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An Efficient Method for the Synthesis of *N*-Acylsulfonamides: One-pot Sulfonylation and Acylation of Primary Arylamines under Solvent-Free Conditions

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Summary. The preparation of *N*-acylsulfonamides is described using primary amines, arylsulfonyl chlorides and acyl chlorides. Reaction of primary aryl amines with arylsulfonyl chlorides in the presence of $NaHCO_3$ produced *N*-arylsulfonamides, which reacted *in situ* with benzoyl chloride furnishing the corresponding *N*-benzoyl-*N*-arylsulfonamides in 72–96% yields. Accordingly, 4-nitrobenzoyl chloride and 3,5-dinitrobenzoyl chloride were used as acylating agents. All the reactions were carried out under solvent-free conditions at room temperature and the products were isolated after simple work-up in high yields and purity.

Keywords. *N*-Acylsulfonamide; Solvent-free; Acylation; Sulfonylation; *N*-Arylsulfonamide; *N*-Acyl-*N*-arylsulfonamide.

Introduction

The *N*-acylsulfonamide moiety is a common structural motif in organic synthesis. Several recent developmental drugs including therapeutic agents for *Alzheimer*'s disease [1], inhibitors of *tRNA* synthetases as antibacterial agents [2], prostaglandin F1a sulfonamides for the potential treatments for osteoporosis [3], antagonists for angiotensin II [4], and leukotriene D_4-receptors [5], incorporate this functionality. In addition, several *N*-acyl-*N*-arylmethansulfonamides have been employed as chemoselective *N*-acylating reagents [6].

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In the majority of reports for the preparation of *N*-acylsulfonamides the parent sulfonamide is used as a starting material. Acylation with acyl chlorides, anhydrides and *N*-acyl benzotriazoles [7–11], direct condensation of carboxylic acid and sulfonamides in the presence of condensing agents (*e.g. EDC*, *DCC*, and carbonyl diimidazole) [2, 3, 12–14], have been employed for this purpose. The reaction of amides with sulfonyl chlorides is also used occasionally for the synthesis of *N*-acylsulfonamides [15–17]. Most of these reports are examples of reactions that were typically carried out in a solvent.

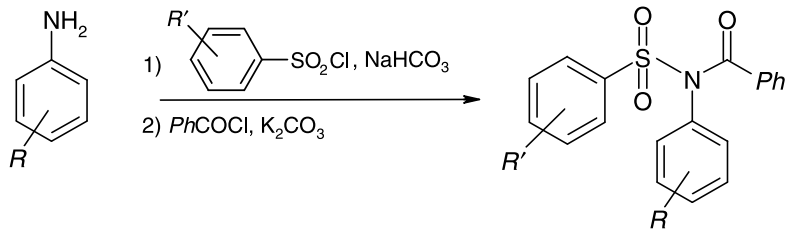
Among the N–H acids in which the acidity is enhanced by neighboring electron withdrawing substituents, *N*-arylsulfonamides ($pKa = 5$–10) [18] were considered as capable of easily undergoing alkylation and acylation. On this basis, *Kondo* and coworkers used *N*-arylsulfonamides as a precursor for the synthesis of *N*-acyl-*N*-arylsulfonamides [6]. They synthesized the starting sulfonamides from the arylamines and appropriate sulfonylchloride in pyridine as solvent in 48–79% yields. These reactions afford the crude product as a mixture of *N*-mono and disulfonylated arylamines. The second step involves the reaction of *N*-arylsulfonamide with 4 equiv of benzoyl chloride in pyridine. Recently, Padmavathi reported the synthesis of a variety of *N*-acyl-*N*-arylsulfonamides from araldoximes and chloramine-T

[19]. In this method reaction of araldoxime with 2 equiv of chloramine-T in refluxing methanol for 48 h followed by purification on silica gel furnished *N*-acyl-*N*-arylsulfonamides in 12–29% yield. These methodologies suffer from some disadvantages such as low yield, prolonged reaction time, use of toxic organic solvent and the requirement of excess reagents. Therefore, an alternative route for the construction of *N*-acylsulfonamides would be highly desirable. Solvent-free reactions have attracted the attention of chemists due to their simplicity in processing and handling [20]. Along this line, we now report an efficient, convenient and facile method for the sulfonylation/acylation of primary aryl amines under solvent-free conditions.

Results and Discussion

Our original plan was to react *N*-benzoyl anilines bearing with different arylsulfonyl groups under solvent-free conditions. However, even after considerable experimentation our attempts remained unsuccessful. In an effort to overcome this problem, we chose to focus on the use of *N*-arylsulfonamides as a precursor of various *N*-acyl-*N*-arylsulfonamides since these starting materials are expected to have lower pK_a values than *N*-benzoyl anilines. At first, sulfonylation of anilines was examined in the presence of anhydrous $NaHCO_3$ as solid base under solvent-free conditions at room temperature. *N*-arylsulfonamides were obtained in high yields and purity. Then, *N*-arylsulfonamides were reacted with benzoyl chloride in the presence of anhydrous K_2CO_3 under solvent-free conditions. The reactions were completed very fast and the corresponding *N*-aryl-*N*-benzoylsulfonamides were obtained in high yields and purity.

