

Phosphotungstic Acid Catalyzed Amidation of Alcohols

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Keywords: Amidation / C–N bond formation / Heteropoly acids / Nucleophilic substitution / Catalyst recycling

Mild nucleophilic substitution reactions of benzhydrylic, benzylic, allylic, and simple aliphatic alcohols with sulfonamides, benzamide, and 4-nitroaniline in the presence of 12-phosphotungstic acid as an efficient, eco-friendly, cheap, and air- and moisture-tolerant catalyst for the construction of C–N bonds has been investigated. The amine derivatives were

obtained in good yields (up to 98 %). The reusable nature of the 12-phosphotungstic acid makes this protocol more attractive.

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Introduction

Amination is a powerful method for the synthesis of amine derivatives, which are highly important intermediates because of their relevance to the synthesis of various pharmaceuticals and fine chemicals.^[1,2] Traditionally, amines are prepared by amination of halides or reduction of nitro compounds, nitriles, oximes, amides, etc. Amines are also extensively synthesized by the reductive amination of aldehydes and ketones.^[3] The amidation of alkenes or alcohols with nitriles, known as the Ritter reaction, is another protocol with broad applications,^[4a] and recent work on the Ritter reaction under catalytic Brønsted acid conditions has been reported.^[4b] A good alternative approach is the nucleophilic substitution of the hydroxy groups in alcohols with various amines. However, the alcohols should usually be preactivated by transformation into halides, carboxylates, carbonates, or other compounds in order to provide good leaving groups. As a result, these protocols produce large quantities of unwanted by-products.^[5] A more atom-economic, eco-friendly, and convenient strategy would thus be highly desirable.

Recently, many elegant procedures focusing on the direct amination of alcohols in the presence of transition metal catalysts have been developed.^[6] These processes have allowed the direct amination of allylic, benzylic, and propargylic alcohols with various nitrogen nucleophiles such as sulfonamides, carboxamides, carbamates, and anilines in the presence of palladium and ruthenium catalysts with ligands.^[7] Very recently, more and more groups have turned their attentions to acid-catalyzed direct *N*-alkylation with

alcohols. Various Lewis acids such as triflate salts,^[8a–8c] BiCl₃,^[8d] FeCl₃,^[8e] NaAuCl₄,^[8f] and MoCl₅,^[8g] as well as Brønsted acids such as *p*-toluenesulfonic acid or polymer-bound *p*-toluenesulfonic acid,^[9a,9b] proton-exchanged montmorillonite,^[9c,9d] and dodecylbenzenesulfonic acid^[9e] have been employed to affect this transformation.

On the other hand, heteropoly acids (HPAs) such as 12-phosphotungstic acid (PWA) and 12-phosphomolybdic acid (PMA) are promising solid acids, act as catalysts both under homogeneous and under heterogeneous conditions,^[10] and exhibit high activities and selectivities in various synthetically useful transformations. HPAs are often regarded as green catalysts in view of their easy commercial availability, stability, recyclability, and clean reaction processes.^[11] Being interested in HPA-catalyzed organic processes, here we report highly efficient nucleophilic substitutions, mediated by 12-phosphotungstic acid, of benzhydrylic, benzylic, and allylic alcohols, and also even of simple aliphatic alcohols, with sulfonamides, benzamide, and 4-nitroaniline.

Results and Discussion

In the choice of benzhydryl alcohol (**1a**) and *p*-toluenesulfonamide (**2a**) as the model substrates, the goal of the initial study was to investigate and compare the catalytic properties of PMA and PWA with regard to the nucleophilic substitution of **1a** with **2a**. The results are listed in Table 1. In 1,4-dioxane, PMA afforded product **3aa** in only 48% isolated yield after stirring at 80 °C for 12 h (Entry 1, Table 1). Much to our pleasure, though, PWA gave the desired product in nearly quantitative yield under the same reaction conditions (Entry 2).

