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Na Zhao[a]; Yanqiu Li[a]; Yulu Wang[a]; Jinye Wang[bc]
[a] Henan Normal University, Xinxiang, Henan, P.R. China [b] Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, P.R. China [c] Shanghai Institute of Organic Chemistry, Shanghai, P.R. China

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RESEARCH ARTICLE

A facile and efficient synthesis of aryl toluenesulfonhydrazides and aryl toluenesulfonates under solvent-free conditions

NA ZHAO†, YANQIU LI†, YULU WANG*† and JINYE WANG‡

†College of Chemistry and Environmental Science, Key Laboratory of Environmental Pollution Control Technology of Henan Province, Henan Normal University, Xinxiang, Henan, 453007, P.R. China
‡Biomedical Engineering, Shanghai Jiao Tong University,1954 Huashan Road, Shanghai, 200030, P.R. China and Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, P.R. China

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A rapid, efficient method is described for synthesis of aryl toluenesulfonhydrazides from toluenesulfonyl chloride and substituted phenylhydrazines and for the synthesis of aryl toluenesulfonates from toluenesulfonyl chloride and substituted phenols. The procedure is simple, environmentally benign and occurs in good yields.

Keywords: p-Toluenesulfonyl chloride; Aryl toluenesulfonates; Aryl toluenesulfonhydrazides; Solvent-free; Co-ground

1. Introduction

Organosulfur compounds are useful materials and most of them have pharmacological properties. Some sulfonyl hydrazides are valuable as inhibitors [1], agrochemical fungicides [2], insecticides and photographic images [3]. Some methods have been reported for preparing these compounds to date. Usually, they were prepared by the reaction of sulfonyl chloride and hydrazines [4] or reduction of azo compounds [5, 6]. However, these reactions were carried out in organic solvent such as pyridine [7–9] and DMF. Furthermore, they gave a mixture of 1,1- and 1,2-sulfonylhydrazines, which lead to difficult separation and low yields. Thus, simple, convenient and environmentally benign methods for synthesis of arylsulfonyl hydrazides are required.

Recently, there was interest in so-called "solvent-free" reaction. This technology can eliminate the use of organic solvents. At the same time, this approach is of interest because of its high efficiency and selectivity, short reaction time, the easy work-up procedure and environmental acceptability [10–14]. All these merits are consistent with green chemistry's requirements of high efficiency and environmental benefits.

*Corresponding author. Email: wyl@henannu.edu.cn

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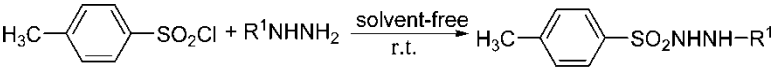
2. Results and discussion

In continuation of our studies on environmentally benign methods under solvent-free conditions, we now wish to report an extremely convenient one-pot synthesis of aryl toluenesulfonhydrazides from readily available p-toluenesulfonyl chloride and substituted phenylhydrazines (scheme 1). The process in its entirety involves a simple mixing of p-toluenesulfonyl chloride and substituted phenylhydrazines in a mortar and grinding the mixture for 10–20 min at room temperature. In this reaction system, p-toluenesulfonyl chloride and phenylhydrazine condensed and the released HCl, when combined with excess phenylhydrazine forms phenylhydrazine hydrochloride. If phenylhydrazine cannot form phenylhydrazine hydrochloride completely, the products are washed with warm dilute hydrochloric acid. The hydrazine salt can then be recycled with dilute sodium hydroxide. This method does not require any catalysts. The yields are excellent (85–97%) and the reaction times are short (10–20 min). We note that the reaction is suitable with many substituents on the phenyl hydrazine. The exceptions are those with strong electron withdrawing groups, where no reaction is observed. For example, when we used p-nitrophenylhydrazine as starting material, no only starting materials were recovered was observed with. The results are summarized in table 1.

Sulfonic esters are important intermediates [15] in organic synthesis and are used as acaricides [16] and thermal recording materials [17]. Traditional methods for preparation sulfonates were by the reaction of sulfonyl chloride with alcohol in the presence of a base [18, 19], or by reacting sulfonic acids reaction with electrophiles [20, 21]. Recently, a synthesis of sulfonic esters using solid-phase bound reagents was reported [22]. However, these methods all require solvent and involve complex procedures.