In a second series of experiments we prepared *N*-aryl-*N*-benzoylsulfonamides directly from arylamines without any need to isolate the intermediate *N*-arylsulfonamides. In order to reach this goal, we had to optimize the reaction conditions. We found that the *N*-arylsulfonamides were rapidly converted into *N*-aryl-*N*-benzoylsulfonamides *in situ* in the presence of 2 equiv benzoyl chloride in anhydrous K_2CO_3 (Scheme 1). The reaction was carried out at



1a: *R*, R′ = H
1b: *R* = 2, 4-CH_3, *R′* = H
1c: *R* = 2-CH_3, *R′* = 4-CH_3
1d: *R* = 2-OCH_3, *R′* = 4-CH_3
1e: *R* = 4-OCH_3, *R′* = 4-CH_3
1f: *R* = 3-Cl, *R′* = 4-CH_3
1g: *R* = 4-Cl, *R′* = 4-CH_3
1h: *R* = 4-CH_3, *R′* = 4-$NHCOCH_3$
1i: *R* = 4-Cl, *R′* = 4-$NHCOCH_3$

Scheme 1

Table 1. One-pot reaction of arylamines with some arylsulfonyl chloride and benzoyl chloride at room temperature

Entry	Arylamine	Arylsulfonyl chloride	Product	Time/min	Yield/%
1	aniline	benzensulfonyl chloride	**1a**	9	92
2	2,4-dimethylaniline	benzensulfonyl chloride	**1b**	20	72
3	2-methylaniline	tosylchloride	**1c**	5	86
4	2-methoxyaniline	tosylchloride	**1d**	7	86
5	4-methoxyaniline	tosylchloride	**1e**	20	72
6	3-chloroaniline	tosylchloride	**1f**	8	95
7	4-chloroaniline	tosylchloride	**1g**	10	96
8	4-methylaniline	4-acetamidobenzensulfonyl chloride	**1h**	17	90
9	4-chloroaniline	4-acetamidobenzensulfonyl chloride	**1i**	35	89

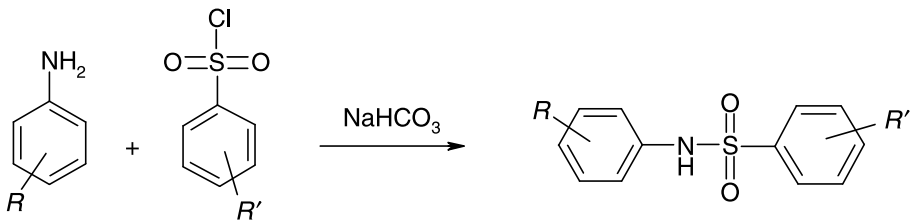
room temperature and the experimental procedure is remarkably simple and requires no toxic solvents or inert atmosphere.

Sulfonylation was achieved with benzenesulfonyl chloride, *p*-methylbenzenesulfonyl chloride and 4-acetamidobenzenesulfonyl chloride in $NaHCO_3$ under vigorous stirring. It was found that in this step the use of K_2CO_3 instead of $NaHCO_3$ as base, gives rise to di-sulfonylated byproduct in some cases. Upon completion of the reaction, K_2CO_3 was added and the mixture was stirred vigorously for a minute. Then, it was treated with benzoyl chloride to afford the *N*-aryl-*N*-benzoylsulfonamides after a very simple work-up (Table 1).

Several functionalities present in the arylamines and arylsulfonyl chloride such as halogen, methyl, and methoxy groups in various positions (*o*, *m*, *p*) were tolerated. In all cases the corresponding *N*-aryl-*N*-benzoylsulfonamides were obtained in good to excellent overall yields. Noteworthy here is that the yield of the reaction was not greatly influenced by the presence of electron-donating or electron-withdrawing groups on the arylamine or arylsulfonyl chloride. Under the same reaction conditions, 4-nitrobenzoyl and 3,5-dinitrobenzoyl chlorides are less reactive than benzoyl chloride and the corresponding *N*-aryl-*N*-4-nitrobenzoylsulfonamides **3a**–**3g** and *N*-aryl-*N*-3,5-dinitrobenzoylsulfonamides **4a**–**4f** were obtained in low yields. For example, treatment of *p*-methoxyaniline (2 mmol) with benzenesulfonyl chloride (2 mmol) in $NaHCO_3$ provided *N*-4-methoxyphenylbenzenesulfonamide; subsequent *in situ* addition of 3,5-dinitrobenzoyl chloride (4 mmol) and K_2CO_3 provided product **4a** in 40% yield after 15 h.