Various solvents were screened (Entries 3–10, Table 1). Only a 61% yield of **3aa** was obtained on conducting the reaction in THF (Entry 3). Surprisingly, however, use of cyclohexane, an apolar solvent, furnished the product in 90% yield, whereas use of a linear aliphatic solvent gave a much

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Table 1. Catalyzed nucleophilic substitution of benzhydryl alcohol (**1a**) with *p*-toluenesulfonamide (**2a**).^[a]

$\text{Ph}-\text{CH}(\text{OH})-\text{Ph} + \text{TsNH}_2 \xrightarrow[\text{solvent, 80 } ^\circ\text{C, 12 h}]{\text{catalyst}} \text{Ph}-\text{CH}(\text{NHTs})-\text{Ph}$			
Entry	Catalyst	Solvent	Yield [%] ^[b]
1	PMA	1,4-dioxane	48
2	PWA	1,4-dioxane	98
3	PWA	THF	61
4	PWA	cyclohexane	90
5	PWA	<i>n</i> -heptane	31
6	PWA	DCE	22
7	PWA	DMSO	trace
8	PWA	DMF	trace
9	PWA	PEG-400	0
10	PWA	ethanol	0
11	PWA	neat	trace
12 ^[c]	PWA	1,4-dioxane	54
13 ^[d]	PWA	1,4-dioxane	15
14	ZnCl ₂	1,4-dioxane	76
15	Zn(OAc) ₂ ·2H ₂ O	1,4-dioxane	46
16	FeCl ₃	1,4-dioxane	90
17	CuSO ₄ ·5H ₂ O	1,4-dioxane	52
18	CeCl ₃ ·7H ₂ O	1,4-dioxane	86
19	SnCl ₄ ·2H ₂ O	1,4-dioxane	64
20	H ₂ SO ₄	1,4-dioxane	56

[a] Unless otherwise specified, all reactions were performed with **1a** (0.25 mmol), **2a** (0.25 mmol), and HPA (5 mg) or other employed catalyst (10 mol-%) in the indicated solvent (2.0 mL) at 80 °C for 12 h. [b] Isolated yield. [c] Reaction was carried out at 50 °C for 20 h. [d] Reaction was carried out at room temperature for 24 h.

lower yield (Entries 4–5). Only traces of product were observed when the reaction was performed in polar aprotic solvents such as DMSO and DMF (Entries 7–8). No reaction occurred when PEG-400 and ethanol were employed as solvents (Entries 9–10, Table 1), and only traces of product were observed when the reaction proceeded without any solvent (Entry 11). Decreasing the reaction temperature made the reaction sluggish and incomplete, furnishing only a 54% yield when performed at 50 °C for 20 h (Entry 12), and only a 15% yield when performed at room temperature for 24 h (Entry 13, Table 1). For comparison with the catalytic activity of PWA, Lewis and Brønsted acids were also examined as catalysts for the reaction between **1a** and **2a** in 1,4-dioxane at 80 °C (Entries 13–19, Table 1). ZnCl₂, Zn(OAc)₂·2H₂O, FeCl₃, CuSO₄·5H₂O, CeCl₃·7H₂O, and SnCl₄·2H₂O exhibited moderate to good catalytic properties (Entries 14–19, Table 1), but all were inferior to PWA (Entry 2). Use of sulfuric acid afforded a 56% yield of product **3aa** (Entry 20). The catalytic activity of PWA was superior to that of conventional Brønsted acids such as H₂SO₄, probably due to the stabilization of formed cationic intermediates (vide infra) by the soft bulky heteropolyanion of PWA.^[10a]

With the optimized reaction conditions at hand, the substrate generality was then investigated. To demonstrate the scope and potential for the PWA-catalyzed dehydrative amination of alcohols, benzhydrylic, benzylic, and allylic

alcohols were examined as the alcohol sources, together with various types of nitrogen nucleophiles including sulfonamides, benzamide, and 4-nitroaniline. The results are summarized in Table 2. When sulfonamides – including *p*-toluenesulfonamide, benzenesulfonamide, and methanesul-

Table 2. PWA-catalyzed nucleophilic substitution of alcohols with nitrogen nucleophiles.^[a]

