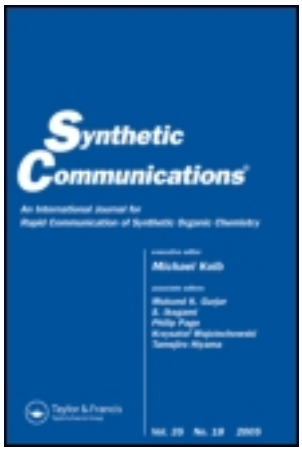

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Solvent-Free Synthesis of Aryl Tosylates Under Microwave Activation

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Solvent-Free Synthesis of Aryl Tosylates Under Microwave Activation

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ABSTRACT

Synthesis of aryl tosylates from phenols requires only several minutes when conducted with controlled microwave heating under solvent-free condition. Eight different aryl tosylates were synthesized and isolated in good yields.

Key Words: Aryl tosylates; Phenols; Microwave activation; Solvent-free synthesis.

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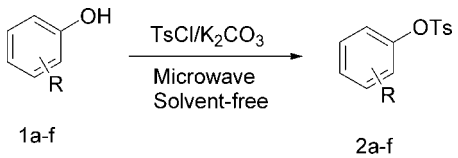
INTRODUCTION

Aryl tosylates are useful starting materials in many types of palladium- and nickel-catalyzed Suzuki and other coupling reactions.[1] For example, palladium-catalyzed alkoxycarbonylation of aryl *p*-toluenesulfonates (tosylates) has been reported.[2] Although tosylates are expected to be less reactive than triflates, Hartwig and Hammann[3a–c] have shown that the tosylate functionality can participate in aniline coupling reactions. Using the ferrocenyl-derivatived ligand, they succeeded in the cross-coupling of aniline with aryl tosylates in high yields. Iron and copper-catalyzed cross couplings of aryl tosylates have also reported.[3d,e]

The most common procedure for the preparation of aryl tosylates is to react toluene-4-sulfonyl-chloride (TsCl) with a phenol in the presence of a toxic base, pyridine or Et_3N. In most cases, reaction times between 12 and 16 hr are needed when employing TsCl. We aimed at finding efficient synthetic conditions for the reduction of the reaction time in order to make the tosylation more adoptable to high-throughput chemistry. In high-throughput and green chemistry there is a need to decrease the reaction times as well as effecture the purification procedures. Conceptual and technological solutions to these issues have been the subjects of intensive research.[4] Automated and focused microwave irradiation was recently proven to improve the preparative efficiency and to dramatically reduce reaction times for several different types of organic and organometallic transformations. And more than, for environmental, economical and safety reasons, solvent free reactions (dry reactions) were successfully used with the microwave activation.[5] Although microwave technique has been widely used for many organic reactions, the preparation of aryl tosylates by a microwave-mediated process was not reported. Herein, we describe the first protocol for fast microwave-promoted tosylation of phenols (Sch. 1).

Eight different phenols were selected as starting materials. The selection was made to include both electron-donating and electron-withdrawing substituents. Na_2CO_3 or K_2CO_3 was chosen due to its ability to act as a drying agent as well as a base. Na_2CO_3 and K_2CO_3 were found to be the same important base. The results from the study outlined in Table 1.



Scheme 1.

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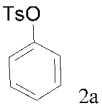
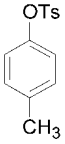
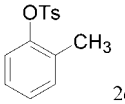
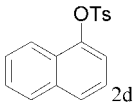
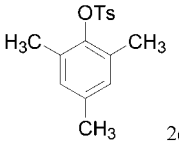
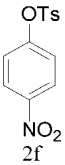
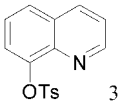
Table 1. Synthesis of aryl tosylates.

		Microwave irradiation		Conventional heating[a] (45°C)	
Entry	Product	Time (min)	Isolated yield (%)	Time (hr)	Isolated yield (%)
1	 2a	3	99	12	91
2	 2b	3	98	12	82
3	 2c	3	98	12	75
4	 2d	3	97	12	85
5	 2e	5	92	14	77
6	 2f	5	98	12	86
7	 3	5	98	16	90

[a]Pyridine was used as a solvent.

