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Regioselective synthesis of 1-aryl-2-p-toluenesulfonyl hydrazides under microwave irradiation

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A series of 1-aryl-2-p-toluenesulfonyl hydrazides were synthesized by microwave irradiation under solvent-free conditions. The regioselectivity was excellent, the reaction time was short, the yields were moderate to high (64–91%), and the manipulation process was simple.

Keywords: Microwave irradiation; Solvent-free; 1-Aryl-2-p-toluenesulfonyl hydrazides; Regioselective synthesis

1. Introduction

Organosulfur compounds are useful materials and some of them have pharmacological properties. Specifically, some sulfonyl hydrazide derivatives are valuable as inhibitors [1], agrochemical fungicides [2], insecticides and photographic images [3]. The methods have been reported for preparing these compounds to date. Usually, they are prepared by the reaction of sulfonyl chloride and hydrazines [4] or reduction of azo compounds [5]. However, these reactions were carried out in organic solvent such as pyridine [6–8] and DMF. Moreover, they gave a mixture of 1,1- and 1,2-sulfonyl hydrazides, which are associated with difficult separation and low yields. Thus, simple, convenient and environmentally benign methods for the synthesis of single arylsulfonyl hydrazide derivatives are required.

We have reported the co-ground method for synthesis of aryl toluenesulfonyl hydrazides [9]. To improve efficiency and simplify the manipulation, we attempted to exploit a more efficient and simple method for synthesis of aryl toluenesulfonyl hydrazides. Initially introduced in 1986 [10], the chemical application of microwaves has now become an area of interest for the

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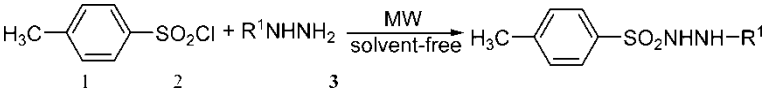
synthesis of a wide variety of compounds and efficient functional group transformations under solvent-free conditions [11–16]. The advantages of microwave-expedited chemical transformations are cleaner reactions, higher efficiency and selectivity, shorter reaction times, and the ease of manipulation. The reactions under solvent-free conditions are especially appealing as they can eliminate the use of organic solvent and increase the efficiency and selectivity, which when combined with microwave irradiation give a more eco-friendly approach required from both economic and environmental standpoints.

2. Results and discussion

In continuation of our studies on environmental methods, we now report a regioselective and microwave-assisted synthesis of 1-aryl-2-p-toluenesulfonyl hydrazides (scheme 1) under solvent-free conditions. The simple process, in its entirety, involves mixing the substrates followed by exposure to microwave irradiation under solvent-free conditions. With microwave irradiation, the experimental conditions were carefully monitored (by TLC) to regulate the ratio of the substrates, irradiation time and power level of the microwave oven to achieve the maximum yield. A 1:2 ratio of p-toluenesulfonyl chloride to arylhydrazine was the most



SCHEME 1

Table 1. Preparation of 1-aryl-2-p-toluenesulfonyl hydrazides under microwave irradiation.[c]

Entry	R^1	Product[a]	Time (min)	Yield[b] (%)	M.P.(°C) Lit: (°C)
1	C_6H_5	**3a**	5	89	154–156 (155) [17]
2	4-MeC_6H_4	**3b**	6	87	136–138 (140) [18]
3	2-MeC_6H_4	**3c**	4	86	140–142 (141.5–143) [9]
4	2,6-$(Me)_2C_6H_3$	**3d**	6	86	121–123 (120–122) [9]
5	2,3-$(Me)_2C_6H_3$	**3e**	8	88	142–143 (141–143) [9]
6	2-ClC_6H_4	**3f**	6	88	146–148 (144–145) [19]
7	2-BrC_6H_4	**3g**	5	91	146–148 (147.5–148) [5]
8	C_6H_5CO	**3h**	8	64	160–162 (164) [20]
9	4-$MeC_6H_4SO_2$	**3i**	5	74	217–219 (219–220) [21]
10	4-FC_6H_4	**3j**	8	80	132–134 (133–134) [9]
11	4-ClC_6H_4	**3k**	5	86	134–136 (136.5–137.5) [9]
12	4-$NO_2C_6H_4$	**3l**	60	0	
13	2,4-$(NO_2)_2C_6H_3$	**3m**	60	0	
14	4-$HO_3SC_6H_4$	**3n**	60	0	

a)All the compounds have been reported previously; b)Isolated yields; c)The power level of the reaction is 600 W.