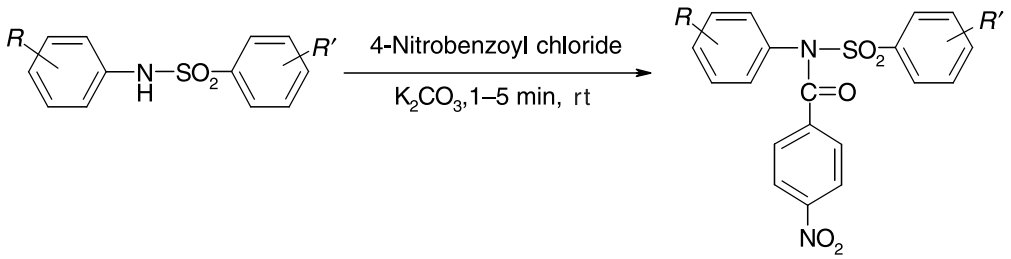
Therefore, we next turned our attention to a stepwise method. It was found that if the product of the sulfonylation reaction of arylamine was isolated and then reacted with nitro substituted benzoyl chloride, the reaction was clean and the product was produced very fast. For this purpose, we synthesized a variety of *N*-arylsulfonamides under solvent-free conditions [20a].

Interestingly, the products of the second step, acylation of *N*-aryl sulfonamides, were obtained by simply grinding of *N*-arylsulfonamides **2a**–**2m** (2 mmol) with 3,5-dinitrobenzoyl chloride or 4-nitrobenzoyl chloride (4 mmol) for 1–5 min at room temperature in the presence of K_2CO_3 under solvent-free conditions (Schemes 3, 4). The results are summarized in Tables 2 and 3. It is worth mentioning that the electronic nature of the substituents on the benzene rings does not have a noticeable effect on the reaction times and the yields of the products. Also, the reaction rates and the yields of products were not greatly affected by the steric bulk of substituents in the vicinity of the nitrogen atom in the starting *N*-arylsulfonamides, which was mentioned as a problem in preceeding reports [6, 7].



2a: *R*, *R′* = H
2b: *R* = 4-CH_3, *R′* = H
2c: *R* = 4-OCH_3, *R′* = H
2d: *R* = 4-Cl, *R′* = H
2e: Ar = $PhCH_2$, *R′* = H
2f: *R* = 4-CH_3, *R′* = 4-CH_3
2g: *R* = 2, 4-CH_3, *R′* = 4-CH_3
2h: *R* = 4-OCH_3, *R′* = 4-CH_3
2i: *R* = 3-Cl, *R′* = 4-CH_3
2j: *R* = 4-OCH_3, *R′* = 4-CH_3
2k: *Ar*NH_2 = 1-Naphthyl, *R′* = 4-CH_3
2l: *R* = H, *R′* = 4-$NHCOCH_3$
2m: *R* = 2, 4-CH_3, *R′* = 4-$NHCOCH_3$

Scheme 2



3a: *R*, *R′* = H
3b: *R* = 4-CH_3, *R′* = H
3c: *R* = 4-OCH_3, *R′* = 4-CH_3
3d: *R* = 2, 4-CH_3, *R′* = 4-CH_3
3e: *R* = 3-Cl, *R′* = 4-CH_3
3f: *Ar*NH_2 = 1-Naphthyl, *R′* = 4-CH_3
3g: *R* = H, *R′* = 4-$NHCOCH_3$

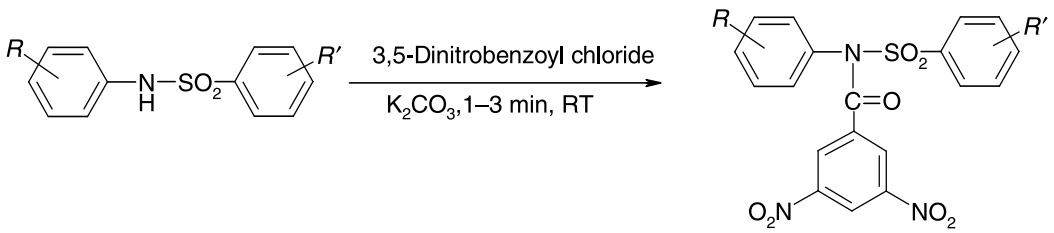
Scheme 3

Table 2. Reaction of some *N*-arylsulfonamides with 4-nitrobenzoyl chloride at room temperature in K_2CO_3 under solvent-free condition

Entry	*N*-Arylsulfonamides	Product	Time/min	Yield/%
1	**2a**	**3a**	1	70
2	**2b**	**3b**	1	80
3	**2j**	**3c**	1	75
4	**2g**	**3d**	1	75
5	**2i**	**3e**	1	81
6	**2k**	**3f**	1	91
7	**2l**	**3g**	5	90

Spectral analysis of *N*-acyl-*N*-arylsulfonamides supports the structure of the products. The IR spectra indicated the absence of N–H bond and exhibited the presence of sulfonyl ($\bar{\nu} = 1150–1180$ and 1350–1380 cm^{-1}) and amide (1660–1700 cm^{-1}) groups. The ^1H NMR spectrum clearly showed the presence of 1,4-disubstituted benzene moieties. The presence of amide groups was further supported by the presence of carbonyl carbon resonance at $\delta = 167–170$ ppm in the ^{13}C NMR spectrum. Finally, the elemental analysis is in accordance with the proposed products.

