL), sulfuryl chloride (6.75 g, 50 mmol) was added dropwise at -15 °C. The mixture was stirred at -15 °C for 80 min and at room temperature for 2.5 h. The resulting mixture was filtered. Concentration and purification through silica gel chromatography (hexane/AcOEt = 2/1) to give 7.92 g of 2-methylpiperidine-1-sulfonyl chloride (40.1 mmol, 80% yield).

Yellow oil; R_f = 0.57 (hexane/AcOEt = 2/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.37 (d, *J* = 6.9 Hz, 3H), 1.58-1.62 (m, 1H), 1.63-1.69 (m, 2H), 1.72-1.76 (m, 2H), 1.90-1.97 (m, 1H), 3.14-3.20 (m, 1H), 3.80-3.83 (m, 1H), 4.37-4.42 (m, 1H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 13.7 (CH_3), 17.5 (CH_2), 24.1 (CH_2), 30.1 (CH_2), 42.7 (CH_2), 52.4 (CH).

IR (ATR): 1170, 1210, 1380, 1440 cm^{-1}.

MS data was not obtained due to the instability.

The compound **1ud** was prepared from 1-acetyl-4-(4-hydroxyphenyl)-piperazine (5.51 g, 25 mmol) with 2-methylpiperidine-1-sulfonyl chloride. Silica gel chromatography (AcOEt/benzene = 1/1 to 5/1) gave 5.05 g of the product (13.2 mmol, 53% yield).

White solid; mp 85-87 °C; R_f = 0.22 (AcOEt/benzene = 5/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (d, *J* = 6.9 Hz, 3H), 1.52-1.68 (m, 5H), 1.75-1.84 (m, 1H), 2.14 (s, 3H), 3.11-3.18 (m, 5H), 3.62 (t, *J* = 5.3 Hz, 2H), 3.68-3.71 (m, 1H), 3.77 (t, *J* = 5.3 Hz, 2H), 4.19-4.25 (m, 1H), 6.89 (d, *J* = 9.2 Hz, 2H), 7.19 (d, *J* = 9.2 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 15.3 (CH_3), 18.0 (CH_2), 21.3 (CH_3), 24.9 (CH_2), 30.2 (CH_2), 41.2 (CH_2), 41.8 (CH_2), 46.1 (CH_2), 49.5 (CH_2), 49.9 (CH_2), 50.6 (CH), 117.4 (CH), 122.6 (CH), 143.8 (C), 149.4 (C), 169.0 (C).

IR (ATR): 750, 1360, 1500, 1640 cm^{-1}.

HRMS (EI) *m/z* (M$^+$) Calcd for $C_{18}H_{27}N_3O_4S$: 381.1722; Found: 381.1722.

4-(4-Acetylpiperazin-1-yl)phenyl diisopropylsulfamate (1ue)

Diisopropylsulfamoyl chloride was prepared according to the literature.[19] To a solution of *i*-Pr_2NH (22.3 g, 220 mmol) in dry Et_2O (55 mL), sulfuryl chloride (13.5 g, 100 mmol) was added dropwise at -15 °C. The mixture was stirred at -15 °C for 80 min and at room temperature for 2.5 h. The resulting mixture was filtered. Concentration and purification through silica gel chromatography (hexane/AcOEt = 2/1) to give 2.84 g of diisopropylsulfamoyl chloride (14.2 mmol, 14% yield).

Yellow solid; mp 43-45 °C; R_f = 0.63 (hexane/AcOEt = 2/1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (d, *J* = 6.5 Hz, 12H), 4.01 (septet, *J* = 6.5 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 20.4 (CH_3), 51.6 (CH).

IR (ATR): 1180, 1200, 1360, 1460 cm^{-1}.

MS data was not obtained due to the instability.

The compound **1ue** was prepared from 1-acetyl-4-(4-hydroxypheny)-piperazine (2.20 g, 10 mmol) with diisopropylsulfamoyl chloride. Silica gel chromatography (AcOEt/benzene = 1/1 to 5/1) gave 608 mg of the product (1.59 mmol, 16% yield).

White solid; mp 153-155 °C; R_f = 0.20 (AcOEt/benzene = 5/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (d, *J* = 6.9 Hz, 12H), 2.14 (s, 3H), 3.10-3.16 (m, 4H), 3.62 (t, *J* = 4.8 Hz, 2H), 3.77 (t, *J* = 4.8 Hz, 2H), 3.87-3.94 (m, 2H), 6.89 (d, *J* = 8.9 Hz, 2H), 7.20 (d, *J* = 8.9 Hz, 2H).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 21.3 (CH_3), 21.4 (CH_3), 41.2 (CH_2), 46.1 (CH_2), 49.6 (CH_2), 49.7 (CH), 50.0 (CH_2), 117.5 (CH), 122.7 (CH), 143.9 (C), 149.3 (C), 168.9 (C).

IR (ATR): 750, 1340, 1510, 1640 cm^{-1}.

HRMS (EI) *m/z* (M$^+$) Calcd for $C_{18}H_{29}N_3O_4S$: 383.1879; Found: 383.1879.

Synthesis of 1v' via the *ortho*-functionalization of 1v

To a solution of 4-methoxyphenyl diethylsulfamate (**1v**)[10d] (778 mg, 3.0 mmol) and TMEDA (453 mg, 3.9 mmol) in dry THF (15 mL), *sec*-BuLi (1.06 M in cyclohexane, 3.7 mL, 3.9 mmol) was added dropwise at -97 °C. After stirring at -97 °C for 1 h, $ClC(O)NEt_2$ (569 mg, 4.2 mmol) was added dropwise. The mixture was allowed to warm to room temperature over 15 min and stirred at room temperature for 2 h. The resulting mixture was quenched with saturated aqueous NH_4Cl solution and diluted with H_2O and AcOEt. The aqueous layer was extracted with AcOEt. The combined organic layers were washed with brine and dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/AcOEt = 1/1) to give 1.01 g of the product (2.82 mmol, 94% yield).

Colorless oil; R_f = 0.27 (hexane/AcOEt = 1/1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.10 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 6H), 1.25 (t, *J* = 7.1 Hz, 3H), 3.15-3.41 (m, 7H), 3.66-3.71 (m, 1H), 3.80 (s, 3H), 6.78 (d, *J* = 2.9 Hz, 1H), 6.90 (dd, *J* = 2.9, 9.1 Hz, 1H), 7.42 (d, *J* = 9.1 Hz, 1H).

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 12.7 (CH_3), 13.6 (CH_3), 13.8 (CH_3), 38.9 (CH_2), 43.1 (CH_2), 43.6 (CH_2), 55.7 (CH_3), 112.4 (CH), 115.2 (CH), 123.7 (CH), 131.7 (C), 139.5 (C), 157.4 (C), 166.7 (C).

IR (ATR): 740, 1020, 1210, 1370, 1630 cm^{-1}.

HRMS (EI) *m/z* (M^+) Calcd for $C_{16}H_{26}N_2O_5S$: 358.1562; Found: 358.1562.

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Supporting Information

Supporting information for this article is available online. Copies of the ^{1}H and ^{13}C NMR spectra were included.

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