$\text{R}^1-\text{CH}(\text{OH})-\text{R}^2 + \text{RNH}_2 \xrightarrow{\text{PWA}} \text{R}^1-\text{CH}(\text{NHR})-\text{R}^2$					
Entry	Alcohol	RNH ₂	Product	Yield [%] ^[b]	
1	1a	2a	3aa	98	
2	1a	2b	3ab	91	
3	1a	2c	3ac	93	
4	1a	2d	3ad	89	
5	1a	2e	3ae	97	
6	1b	2a	3ba	94	
7	1b	2b	3bb	93	
8	1b	2c	3bc	97	
9	1b	2d	3bd	90	
10	1b	2e	3be	92	
11 ^[c]	1c	2a	3ca	87	
12 ^[c]	1c	2b	3cb	90	
13	1c	2d	3cd	88	
14	1d	2a	3da	86	
15	1d	2d	3dd	70	
16	1e	2a	3ea	98	
17	1e	2b	3eb	94	
18	1e	2d	3ed	96	
19	1e	2e	3ee	91	
20	1f	2a	3fa	53	
21 ^[d]	1g	2a	3ga	68	
22 ^[e]	1h	2a	3ha	58	
23 ^[e]	1i	2a	3ia	66	

[a] Unless otherwise specified, all reactions were performed with alcohol (0.25 mmol), amine (0.25 mmol), and PWA (5 mg) in 1,4-dioxane (2.0 mL) at 80 °C for 12 h. [b] Isolated yield. [c] Reactions were performed with alcohol **1** (0.25 mmol), nitrogen nucleophile **2** (0.25 mmol), PWA (5 mg), and MS (4 Å, 500 mg) in 1,4-dioxane (2.0 mL) at 80 °C for 12 h. [d] Reactions were performed with cyclohexanol (2.5 mmol), *p*-toluenesulfonamide (**2a**, 0.25 mmol), and PWA (5 mg) without any solvent in a sealed tube at 120 °C for 3 h. [e] Reactions were performed with alcohol (2.5 mmol), *p*-toluenesulfonamide (**2a**, 0.25 mmol), and PWA (5 mg) without any solvent in a sealed tube at 140 °C for 4 h.

sulfonamide – were employed, the final products were obtained in excellent yields in the cases of benzhydrylic alcohols substituted either with electron-donating or with electron-withdrawing groups (Entries 1–3, 6–8, 11, 12, Table 2) and of 1-phenylethanol (Entry 14, Table 2). The substituents on the phenyl rings of benzhydrylic alcohols had little influence on the product yields, with the coupling products being obtained in yields of up to 98%. Benzamide was also utilized in reactions with benzhydrylic alcohols, and good yields (88–90%) were observed (Entries 4, 9, 13). When 1-phenylethanol was used, **3da** was obtained in a decreased yield (70%, Entry 15, Table 2). To our delight, 4-nitroaniline reacted smoothly and efficiently with benzhydrylic alcohols to afford the coupling products in 92–97% yields (Entries 5 and 10).

Furthermore, *trans*-1,3-diphenylprop-2-en-1-ol, which in Sanz's work was used to react with multifarious nucleophiles,^[9b] was examined with sulfonamides, benzamide, and 4-nitroaniline. The final products, [(*E*)-1,3-diphenylallyl]-amine derivatives, were obtained in high yields (91–98%, Entries 16–19, Table 2). However, when benzyl alcohol was employed, the reaction proceeded with lower yield (Entry 20).

Finally, simple aliphatic alcohols were examined to demonstrate the high efficiency of our protocol further. Much to our delight, cyclohexanol proved to be transformable into amide **3fa** with *p*-toluenesulfonamide (**2a**) in a sealed tube at 140 °C without any solvent (68% yield, Entry 20, Table 2). Acyclic aliphatic alcohols such as methanol and ethanol were also tolerated under similar reaction conditions, giving the final products in moderate yields with *p*-toluenesulfonamide **2a** (Entries 21 and 22, Table 2).