In order to evaluate the generality of solvent-free synthesis, we attempted to synthesize aryl toluenesulfonates by co-grinding p-toluenesulfonyl chloride and phenol, but the reaction was unsuccessful and p-toluenesulfonyl chloride remained unchanged after 60 min grinding in a



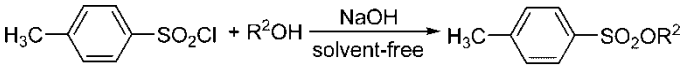
1 2 3

SCHEME 1

Table 1. Preparation of aryl toluenesulfonhydrazides under solvent-free conditions.

Entry	R^1	Product[a]	Time (min)	Yield (%)[b]
1	C_6H_5	**3a**	10	91
2	4-MeC_6H_4	**3b**	15	93
3	2-MeC_6H_4	**3c**	10	91
4	2,5-$(Me)_2C_6H_3$	**3d**	20	91
5	2,6-$(Me)_2C_6H_3$	**3e**	8	94
6	2,3-$(Me)_2C_6H_3$	**3f**	20	93
7	4-ClC_6H_4	**3g**	10	97
8	2-ClC_6H_4	**3h**	10	91
9	2-BrC_6H_4	**3i**	5	91
10	4-FC_6H_4	**3j**	13	85
11	4-$HO_3SC_6H_4$	**3k**	60	0
12	4-$NO_2C_6H_4$	**3l**	60	0
13	$C_6H_4SO_2$	**3m**	60	0

[a]Compounds **3c–g, 3j** have not been reported previously.
[b]isolated yields.



1 **4** **5**

SCHEME 2

Table 2. Preparation of aryl toluenesulfonates under solvent-free conditions.

Entry	R^2	Product[a]	Time (min)	Yield (%)[b]
1	C_6H_5	**5a**	5	98
2	4-ClC_6H_4	**5b**	10	91
3	2-ClC_6H_4	**5c**	10	91
4	1-$C_{10}H_7$	**5d**	8	91
5	2-$C_{10}H_7$	**5e**	18	92
6[c]	1-NO-2-$C_{10}H_6$	**5f**	20	80
7	2-$O_2NC_6H_4$	**5g**	60	86
8	4-$O_2NC_6H_4$	**5h**	60	81
9	C_6Cl_5	**5i**	90	0

[a]Compound **5f** has not been reported previously.
[b]isolated yields.
[c]1-nitroso-2-naphthol exists in the 1,2-naphthoquinone 1-oxime form, and is tosylated on the oxime oxygen atom.

mortar. To solve the low reactivity of p-toluenesulfonyl chloride towards phenols, we added NaOH in the reaction mixture. $NaHCO_3$ was also used instead of NaOH, but no reaction occurred. We are working under the hypothesis that it is the phenol sodium salt that reacts with p-toluenesulfonyl chloride (scheme 2). The synthetic protocol does not require organic solvent until the recrystallization stage, which makes the process environmental beneficial. Phenols bearing an electron-withdrawing group show lower reactivity. For example, p-nitrophenol and o-nitrophenol afford the corresponding products in an hour. This time frame is comparable to reactions in a solvent. We report the preparation of a number of aryl toluenesulfonates in table 2.

3. Conclusions

In summary, a simple, efficient and environmentally benign nature method has been developed for preparation of aryl toluenesulfonhydrazides and aryl toluenesulfonates under solvent-free conditions. This method is superior from the view of yield, reaction time and its facile work-up, compared to reported methods.

4. Experimental

Melting points were uncorrected. IR spectra were recorded on a FTS-40 spectrophotometer in KBr. ^{1}H NMR were measured on a Bruker DPX-400M spectrometer using TMS as internal standard. Elemental analyses were performed on PE-2400 CHN elemental analyzer.

4.1 *Typical procedure for preparation of aryl toluenesulfonylhydrazides*

P-toluenesulfonyl chloride (1 mmol) and phenyl hydrazine (2 mmol) were mixed thoroughly in an agate mortar and co-ground for 10 min at room temperature (monitored by TLC). After

the reaction was completed, the powder was obtained. Then, the reaction mixture was washed with warm dilute hydrochloric acid. The crude product was recrystallized in 95% alcohol.

4.2 *Typical procedure for preparation of aryl toluenesulfonates*

P-toluenesulfonyl chloride (1 mmol), phenol (1 mmol) and NaOH (1.2 mmol) were mixed thoroughly in an agate mortar and co-ground for 5 min at room temperature (monitored by TLC). After the reaction was completed, the white powder was obtained. Then, the reaction mixture was washed with water. The crude product was recrystallized in 95% alcohol.