In conclusion, we have described a convenient synthetic method for the preparation of *N*-acyl-*N*-arylsulfonamides from sterically and electronically diverse arylamines or *N*-arylsulfonamides. The key feature is the one-pot condensation of arylamines with arylsulfonyl chlorides and acyl chlorides, especially benzoyl chloride, under solvent-free conditions in the presence of $NaHCO_3/K_2CO_3$ as base at room temperature. All of the reactions are easy to operate, proceed very fast, use inexpensive reagents and furnish the products after simple work-up. Thus, this method obeying several principles of green chemistry should be widely applicable to the synthesis of various *N*-acyl-*N*-arylsulfonamides.



4a: *R* = 4-OCH_3, *R′* = H
4b: *R* = 4-Cl, *R′* = H
4c: *Ar*NH_2 = *Ph*CH_2, *R′* = H
4d: *R*, *R′* = 4-CH_3
4e: *R* = 2-OCH_3, *R′* = 4-CH_3
4f: *R* = 2, 4-CH_3, *R′*=4-$NHCOCH_3$

Scheme 4

Table 3. Reaction of some *N*-arylsulfonamides with 3,5-dinitrobenzoyl chloride at room temperature in K_2CO_3 under solvent-free condition

Entry	*N*-Arylsulfonamides	Product	Time/min	Yield/%
1	**2c**	**4a**	1	73
2	**2d**	**4b**	1	84
3	**2e**	**4c**	1	70
4	**2f**	**4d**	1	80
5	**2h**	**4e**	1	95
6	**2m**	**4f**	3	86

Experimental

All chemicals were purchased from Merck and Fluka. The products were characterized by comparing the physical data with those of known samples or by their spectral data. Infrared spectra were recorded on a Nicolet (Impact 400D model) FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX 500 Avance spectrophotometer in $CDCl_3$, acetone-d_6, or *DMSO*-d_6 as the solvent and *TMS* as internal standard. Column chromatography was performed using silica gel 60 (230–400 mesh, Merck). All yields refer to isolated yields. Results of elemental analysis were found to agree with calculated values.

General Procedure for the Prepration of N-Aryl-N-benzoylsulfonamides

An amine (2 mmol) and anhydrous $NaHCO_3$ (1 g) were ground together into fine powder in a mortar and arylsulfonyl chloride (2 mmol) was added under vigorous stirring with a magnetic stirrer at room temperature. The progress of the reaction was monitored by TLC until the conversion of amine was completed. In all cases the crude products showed one spot on TLC and were used in the second step without prior purification. Benzoyl chloride (4 mmol) and anhydrous K_2CO_3 were added to the mixture and stirred vigorously at room temperature. The reaction was monitored by TLC. Upon completion of the reaction, water was added and the mixture was stirred for a few minutes. The product was collected by filtration of the suspension through a sintered glass funnel and washed with additional water. The crude product was purified by column chromatography on silica gel (60–120 mesh, *Et*O*Ac*-petroleum ether) or recrystallized (ethyl acetate–*n*-hexane mixed solvent) to afford the corresponding *N*-aryl *N*-benzoylsulfonamides in good to high yield.

N-Phenyl-N-(phenylsulfonyl)benzamide (**1a**, $C_{19}H_{15}NO_3S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **1a** as a colorless powder, mp 123–125°C; yield 92%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.20$ (4H, m), 7.32 (4H, m), 7.49 (2H, d, $J = 7.5$ Hz), 7.57 (2H, m), 7.70 (1H, m), 7.99 (2H, d, $J = 7.5$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 121.6$, 124.4, 127.3, 127.5, 127.7, 128.9, 129, 129.1, 132.0, 132.2, 134.2, 139.7, 165.0 ppm; IR: $\bar{\nu} = 1691$, 1365, 1266, 1186, 1093, 582 cm^{-1}.

N-(2,4-Dimethylphenyl)-N-(phenylsulfonyl)benzamide (**1b**, $C_{21}H_{19}NO_3S$)
Purification by silica gel column chromatography (ethyl acetate–petroleum ether) afforded pure **1b** as a colorless powder, mp 168–170°C; yield 72%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.18$ (3H, s), 2.31 (3H, s), 6.99 (2H, m), 7.06 (1H, d, $J = 8.0$ Hz), 7.19 (2H, m), 7.32 (1H, m), 7.38 (2H, d, $J = 7.0$ Hz), 7.59 (2H, m), 7.72 (1H, m), 8.11 (2H, d, $J = 7.5$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 18.22$, 20.98, 127.03, 127.39, 127.72, 128.51, 128.56, 128.81, 129.55, 130.90, 131.35, 132.13, 133.42, 133.71, 133.83, 137.63, 138.81, 139.66, 169.63 ppm; IR: $\bar{\nu} = 1686$, 1453, 1366, 1280, 1173 cm^{-1}.