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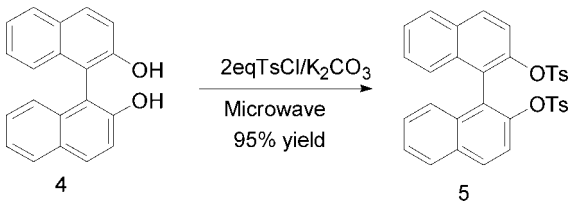
Using controlled microwave heating we succeeded in reducing the reaction time to 3 min. To compare the efficacy of microwave irradiation with those of conventional heating, the reaction was performed under previous reported conditions. The results suggested that microwave heating presented improvements in yields even with large amounts of products. Aryl tosylates have been proven to be surprisingly stable at high temperatures,[6] and the reactions were found not to be sensitive to air or moisture, hence there was no need for an inert atmosphere. All the phenols were smoothly converted to aryl tosylates in isolated yields between 92% and 99%. There was no clear correlation between the reaction outcome and the electron density of the substituents, and a large group in the *ortho*-position did not reduce the yield to any extent. The reaction condition was successfully applied to 2,2′-dihydroxy-1,1′-binaphthyl (BINOL). Under the same conditions, 5 min microwave heating was give the title product with high yield (95% yield, Sch. 2). It is notable that, the solvent-free reaction gave simple, clean, and green work-up procedure in purification.

In summary, we have developed a convenient, solvent-free, economical, clean, and high-speed method for synthesis of aryl tosylates.

EXPERIMENTAL

General

All regeants were used without further purification. Microwave assisted reactions were carried out using a Galanz microwave oven model WP800SL23 of variable radiofrequency. Melting points: X-4 (Beijing) are uncorrected; infrared spectra were performed in a Nicolet 10DX FT-IR spectrophotometer; NMR spectra were recorded on a AM-400 Bruker; Mass spectra were obtained on a GC/MS HP6890/5973.



Scheme 2.

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Synthesis of Aryl Tosylates: General Procedure

A dry 100 mL, single-necked, round-bottomed flask was charged with 110 mmol phenol, 100 mmol TsCl, and 200 mmol K_2CO_3. The reaction mixture was irradiation for 3 min (or 5 min) at 250 W. After cooling to room temperature, the remaining mixture was dissolved in 50 mL of water and stirred for several minutes. The pure product was easily obtained by filtration, wash with a 0.1 N aqueous sodium hydroxide solution, water, and then dried in vacuo. The yields as given below.

Phenyl tosylate (2a).[7] The general procedure gave 24.55 g (99% yield based on TsCl) of white solid: m.p. 90–91°C. ^{1}H NMR ($CDCl_3$): δ 7.70 (d, $J = 8.2$ Hz, 2H), 7.31–3.25 (m, 5H), 7.01 (d, $J = 7.7$ Hz, 2H), 2.42 (s, 3H). GC-MS (IE, 70 eV) m/z (%) 91 (100), 155 (91), 65 (44), 248 (14, M+), 63 (11), 51 (9), 92 (7), 89 (6). IR (KBr, cm^{-1}): 2909, 2859, 1454, 1382, 1192, 865, 774, 725, 688, 656.

4-Methylphenyl tosylate (2b).[7] The general procedure gave 25.68 g (98% yield) of white solid: m.p. 59–60°C. ^{1}H NMR ($CDCl_3$): δ 7.67 (d, $J = 8.3$ Hz, 2H), 7.29 (d, $J = 7.8$ Hz, 2H), 7.03 (d, $J = 8.1$ Hz, 2H), 6.83 (d, $J = 8.5$ Hz, 2H), 2.43 (s, 3H), 2.28 (s, 3H). GC-MS (IE, 70 eV) m/z (%) 91 (100), 155 (50), 65 (31), 77 (29), 107 (24), 262 (18, M+), 79 (14), 52 (11). IR (KBr, cm^{-1}) 2928, 2854, 1593, 1505, 1461, 1378, 1197, 866, 782, 728, 692, 656.

2-Methylphenyl tosylate (2c).[7] The general procedure gave 25.68 g (98% yield) of white solid: m.p. 60–61°C. ^{1}H NMR ($CDCl_3$): 7.71 (d, $J = 8.4$ Hz, 2H), 7.30 (d, $J = 8.1$ Hz, 2H), 7.03–6.97 (m, 4H), 2.43 (s, 3H), 2.06, (s, 3H). GC-MS (IE, 70 eV) m/z (%) 91 (100), 155 (46), 65 (28), 77 (24), 51 (19), 262 (14, M+), 101 (13), 52 (10). IR (KBr, cm^{-1}): 2927, 2853, 1460, 1377, 1194, 873, 751, 660.