acceptable ratio in terms of efficiency and safety; a power level of 600W was the most suitable. In this reaction, p-toluenesulfonyl chloride reacted with arylhydrazine to give the desired products **3a–3k**. The by-product, hydrogen chloride, is quenched by the second equivalent of arylhydrazine generating hydrazine hydrochloride in the course of the reaction thereby avoiding its release to the air and defining an additional environmentally friendly synthetic advantage. It should be pointed out that generally the yield of the reaction was not greatly influenced by the presence of electro-donating or electro-withdrawing substituents except for the very strong electro-withdrawing groups. For example, when we used p-nitrophenylhydrazine, 2,4-dinitrophenylhydrazine or p-hydrazinobenzenesulfonic acid as starting materials, no reaction was observed. Since the boiling points of aliphatic hydrazines are usually very low, they would evaporate under microwave irradiation even if at the lowest power. Hence we did not pursue the reactions between p-toluenesulfonyl chloride and aliphatic hydrazines. This method does not require any base (beyond excess hydrazine) and any catalyst and no 1-aryl-1-p-toluenesulfonyl hydrazides were detected (by TLC). The yields are moderate to high (64–91%) and the reaction times are short (4–8 min). The results are reported in table 1.

3. Conclusions

In summary, a simple, efficient, microwave-assisted and environmentally benign method has been developed for preparation of 1-aryl-2-p-toluenesulfonyl hydrazides under solvent-free conditions. This method is superior from the view of yield, reaction time, selectivity and easier operation to the 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. The reactions took place in the Galanz WD750S microwave oven.

4.1 *A typical procedure for preparation of 1-aryl-2-p-toluenesulfonyl hydrazide*

p-Toluenesulfonyl chloride (0.25 mmol) and phenylhydrazine (0.5 mmol) were mixed thoroughly in a crucible and exposure to microwave oven for 5 min under solvent-free conditions (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 *Physical and spectra data of partial products*

4.2.1 Compound 3c. Pale yellow needles, m.p. 140–142 °C (lit. [9] 141.5–143 °C). IR (KBr) ν (cm^{-1}): 3358, 3232, 3021, 2925, 1609, 1525, 1483, 1321, 1156; ^{1}H NMR (400 MHz, DMSO-d$_6$) δ: 9.36 (s, 1H, NH), 6.91 (s, 1H, NH), 6.75 (d, 1H, ArH), 6.93–6.98 (m, 3H, ArH), 7.39 (d, 2H, ArH), 7.83 (d, 2H, ArH), 2.42 (s, 3H, CH_3), 2.13 (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, 60.63; H, 5.75; N, 10.36.

4.2.2 Compound 3d. White needles, m.p. 121–123 °C (lit. [9] 120–122 °C). IR (KBr) ν (cm^{-1}): 3358, 3275, 3032, 2956, 1594, 1525, 1475, 1324, 1152; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.22 (s, 1H, NH), 6.08 (s, 1H, NH), 6.70–6.72 (t, 1H, ArH), 6.80 (d, 2H, ArH), 7.29 (d, 2H, ArH), 7.54 (d, 2H, ArH), 2.32 (s, 3H, CH_3), 2.15 (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, 61.95; H, 6.11; N, 9.75.

4.2.3 Compound 3e. Yellow needles, m.p. 142–143 °C (lit. [9] 141–143 °C). IR (KBr) ν (cm^{-1}): 3375, 3248, 3034, 2925, 1596, 1477, 1325, 1168; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.26 (s, 1H, NH), 6.95 (s, 1H, NH), 6.56 (d, 1H, ArH), 6.86–6.89 (m, 1H, ArH), 6.93 (d, 1H, ArH), 7.39 (d, 2H, ArH), 7.78 (d, 2H, ArH), 2.36 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 1.82 (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, 61.85; H, 6.12; N, 9.80.

4.2.4 Compound 3j. White needles, m.p. 132–134 °C (lit. [9] 133–134 °C). IR (KBr) ν (cm^{-1}): 3332, 3188, 3059, 2931, 1595, 1519, 1325, 1156; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.46 (s, 1H, NH), 7.50 (s, 1H, NH), 6.78 (d, 2H, ArH), 6.93 (d, 2H, ArH), 7.41 (d, 2H, ArH), 7.75 (d, 2H, 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, 55.58; H, 4.56; N, 10.12.

4.2.5 Compound 3k. White needles, m.p. 134–136 °C (lit. [9] 136.5–137.5 °C). IR (KBr) ν (cm^{-1}): 3344, 3241, 3062, 2925, 1599, 1495, 1325, 1165; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.50 (s, 1H, NH), 7.75 (s, 1H, NH), 6.84 (d, 2H, ArH), 7.13 (d, 2H, ArH), 7.41 (d, 2H, ArH), 7.76 (d, 2H, ArH), 2.38 (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, 52.49; H, 4.22; N, 9.61.

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