N-o-Tolyl-N-tosylbenzamide (**1c**, $C_{21}H_{19}NO_3S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **1c** as a colorless powder, mp 156–158°C; yield 86%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.25$ (3H, s), 2.51 (3H, s), 7.18 (5H, m), 7.25 (1H, m), 7.30 (1H, m), 7.38 (4H, dd, $J = 13.5$, 8.0 Hz), 8.00 (2H, d, $J = 8.0$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 15.2$, 24.3, 121.5, 124.3, 126.0, 127.2, 127.5, 128.9, 129.3, 129.4, 134.2, 134.3, 136.7, 138.5, 141.6, 165.0 ppm; IR: $\bar{\nu} = 1676$, 1596, 1348, 1281, 1167, 580 cm^{-1}.

N-(2-Methoxyphenyl)-N-tosylbenzamide (**1d**, $C_{21}H_{19}NO_4S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **1d** as a colorless powder, mp 213–215°C; yield 86%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.48$ (3H, s), 3.49 (3H, s), 6.71 (1H, d, $J = 8.0$), 6.99 (2H, m), 7.16 (2H, m), 7.28 (1H, m), 7.35 (2H, d, $J = 8.0$ Hz), 7.41 (2H, d, $J = 7.0$ Hz), 7.50 (1H, dd, $J = 8.0$, 1.5 Hz), 7.94 (2H, d, $J = 8.0$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 24.3$, 55.9, 114.5, 121.3, 122.6, 123.8, 125.4, 127.2, 128.9, 129.4, 132.2, 134.2, 136.7, 141.6, 152.8, 165.1 ppm; IR: $\bar{\nu} = 1703$, 1596, 1449, 1361, 1261, 1167, 713 cm^{-1}.

N-(4-Methoxyphenyl)-N-tosylbenzamide (**1e**, $C_{21}H_{19}NO_4S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **1e** as a colorless powder, mp 178–180°C; yield 72%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.49$ (3H, s), 3.80 (3H, s), 6.81 (2H, d, $J = 8.5$ Hz), 7.09 (2H, d, $J = 8.5$ Hz), 7.22 (2H, m), 7.31 (1H, m), 7.36 (2H, d, $J = 8.0$ Hz), 7.49 (2H, d, $J = 8.0$ Hz), 7.87 (2H, d, $J = 8.0$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 24.4$, 55.9, 114.7, 120.0, 122.6, 127.2, 127.5, 128.9, 129.4, 132.2, 134.2, 136.7, 141.6, 156.3, 165.2 ppm; IR: $\bar{\nu} = 1690$, 1509, 1368, 1261, 1174 cm^{-1}.

N-(3-Chlorophenyl)-N-tosylbenzamide (**1f**, $C_{20}H_{16}ClNO_3S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **1f** as a colorless powder, mp 136–138°C; yield 95%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.50$ (3H, s), 7.05 (1 H, d, $J = 8.0$ Hz), 7.25 (4H, m), 7.31 (1H, m), 7.37 (3H, m),

7.48 (2H, d, $J = 8.0$ Hz), 7.86 (2H, d, $J = 8.0$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.64$, 128.13, 128.52, 129.26, 129.30, 129.34, 129.40, 129.83, 130.40, 132.00, 133.26, 134.53, 134.91, 138.40, 145.07, 160.50; IR: $\bar{\nu} = 1690$, 1583, 1375, 1267, 1180, 1086 cm^{-1}.

N-(4-Chlorophenyl)-N-tosylbenzamide (**1g**, $C_{20}H_{16}ClNO_3S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **1g** as a colorless powder, mp 163–165°C; yield 96%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.50$ (3H, s), 7.12 (2H, d, $J = 8.5$ Hz), 7.24 (2H, m), 7.30 (2H, dd, $J =$ 8.5, 1.7 Hz), 7.37 (3H, m), 7.47 (2H, d, $J = 8.5$ Hz), 7.85 (2H, d, $J = 8.5$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 24.3$, 123.0, 125.8, 127.1, 127.8, 128.9, 129.1, 129.3, 132.5, 134.2, 136.7, 141.6, 165.7 ppm; IR: $\bar{\nu} = 1688$, 1367, 1274, 1167 cm^{-1}.

N-(4-Acetamidophenylsulfonyl)-N-p-tolylbenzamide
(**1h**, $C_{22}H_{20}N_2O_4S$)
Purification by silica gel column chromatography (ethyl acetate–petroleum ether) afforded pure **1h** as a colorless powder, mp 192–194°C; yield 90%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.20$ (3H, s), 2.34 (3H, s), 7.06 (2H, d, $J = 8.0$ Hz), 7.11 (2H, d, $J = 8.0$ Hz), 7.22 (2H, m), 7.35 (1H, m), 7.47 (2H, d, $J = 8.0$ Hz), 7.73 (2H, d, $J = 8.0$ Hz), 7.91 (2H, d, $J =$ 8.0 Hz), 9.85 (1, s) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.09$, 24.50, 118.70, 128.05, 129.17, 129.88, 130.02, 130.67, 131.77, 132.14, 133.62, 134.43, 139.51, 143.40, 169.31, 170.50 ppm; IR: $\bar{\nu} = 3339$, 1710, 1656, 1368, 1254, 1174 cm^{-1}.