It is known that acids such as *p*-toluenesulfonic acid could promote ether formation from alcohols.^[8f] However, PWA preferably catalyzed C–N bond formation under our conditions. Even though small amounts of the corresponding ethers could be observed by TLC during the reaction processes, they had been converted into the amine products at the ends of the reactions, presumably thanks to the equilibria formed between the alcohols and ethers in the presence of PWA.^[8a,9d] It should be emphasized that the yields for all of the examined reactions were outstanding, and are higher than most of procedures described by others.^[8a,8b,8f,8g,9c,9d] As examples, the reactions of 1-phenylethanol with *p*-toluenesulfonamide and benzamide under our conditions afforded products **3da** and **3dd** in 86% and 70% yields, respectively, clearly better than the 60% reported for **3da** (catalyzed by proton-exchanged montmorillonite)^[9c,9d] and the 46% reported for **3dd** [catalyzed by Hf(OTf)₃].^[8a]

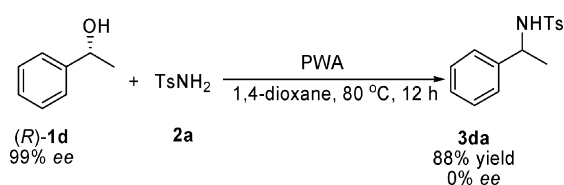
To demonstrate further the significant advantage of PWA – that it can be easily separated from substrates and products through filtration, owing to the insolubility of PWA in 1,4-dioxane – the recovered PWA was reused to catalyze the nucleophilic substitution of **1a** with **2a**. The results are summarized in Table 3. Clearly, the recovered PWA could be reused for at least four times with only slight loss of activity.

Table 3. Recycling of PWA for the nucleophilic substitution of **1a** with **2a**.^[a]

Run	1	2	3	4
Reaction time [h]	12	12	12	15
Yield [%] ^[b]	98	98	96	93

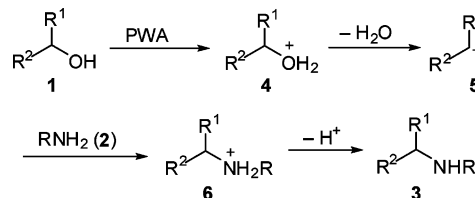
[a] All reactions were performed with **1a** (0.25 mmol), **2a** (0.25 mmol), and PWA (5 mg) in 1,4-dioxane (2.0 mL) at 80 °C. [b] Isolated yield.

To probe the reaction mechanism of this PWA-catalyzed amidation reaction, (*R*)-1-phenylethanol [(*R*)-**1d**, 99% *ee*] was treated with *p*-toluenesulfonamide (**2a**) under the typical reaction conditions (Scheme 1). After 12 h, product **3da** was isolable in 88% yield as a racemic mixture. No chirality transfer was observed.



Scheme 1. Amidation reaction of (*R*)-**1d** with **2a**.

Even though the exact reaction mechanism is not quite clear at the moment, the amidation of the investigated benzylic alcohols most likely proceeds by a pathway as shown in Scheme 2. In the presence of PWA, alcohol **1** is protonated to give oxonium ion **4**. Subsequent dehydration of **4** results in the formation of carbocation intermediate **5**. Quick binding of cation **5** with amine **2**, followed by the release of H⁺, generates the final amine derivative **3**. This S_N1 pathway is well supported by the above chirality-transfer experiment. However, the alternative S_N2 pathway might operate when simple aliphatic alcohols are employed. The corresponding carbocations of simple aliphatic alcohols should not be sufficiently stable, and hence difficult to form, under the present conditions, due to the lack of conjugation with adjacent π -bonding electrons.



Scheme 2. Possible pathway of the amidation process.

Conclusions

We have successfully employed 12-phosphotungstic acid as an efficient and reusable catalyst to promote nucleophilic substitution reactions of benzhydrylic, benzylic, and allylic alcohols, and also even of simple aliphatic alcohols, with sulfonamides, benzamide, and 4-nitroaniline, affording the

amine derivatives in yields of up to 98%. The very low catalyst loadings (ca. 0.6 mol-%) and recyclability of the 12-phosphotungstic acid made this protocol attractive.