4.3 *Physical and spectra data of the products*

4.3.1 Compound 3a. Pale yellow needles, m.p. 125.5–126 °C (lit. [23] 155 °C) IR (KBr) ν (cm^{-1}): 3344, 3239, 3033, 2954, 1604, 1496, 1453, 1326, 1162; ^{1}H NMR (400-MHz, DMSO-d_6) δ: 9.44 (s, 1H, NH), 7.57 (s, 1H, NH), 6.71–7.72 (m, 9H, ArH), 2.40 (s, 3H, CH_3); Anal. Calcd. for $C_{13}H_{14}N_2O_2S$: C, 59.54; H, 5.34; N, 10.69. Found: C, 59.46; H, 5.21; N, 10.50.

4.3.2 Compound 3b. Pale yellow needles, m.p. 145–147 °C (lit. [24] 140 °C). IR (KBr) ν (cm^{-1}): 3342, 3242, 3032, 2922, 1616, 1518, 1325, 1159; ^{1}H NMR (400-MHz, DMSO-d_6) δ: 9.37 (s, 1H, NH), 7.39 (s, 1H, NH), 6.70–7.72 (m, 8H, ArH), 2.40 (s, 3H, CH_3), 2.16 (s, 3H, CH_3); Anal. Calcd. for $C_{14}H_{16}N_2O_2S$: C, 60.87; H, 5.80; N, 10.14. Found: C, 60.60; H, 5.85; N, 10.41.

4.3.3 Compound 3c. Pale yellow needles, m.p. 141.5–143 °C; IR (KBr) ν (cm^{-1}): 3362, 3237, 3024, 2928, 1609, 1520, 1480, 1325, 1158; ^{1}H NMR (400-MHz, DMSO-d_6) δ: 9.32 (s, 1H, NH), 6.96 (s, 1H, NH), 6.65–7.73 (m, 8H, ArH), 2.39 (s, 3H, CH_3), 2.03 (s, 3H, CH_3); Anal. Calcd. for $C_{14}H_{16}N_2O_2S$: C, 60.87; H, 5.80; N, 10.14. Found: C, 60.62; H, 5.77; N, 10.32.

4.3.4 Compound 3d. Yellow needles, m.p. 135–136 °C; IR (KBr) ν (cm^{-1}): 3345, 3270, 3030, 2920, 1599, 1523, 1326, 1158; ^{1}H NMR (400-MHz, DMSO-d_6) δ: 9.29 (s, 1H, NH), 6.89 (s, 1H, NH), 6.45–7.71 (m, 7H, ArH), 2.38 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 1.98 (s, 3H, CH_3); Anal. Calcd. for $C_{15}H_{18}N_2O_2S$: C, 62.07; H, 6.21; N, 9.66. Found: C, 61.89; H, 6.11; N, 9.81.

4.3.5 Compound 3e. White needles, m.p. 120–122 °C; IR (KBr) ν (cm^{-1}): 3358, 3271, 3035, 2959, 1596, 1520, 1477, 1326, 1154; ^{1}H NMR (400-MHz, DMSO-d_6) δ: 9.25 (s, 1H, NH), 6.10 (s, 1H, NH), 6.72–7.57 (m, 7H, ArH), 2.35 (s, 3H, CH_3), 2.18 (s, 6H, CH_3); Anal. Calcd. for $C_{15}H_{18}N_2O_2S$: C, 62.07; H, 6.21; N, 9.66. Found: C, 61.91; H, 6.10; N, 9.76.

4.3.6 Compound 3f. Yellow needless, m.p. 141–143 °C; IR (KBr) ν (cm^{-1}): 3370, 3247, 3030, 2922, 1593, 1477, 1328, 1162; ^{1}H NMR (400-MHz, DMSO-d_6) δ: 9.29 (s, 1H, NH), 6.90 (s, 1H, NH), 6.59–7.73 (m, 7H, ArH), 2.39 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.92 (s, 3H, CH_3); Anal. Calcd. for $C_{15}H_{18}N_2O_2S$: C, 62.07; H, 6.21; N, 9.66. Found: C, 61.87; H, 6.13; N, 9.78.

4.3.7 Compound 3g. White needles, m.p. 136.5–137.5 °C; IR (KBr) ν (cm^{-1}): 3344, 3241, 3062, 2928, 1599, 1490, 1325, 1160; ^{1}H NMR (400-MHz, DMSO-d_6) δ: 9.53 (s, 1H, NH), 7.78 (s, 1H, NH), 6.81–7.73 (m, 8H, ArH), 2.40 (s, 3H, CH_3); Anal. Calcd. for $C_{13}H_{13}ClN_2O_2S$: C, 52.61; H, 4.38; N, 9.44. Found: C, 52.47; H, 4.25; N, 9.57.