N-(4-Acetamidophenylsulfonyl)-N-(4-chlorophenyl)-benzamide (**1i**, $C_{21}H_{17}ClN_2O_4S$)
Purification by silica gel column chromatography (ethyl acetate–petroleum ether) afforded pure **1i** as brownish white powder, mp 240–242°C; yield 89%; ^{1}H NMR (500 MHz, acetone-d_6): $\delta = 2.17$ (3H, s), 7.29 (4H, m), 7.39 (3H, m), 7.52 (2H, d, $J = 7.5$ Hz), 7.89 (4H, d, $J = 5.0$ Hz), 9.79 (1H, s); ^{13}C NMR (125 MHz, acetone-d_6): $\delta = 22.9$, 121.9, 123.1, 125.8, 127.5, 128.9, 129.1, 130.0, 132.2, 134.5, 135.3, 141.7, 165.1, 168.9 ppm; IR: $\bar{\nu} = 3347$, 1709, 1662, 1367, 1254, 1173 cm^{-1}.

General Procedure for the Preparation of N-Aryl-N-3,5-dinitrobenzoylsulfonamides and N-Aryl-N-4-nitrobenzoyl-sulfonamides

Step 1. Synthesis of N-arylsulfonamides: An amine (2 mmol) and anhydrous $NaHCO_3$ (1 g) were ground together into fine powder in a mortar, and arylsulfonyl chloride (2 mmol) was added under vigorous stirring with a magnetic stirrer at room temperature. The progress of the reaction was monitored by TLC until the conversion of the amine was complete. The product was obtained by one of the following two work-up methods: Method A: water was added to the mixture and the solid sulfonamide was collected by filtration and washed with additional water. Method B: a suitable solvent such as diethyl ether was added, the solid base was removed by filtration. The filter cake was washed with additional solvent. The combined filtrates were evaporated and the product was obtained as a solid or liquid. The work-up method B was used preferentially for liquid products. The products were obtained very pure and can be used for the next reaction step without any further purification.

Step 2. Acylation of N-arylsulfonamides: A mortar was charged with anhydrous K_2CO_3 (1 g) and *N*-arylsulfonamide (2 mmol); the mixture was ground with a pestle and 3,5-dinitrobenzoyl chloride or 4-nitrobenzoyl chloride (4 mmol) was added to the mixture. The reaction was ground for 1–5 min and the progress of the reaction was monitored by TLC. After completion of the reaction, water was added and the product was collected by filtration through a sintered glass funnel and washed with additional water. The crude product was purified by column chromatography on silica gel (60–120 mesh, *Et*O*Ac*-petroleum ether) or recrystallized (ethyl acetate-*n*-hexane mixed solvent) to afford the products in good to high yield.

4-Nitro-N-phenyl-N-(phenylsulfonyl)benzamide
(**3a**, $C_{19}H_{14}N_2O_5S$)
Purification by silica gel column chromatography (ethyl acetate–petroleum ether) afforded pure **3a** as a colorless powder, mp 192–194°C; yield 70%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.15$ (2H, d, $J = 7.0$), 7.31 (3H, d, $J = 7.0$), 7.56 (4H, m), 7.68 (1H, t, $J = 7.0$), 7.97 (2H, d, $J = 8.0$), 8.01(2H, d, $J = 8.0$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 123.27$, 128.87, 129.48, 129.61, 129.85, 130.14, 130.40, 134.27, 136.42, 137.71, 139.54, 149.09, 167.83 ppm; IR: $\bar{\nu} =$ 3107, 1696, 1602, 1528, 1374, 1280, 1179, 1092, 581 cm^{-1}.

4-Nitro-N-(phenylsulfonyl)-N-p-tolylbenzamide
(**3b**, $C_{20}H_{16}N_2O_5S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **3b** as a colorless powder, mp 234–236°C; yield 80%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.31$ (3H, s), 7.02 (2H, d, $J = 7.5$ Hz), 7.10 (2H, d, $J = 7.5$ Hz), 7.56 (4H, m), 7.69 (1H, m), 7.98 (2H, d, $J = 8.0$ Hz), 8.02 (2H, d, $J = 8.0$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.14$, 123.18, 128.74, 129.45, 130.02, 130.04, 130.21, 133.65, 134.09, 137.74, 139.62, 140.18, 149.01, 167.80 ppm; IR: $\bar{\nu} =$ 3108, 1688, 1602, 1529, 1377, 1277, 1117, 1091, 581 cm^{-1}.