Experimental Section

General: Reagents and solvents were obtained from commercial sources and were not further purified before use. All melting points are uncorrected. IR spectra were recorded in KBr pellets and are reported in cm^{-1} . ^1H NMR spectra were recorded at 300 MHz and are reported in parts per million (ppm) relative to tetramethylsilane ($\delta = 0.00$ ppm). ^{13}C NMR spectra were recorded at 75 MHz and are reported in parts per million (ppm) relative to CDCl_3 ($\delta = 77.0$ ppm). High-resolution mass spectra (HRMS) were recorded with the EI mode.

Typical Procedure for the Nucleophilic Substitution of Benzylic Alcohols with Nitrogen Nucleophiles: 12-Phosphotungstic acid (5 mg) was added to a solution of alcohol **1** (0.25 mmol) and nitrogen nucleophile **2** (0.25 mmol) in 1,4-dioxane (2 mL) in a test tube. The tube was sealed, and the mixture was stirred at 80 °C for 12 h. Upon completion, the reaction mixture was filtered to remove PWA, and the organic solution was concentrated to dryness in vacuo. The residue was separated on a silica gel column with petroleum ether/ethyl acetate (4:1) as the eluent to provide the desired product **3**: **3aa** (82.6 mg, 98%), **3ab** (73.5 mg, 91%), **3ac** (60.7 mg, 93%), **3ad** (63.9 mg, 89%), **3ae** (73.7 mg, 97%), **3ba** (87.2 mg, 94%), **3bb** (83.2 mg, 93%), **3bc** (71.6 mg, 97%), **3bd** (72.4 mg, 90%), **3be** (77.9 mg, 92%), **3ca** (76.3 mg, 87%), **3cb** (75.8 mg, 90%), **3cd** (66.2 mg, 88%), **3da** (59.1 mg, 86%), **3dd** (39.4 mg, 70%), **3ea** (88.9 mg, 98%), **3eb** (82.0 mg, 94%), **3ed** (75.1 mg, 96%), **3ee** (75.1 mg, 91%), and **3fa** (34.5 mg, 53%).

Typical Procedure for the Nucleophilic Substitution of Simple Aliphatic Alcohols with *p*-Toluenesulfonamide (2a): 12-Phosphotungstic acid (5 mg) was added to a solution of alcohol **1** (2.5 mmol) and *p*-toluenesulfonamide (**2a**, 0.25 mmol) in a test tube. The tube was sealed, and the mixture was stirred at a given temperature for a designated time (monitored by TLC). Upon completion, the reaction mixture was filtered to remove PWA, and the organic solution was concentrated to dryness in vacuo. The residue was separated on a silica gel column with petroleum ether/ethyl acetate (4:1) as the eluent to afford the desired product **3**: **3ga** (43.0 mg, 68%), **3ha** (26.4 mg, 58%), and **3ia** (32.6 mg, 66%).

Compounds **3aa**,^[8f] **3ab**,^[8f] **3ac**,^[12] **3ad**,^[13] **3ae**,^[8f] **3ba**,^[14] **3be**,^[8f,9d] **3da**,^[8a,15] **3dd**,^[8a,16] **3ea**,^[17] **3eb**,^[18] **3ed**,^[18] **3ee**,^[9b] **3fa**,^[19] **3ga**,^[15] **3ha**,^[20] and **3ia**^[21] had been reported previously, and their identities were confirmed by comparison of their melting points and spectroscopic data with the reported data. Characterization data for the new compounds **3bb**, **3bc**, **3bd**, **3ca**, **3cb**, and **3cd** are shown below.