1-Naphtyl tosylate (2d).[8] The general procedure gave 29 g (97% yield) of white solid: m.p. 84–86°C. ^{1}H NMR ($CDCl_3$): 7.92 (d, $J = 7.9$ Hz, 1H), 7.82–7.73 (m, 4H), 7.51–7.35 (m, 3H), 7.29–7.21 (m, 3H), 2.40 (s, 3H). GC-MS (IE, 70 eV) m/z (%) 115 (100), 143 (89), 91 (56), 65 (34), 298 (19, M+), 89 (18), 155 (16), 63 (17), 144 (12), 116 (11). IR (KBr, cm^{-1}): 2926, 2856, 1598, 1369, 1215, 1178, 890, 768, 711, 661.

2,3,6-Trimethylphenyl tosylate (2e).[1b,7] The general procedure gave 26.56 g (92% yield) of white solid: m.p. 58–60°C. ^{1}H NMR ($CDCl_3$): 7.82 (d, $J = 8.3$ Hz, 1H), 7.34 (d, $J = 8.3$ Hz, 2H), 6.95 (d, $J = 7.6$ Hz, 2H), 2.46 (s, 3H), 2.21 (s, 3H), 2.10 (s, 3H), 2.01 (s, 3H). GC-MS (IE, 70 eV) m/z (%) 135 (100), 91 (70), 65 (24), 155 (19), 290 (14, M+), 79 (12), 136 (11), 77 (9), 92 (8). IR (KBr, cm^{-1}): 2929, 2856, 1595, 1462, 1176, 892, 778, 731, 671.

4-Nitrophenyl tosylate (2f).[1b,7] The general procedure gave 28.81 g (98% yield) of white solid: m.p. 96–97°C. ^{1}H NMR ($CDCl_3$): 8.19

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(d, $J = 9.1$ Hz, 2H), 7.73 (d, $J = 8.2$ Hz, 2H), 7.35 (d, $J = 8.1$ Hz, 2H), 7.18 (d, $J = 9.1$ Hz, 2H), 2.47 (s, 3H). GC-MS (IE, 70 eV) m/z (%) 91 (100), 155 (75), 65 (21), 292 (5). IR (KBr, cm^{-1}): 3118, 2926, 2870, 1618, 1591, 1484, 1170, 1089, 870, 728, 665.

8-Quinoline tosylate (4). The general procedure gave 29.30 g (98% yield) of white solid: m.p. 85–86°C. ^{1}H NMR ($CDCl_3$): 8.80 (d, $J = 5.5$ Hz, 1H), 8.08 (d, $J = 8.3$ Hz, 1H), 7.84 (d, $J = 9.4$ Hz, 2H), 7.70 (d, $J = 7.9$ Hz, 1H), 7.45 (m, $J = 8.0$ Hz, 1H), 7.35 (m, $J = 8.3$ Hz, 1H), 7.21 (d, $J = 8.1$ Hz, 2H), 2.35 (s, 3H). IR (KBr, cm^{-1}): 3064, 2918, 1597, 1498, 1470, 1374, 1311, 1179, 1081, 887, 831, 777, 663.

1,1′-Binaphtyl 2,2′-ditosylate (6). BINOL (100 mmol, 28.6 g), K_2CO_3 (0.4 mol, 55.2 g), and the TsCl (200 mmol, 38 g) were taken in the reaction flask and the resultant mixture was placed in the microwave oven. And the worked up procedure as same as above. The general procedure gave 56.43 g (95% yield) of white solid: m.p. 183–184°C. ^{1}H NMR ($CDCl_3$): 7.90 (d, $J = 9.0$, 2H), 7.83 (d, $J = 8.2$ Hz, 2H), 7.70 (d, $J = 9.0$ Hz, 2H), 7.41 (m, $J = 7.2$ Hz, 2H), 7.09 (m, $J = 7.6$ Hz, 2H), 7.00 (d, $J = 8.1$ Hz, 4H), 6.76 (d, $J = 8.5$ Hz, 2H), 6.67 (d, $J = 8.9$ Hz, 4H), 2.20 (s, 6H). IR (KBr, cm^{-1}): 3060, 2922, 1596, 1508, 1376, 1171, 1092, 970, 937, 824, 771, 677.

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