N-(4-Methoxyphenyl)-4-nitro-N-tosylbenzamide
(**3c**, $C_{21}H_{18}N_2O_6S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **3c** as a brownish white powder, mp 171–173°C; yield 75%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.44$ (3H, s), 3.73 (3H, s), 6.77 (2H, d, $J = 8.0$ Hz), 7.03 (2H, d, $J = 8.0$ Hz), 7.33 (2H, d, $J = 8.0$ Hz), 7.56 (2H, d, $J =$ 8.0 Hz), 7.84 (2H, d, $J = 8.0$ Hz), 8.01 (2H, d, $J = 8.0$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.74$, 55.46, 114.72, 123.24, 128.77, 129.47, 129.51, 130.03, 131.57, 134.71, 139.92, 145.38, 148.95, 160.35, 167.89 ppm; IR: $\bar{\nu} = 3111$, 1689, 1603, 1517, 1365, 1286, 1252, 1173, 1034, 578 cm^{-1}.

N-(2,4-Dimethylphenyl)-4-nitro-N-tosylbenzamide (**3d**, $C_{22}H_{20}N_2O_5S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **3d** as a colorless powder, mp 172–174°C; yield 75%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.19$ (3H, s), 2.27 (3H, s), 2.47 (3H, s), 6.97 (3H, m), 7.37 (2H, d, $J = 6.0$ Hz), 7.47 (2H, d, $J = 6.0$ Hz), 7.96 (2H, d, $J = 6.0$ Hz), 8.00 (2H, d, $J = 6.0$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 18.37$, 21.14, 21.77, 123.10, 127.86, 129.33, 129.48, 129.78, 130.79, 132.54, 132.82, 135.35, 137.75, 140.08, 140.52, 145.51, 148.86, 167.76 ppm; IR: $\bar{\nu} = 3100$, 1690, 1602, 1522, 1367, 1287, 1172, 1092, 581 cm^{-1}.

N-(3-Chlorophenyl)-4-nitro-N-tosylbenzamide (**3e**, $C_{20}H_{15}ClN_2O_5S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **3e** as a colorless powder, mp 152–154°C; yield 81%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.47$ (3H, s), 7.01 (1H, d, $J = 7.0$ Hz), 7.23 (2H, m), 7.31 (1H, d, $J = 7.5$ Hz), 7.36 (2H, d, $J = 7.5$ Hz), 7.58 (2H, d, $J = 8.0$ Hz), 7.83 (2H, d, $J = 7.5$ Hz), 8.05 (2H, d, $J = 8.0$ Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.78$, 123.44, 128.63, 129.53, 129.61, 130.07, 130.34, 130.48, 134.42, 135.10, 137.54, 139.27, 145.79, 149.25, 167.54 ppm; IR: $\bar{\nu} = 3125$, 1692, 1587, 1527, 1369, 1283, 1171, 1091, 590 cm^{-1}.

N-(Naphthalen-1-yl)-4-nitro-N-tosylbenzamide (**3f**, $C_{24}H_{18}N_2O_5S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **3f** as a colorless powder, mp 172–174°C; yield 91%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.46$ (3H, s), 7.28 (1H, d, $J = 7.0$ Hz), 7.34 (3H, m), 7.40 (2H, d, $J = 8.5$ Hz), 7.50 (1H, m), 7.58 (1H, m), 7.80 (3H, m), 7.98 (3H, m), 8.02 (1H, d, $J = 8.5$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.80$, 122.91, 123.17, 125.18, 127.04, 128.09, 128.64, 128.70, 129.45, 129.53, 130.06, 131.00, 132.20, 133.03, 134.41, 134.82, 139.99, 145.75, 148.77, 168.45 ppm; IR: $\bar{\nu} =$ 3066, 1690, 1596, 1528, 1360, 1293, 1172, 1078, 581 cm^{-1}.

N-(4-Acetamidophenylsulfonyl)-4-nitro-N-phenylbenzamide (**3g**, $C_{21}H_{17}N_3O_6S$)
Purification by silica gel column chromatography (ethyl acetate–petroleum ether) afforded pure **3g** as a brownish white powder, mp 202–204°C; yield 90%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.11$ (3H, s), 7.33 (5H, m), 7.67 (2H, d, $J =$ 8.0 Hz), 7.86 (4H, m), 8.03 (2H, d, $J = 8.0$ Hz), 10.52 (1H, s) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 24.16$, 118.37, 123.19, 129.35, 129.66, 129.75, 130.26, 130.49, 130.74, 135.79, 139.76, 144.64, 148.47, 167.60, 169.29 ppm; IR: $\bar{\nu} = 3368$, 3110, 1705, 1683, 1588, 1526, 1369, 1167, 1087, 576 cm^{-1}.

N-(4-Methoxyphenyl)-3,5-dinitro-N-(phenylsulfonyl)-benzamide (**4a**, $C_{20}H_{15}N_3O_8S$)
Purification by silica gel column chromatography (ethyl acetate–petroleum ether) afforded pure **4a** as brownish white powder, mp 202–204°C; yield 73%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.78$ (3H, s), 6.84 (2H, d, $J = 8.5$ Hz), 7.10 (2H, d, $J = 8.5$ Hz), 7.58 (2H, m), 7.72 (1H, m), 7.96 (2H, d, $J = 7.5$ Hz), 8.57 (2H, s), 8.94 (1H, s) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 55.58$, 115.25, 121.02, 128.10, 128.98, 129.04, 129.56, 131.50, 134.53, 137.21, 137.38, 148.06, 160.83, 165.12 ppm; IR: $\bar{\nu} = 3092$, 1693, 1627, 1547, 1348, 1255, 1176, 1096, 572 cm^{-1}.