***N*-[4-(4-Chlorophenyl)(phenyl)methyl]benzenesulfonamide (3bb):** ^1H NMR (300 MHz, CDCl_3): $\delta = 7.67$ (d, $J = 7.8$ Hz, 2 H), 7.50 (t, $J = 7.4$ Hz, 1 H), 7.36 (t, $J = 7.7$ Hz, 2 H), 7.22–7.17 (m, 5 H), 7.07–7.02 (m, 4 H), 5.58 (d, $J = 6.8$ Hz, 1 H), 5.05 (d, $J = 6.8$ Hz, 1 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): $\delta = 140.41$ (C), 140.08 (C), 139.04 (C), 133.77 (C), 132.73 (CH), 129.02 (2 × CH), 128.95 (4 × CH), 128.85 (2 × CH), 128.15, 127.43 (2 × CH), 127.30 (2 × CH), 60.97 ppm. IR (KBr): $\tilde{\nu} = 3251$, 3056, 1599, 1490, 1449, 1436, 1319, 1162, 1091, 1048, 927, 845, 804, 753, 725, 686, 591, 559, 479 cm^{-1} . HRMS (EI-TOF): m/z [$M - 2\text{H}$]⁺ calcd. for $\text{C}_{19}\text{H}_{14}^{35}\text{ClNO}_2\text{S}$ 355.0434; found 355.0435.

***N*-[4-(4-Chlorophenyl)(phenyl)methyl]methanesulfonamide (3bc):** ^1H NMR (300 MHz, CDCl_3): $\delta = 7.38$ –7.25 (m, 9 H), 5.74 (d, $J =$

7.1 Hz, 1 H), 5.04 (d, $J = 7.1$ Hz, 1 H), 2.70 (s, 3 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): $\delta = 140.36$ (C), 139.41 (C), 134.04 (C), 129.22 (2 × CH), 129.17 (2 × CH), 128.93 (2 × CH), 128.40 (CH), 127.47 (2 × CH), 60.79 (CH), 42.11 (CH) ppm. IR (KBr): $\tilde{\nu} = 3279$, 3058, 2928, 1598, 1491, 1449, 1320, 1153, 1092, 1054, 977, 906, 846, 808, 763, 744, 699, 560, 520 cm^{-1} . HRMS (EI-TOF): m/z [$M - 2\text{H}$]⁺ calcd. for $\text{C}_{14}\text{H}_{12}^{35}\text{ClNO}_2\text{S}$ 293.0277; found 293.0273.

***N*-[4-(4-Chlorophenyl)(phenyl)methyl]benzamide (3bd):** ^1H NMR (300 MHz, CDCl_3): $\delta = 7.82$ (d, $J = 7.2$ Hz, 2 H), 7.52 (t, $J = 7.2$ Hz, 1 H), 7.44 (t, $J = 7.5$ Hz, 2 H), 7.39–7.23 (m, 9 H), 6.61 (d, $J = 7.4$ Hz, 2 H), 6.43 (d, $J = 7.4$ Hz, 1 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): $\delta = 166.66$ (C=O), 141.12 (C), 140.14 (C), 134.18 (C), 133.52 (C), 131.94 (CH), 129.05 (2 × CH), 128.99 (2 × CH), 128.93 (2 × CH), 128.80 (2 × CH), 128.00 (CH), 127.69 (2 × CH), 127.19 (2 × CH), 57.09 (CH) ppm. IR (KBr): $\tilde{\nu} = 3254$, 3058, 3028, 1635, 1579, 1535, 1490, 1449, 1411, 1323, 1252, 1178, 1087, 1014, 931, 853, 839, 791, 751, 719, 695, 613, 582, 480 cm^{-1} . HRMS (EI-TOF): m/z [M]⁺ calcd. for $\text{C}_{20}\text{H}_{16}^{35}\text{ClNO}$ 321.0920; found 321.0914.