4.3.8 Compound 3h. White needles, m.p. 147–148 °C (lit. [25] 144–145 °C) IR (KBr) ν (cm^{-1}): 3350, 3240, 3030, 2949, 1598, 1508, 1455, 1330, 1160; ^{1}H NMR (400-MHz, DMSO-d_6) δ: 9.51 (s, 1H, NH), 7.21 (s, 1H, NH), 6.76–7.74 (m, 8H, ArH), 2.39 (s, 3H, CH_3); Anal. Calcd. for $C_{13}H_{13}ClN_2O_2S$: C, 52.61; H, 4.38; N, 9.44. Found: C, 52.43; H, 4.27; N, 9.55.

4.3.9 Compound 3i. White needles, m.p. 145–147 °C (lit. [26] 147.5–148 °C). IR (KBr) ν (cm^{-1}): 3347, 3241, 3067, 2954, 1596, 1509, 1453, 1329, 1160.

4.3.10 Compound 3j. White needles, m.p. 133–134 °C; IR (KBr) ν (cm^{-1}): 3336, 3188, 3062, 2933, 1597, 1519, 1328, 1156; ^{1}H NMR (400-MHz, DMSO-d_6) δ: 9.48 (s, 1H, NH), 7.55 (s, 1H, NH), 6.82–7.73 (m, 8H, ArH), 2.40 (s, 3H, CH_3); Anal. Calcd. for $C_{13}H_{13}FN_2O_2S$: C, 55.71; H, 4.64; N, 10.00. Found: C, 55.55; H, 4.59; N, 10.10.

4.3.11 Compound 5a. White needles, m.p. 92–94 °C (lit. [27] 94–95 °C). IR (KBr) ν (cm^{-1}): 3059, 2971, 1595, 1489, 1456, 1378, 1173; ^{1}H NMR (400-MHz, $CDCl_3$) δ: 7.00–7.72 (m, 9H, ArH), 2.46 (s, 3H, CH_3).

4.3.12 Compound 5b. White needles, m.p. 80–81 °C (lit. [28] 79.6–80.6 °C). IR (KBr) ν (cm^{-1}): 3063, 2966, 1596, 1486, 1449, 1379, 1169; ^{1}H NMR (400-MHz, $CDCl_3$) δ: 6.92–7.69 (m, 8H, Ar-H), 2.45 (s, 3H, -CH_3); Anal. Calcd. for $C_{13}H_{11}ClO_3S$: C, 55.22; H, 3.89. Found: C, 55.21; H, 3.91.

4.3.13 Compound 5c. White needle, m.p. 69–71 °C; IR (KBr) ν(cm^{-1}): 3068, 2929, 1598, 1474, 1446, 1373, 1181; ^{1}H NMR (400-MHz, $CDCl_3$) δ: 7.19–7.79 (m, 8H, Ar-H), 2.47 (s, 3H, -CH_3); Anal. Calcd. for $C_{13}H_{11}ClO_3S$: C, 55.22; H, 3.89. Found: C, 55.20; H, 3.90.

4.3.14 Compound 5d. White needles, m.p. 88–89 °C (lit. [29] 83–84 °C). IR (KBr) ν (cm^{-1}): 3068, 2923, 1597, 1574, 1508, 1368, 1178; ^{1}H NMR (400-MHz, $CDCl_3$) δ: 7.23–7.93 (m, 11H, Ar-H), 2.44 (s, 3H, -CH_3); Anal. Calcd. for $C_{17}H_{14}O_3S$: C, 68.46; H, 4.70. Found: C, 68.36; H, 4.71.

4.3.15 Compound 5e. White needles, m.p. 122–124 °C (lit. [30] 125 °C).

4.3.16 Compound 5f. Yellow crystals, m.p. 99–101 °C; IR (KBr) ν (cm^{-1}): 3068, 2923, 1680, 1599, 1556, 1508, 1379, 1196; ^{1}H NMR (400-MHz, $CDCl_3$) δ: 6.31–8.56 (m, 10H, Ar-H), 2.47 (s, 3H, -CH_3); Anal. Calcd. for $C_{17}H_{13}NO_4S$: C, 62.39; H, 3.98; N, 4.28. Found: C, 62.44; H, 3.90; N, 4.23.

4.3.17 Compound 5g. White needles, m.p. 81–82 °C (lit. [26] 80–81 °C).

4.3.18 Compound 5h. White needles, m.p. 95–97 °C (lit. [31] 97–97.5 °C).

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