N-(4-Chlorophenyl)-3,5-dinitro-N-(phenylsulfonyl)-benzamide (**4b**, $C_{19}H_{12}ClN_3O_7S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **4b** as brownish white powder, mp 215–217°C; yield 84%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.15$ (2H, d, $J = 8.5$ Hz), 7.35 (2H, d, $J = 8.5$ Hz), 7.60 (2H, m), 7.75 (1H, m), 7. 95 (2H, d, $J = 7.5$ Hz), 8.59 (2H, d, $J = 2.0$ Hz), 9.00 (1H, s) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 121.40$, 128.96, 129.13, 129.55, 130.37, 131.42, 134.34, 134.81, 136.89, 136.97, 148.21, 164.97 ppm; IR: $\bar{\nu} = 3098$, 1699, 1627, 1547, 1373, 1249, 1156, 1090, 586 cm^{-1}.

N-Benzyl-3,5-dinitro-N-(phenylsulfonyl)benzamide (**4c**, $C_{20}H_{15}N_3O_7S$)
Purification by silica gel column chromatography (ethyl acetate–petroleum ether) afforded pure **4c** as a colorless powder, mp 188–190°C; yield 70%; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 5.05$ (2H, s), 7.28 (5H, m), 7.58 (2H, s), 7.78 (3H, m), 8.46 (2H, s), 8.88 (1H, s) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6): $\delta = 51.04$, 118.53, 120.79, 127.27, 127.41, 127.76, 128.19, 128.70, 129.62, 134.81, 136.35, 137.22, 137.91, 147.74, 166.90 ppm; IR: $\bar{\nu} = 3086$, 1686, 1626, 1547, 1349, 1171, 722, 596 cm^{-1}.

3,5-Dinitro-N-p-tolyl-N-tosylbenzamide (**4d**, $C_{21}H_{17}N_3O_7S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **4d** as a colorless powder, mp 173–175°C; yield 80%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.31$ (3H, s), 2.48 (3H, s), 7.07(2H, d, $J = 7.5$ Hz), 7.15 (2H, d, $J = 7.5$ Hz), 7.37 (2H, d, $J = 7.5$ Hz), 7.83 (2H, d, $J = 7.5$ Hz), 8.55 (2H, s), 8.92 (1H, s) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.12$, 21.69, 120.86, 128.93, 129.50, 129.98, 130.60, 133.22, 134.22, 137.37, 140.79, 145.75, 147.93, 165.01 ppm; IR: $\bar{\nu} = 3087$, 1676, 1629, 1549, 1347, 1159, 1085, 568 cm^{-1}.

N-(2-Methoxyphenyl)-3,5-dinitro-N-tosylbenzamide (**4e**, $C_{21}H_{17}N_3O_8S$)
Purification by recrystallization (ethyl acetate–*n*-hexane) afforded pure **4e** as a colorless powder, mp 186–188°C; yield 95%; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.48$ (3H, s), 3.64 (3H, s), 6.79 (1H, s), 6.97 (1H, s), 7.36 (4H, s), 7.91 (2H, s), 8.56 (2H, s), 8.89 (1H, s) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.73$, 55.55, 112.21, 120.62, 121.64, 124.83, 128.10, 129.27, 129.67, 131.89, 132.33, 135.06, 137.81, 145.53, 147.80, 155.25, 165.52 ppm; IR: $\bar{\nu} = 3100$, 1701, 1596, 1549, 1501, 1360, 1260, 1179, 575 cm^{-1}.

N-(4-Acetamidophenylsulfonyl)-N-(2,4-dimethylphenyl)-3,5-dinitrobenzamide (**4f**, $C_{23}H_{20}N_4O_8S$)
Purification by silica gel column chromatography (ethyl acetate–petroleum ether) afforded pure **4f** as brownish white powder, mp 255–257°C; yield 86%; ^{1}H NMR (500 MHz,

DMSO-d_6): $\delta = 2.05$ (3H, s), 2.11 (3H, s), 2.21 (3H, s), 7.06 (2H, m), 7.28 (1H, d, J = 6.0 Hz), 7.89 (4H, m), 8.46 (2H, s), 8.73 (1H, s), 10.57 (1H, s) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6): $\delta = 17.79$, 20.53, 24.14, 118.31, 120.91, 127.85, 128.21, 128.33, 130.42, 130.66, 131.03, 132.04, 132.20, 136.30, 137.52, 140.14, 144.87, 147.44, 164.87, 169.31 ppm; IR: $\bar{\nu} = 3398$, 3089, 1712, 1680, 1589, 1544, 1345, 1165, 1087, 572 cm^{-1}.

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