***N*-[Phenyl(*p*-tolyl)methyl]-*p*-toluenesulfonamide (3ca):** ^1H NMR (300 MHz, CDCl_3): $\delta = 7.56$ (d, $J = 8.1$ Hz, 2 H), 7.21–7.19 (m, 3 H), 7.15–7.08 (m, 4 H), 7.02 (d, $J = 8.1$ Hz, 2 H), 6.97 (d, $J = 8.1$ Hz, 2 H), 5.52 (d, $J = 6.9$ Hz, 1 H), 4.94 (d, $J = 6.9$ Hz, 1 H), 2.38 (s, 3 H), 2.28 (s, 3 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): $\delta = 143.26$ (C), 140.86 (C), 137.83 (C), 137.62 (C), 137.50 (CH), 129.46 (2 × CH), 129.37 (2 × CH), 128.64 (2 × CH), 127.62 (CH), 127.45 (4 × CH), 127.38 (2 × CH), 61.29 (CH), 21.60 (CH_3), 21.14 (CH_3) ppm. IR (KBr): $\tilde{\nu} = 3261$, 3058, 3028, 2922, 1599, 1513, 1493, 1433, 1321, 1163, 1093, 1045, 932, 905, 842, 810, 701, 677, 573 cm^{-1} . HRMS (EI-TOF): m/z [M]⁺ calcd. for $\text{C}_{21}\text{H}_{21}\text{NO}_2\text{S}$ 351.1293; found 351.1299.

***N*-[Phenyl(*p*-tolyl)methyl]benzenesulfonamide (3cb):** ^1H NMR (300 MHz, CDCl_3): $\delta = 7.67$ (d, $J = 7.2$ Hz, 2 H), 7.46 (t, $J = 7.5$ Hz, 1 H), 7.32 (t, $J = 7.7$ Hz, 2 H), 7.20–7.14 (m, 3 H), 7.11–7.07 (m, 2 H), 7.00 (d, $J = 8.1$ Hz, 2 H), 6.96 (d, $J = 8.1$ Hz, 2 H), 5.56 (d, $J = 6.9$ Hz, 1 H), 5.25 (d, $J = 6.9$ Hz, 1 H), 2.27 (s, 3 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): $\delta = 140.69$ (C), 140.60 (C), 137.69 (C), 137.54 (C), 132.44 (CH), 129.39 (2 × CH), 128.86 (2 × CH), 128.66 (2 × CH), 127.68 (CH), 127.44 (2 × CH), 127.42 (2 × CH), 127.30 (2 × CH), 61.32 (CH), 21.13 (CH_3) ppm. IR (KBr): $\tilde{\nu} = 3251$, 3053, 2926, 1510, 1449, 1435, 1317, 1160, 1090, 1049, 928, 844, 755, 723, 702, 687, 592, 555, 480 cm^{-1} . HRMS (EI-TOF): m/z [M]⁺ calcd. for $\text{C}_{20}\text{H}_{19}\text{NO}_2\text{S}$ 337.1137; found 337.1144.

***N*-[Phenyl(*p*-tolyl)methyl]benzamide (3cd):** ^1H NMR (300 MHz, CDCl_3): $\delta = 7.81$ (d, $J = 6.9$ Hz, 2 H), 7.51 (t, $J = 7.2$ Hz, 1 H), 7.43 (t, $J = 7.4$ Hz, 2 H), 7.37–7.27 (m, 5 H), 7.19 (d, $J = 8.1$ Hz, 2 H), 7.15 (d, $J = 8.1$ Hz, 2 H), 6.64 (d, $J = 7.8$ Hz, 1 H), 6.41 (d, $J = 7.8$ Hz, 1 H), 2.34 (s, 3 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): $\delta = 166.59$ (C=O), 141.79 (C), 138.72 (C), 137.39 (C), 134.49 (C), 132.73 (CH), 129.55 (2 × CH), 128.81 (2 × CH), 128.72 (2 × CH), 127.58 (3 × CH), 127.55 (2 × CH), 127.18 (2 × CH), 57.34 (CH), 21.18 (CH_3) ppm. IR (KBr): $\tilde{\nu} = 3311$, 3056, 3031, 2920, 1639, 1579, 1522, 1489, 1357, 1317, 1247, 1181, 1082, 1054, 1026, 927, 856, 796, 776, 741, 703, 691, 577, 479 cm^{-1} . HRMS (EI-TOF): m/z [M]⁺ calcd. for $\text{C}_{21}\text{H}_{19}\text{NO}$ 301.1467; found 301.1461.

Acknowledgments

The authors are grateful for the financial support from the National Natural Science Foundation of China (Nos. 20621061 and 20772117).

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Received: April 27, 2008

Published Online: July 17, 2008