Convenient synthesis of sulfonyl azides using PEG-400 as an efficient and eco-friendly reaction medium

Hongyao Zeng\textsuperscript{a,b} and Huawu Shao\textsuperscript{a*}

\textsuperscript{a}Natural Products Research Center, Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu, PR China; \textsuperscript{b}University of Chinese Academy of Sciences, Beijing, China

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Sulfonyl azides have efficiently been synthesized via a convenient and environmentally benign procedure, in which sulfonyl chlorides undergo nucleophilic substitution reaction with sodium azide in PEG-400 under mild conditions. The sulfonyl azides were obtained in 84–97% isolated yields.

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\begin{array}{c}
\text{O} \quad \text{O} \\
\text{R} \quad \text{S} \quad \text{Cl} \quad + \quad \text{Na}_2\text{N}_3 \\
1 \quad 2 \quad \text{PEG-400} \quad \text{r.t.} \\
10–40\text{min} \quad 84–97\%
\end{array}
\]

\( R = \) alkyl, aryl, cinnamyl and heteroaryl

Keywords: sulfonyl azides; PEG-400; reaction medium; sodium azide

Introduction

Sulfonyl azides are very valuable reagents in organic chemical transformations such as the preparation of \( \alpha \)-diazo carbonyl compounds [1], the hydro-hydrazination or/and hydroazidation of olefins [2,3], the aziridination of olefins [4], the radical amination [5,6], and metal-catalyzed coupling reactions [7]. Due to a wide range of applications, there are many methods available for the preparation of sulfonyl azides. For example, sulfonyl azides were prepared by reacting sulfonyl anhydrides [8], \( \alpha \)-disulfoines [9], or 1-sulfonylbenzotriazole [10] with sodium azide. These procedures may suffer from the unavailability of starting materials or their difficulty in preparation. Additionally, diazotization of sulfonyl hydrazides with NO\textsuperscript{+} has also been employed but still requires the availability of the hydrazides [11]. However, the most practical laboratory methods for preparing sulfonyl azides by nucleophilic substitution reaction of sulfonyl chlorides with sodium azide in various solvents are such as alcohol/H\textsubscript{2}O, acetone/H\textsubscript{2}O, DME/H\textsubscript{2}O, and so on [3,12–17]. Since nucleophilic substitution reactions of sulfonyl chloride involve a nonpolar organic compound and a polar ionic salt, sodium azide, the heterogenous reactions are often troublesome because the polar and nonpolar reagents are often not soluble in a single solvent system. Consequently, to improve the yields and to facilitate the product isolation, the nucleophilic displacement reactions are carried out under phase-transfer catalysis conditions [18,19]. However, these methodologies often suffer from complex procedures, long reaction times, and low yields. Thus, there is a great demand for the development of new convenient and eco-friendly synthetic methods toward assessing sulfonyl azides.

In the recent years, polyethylene glycols (PEGs) have attracted great interest and have been explored as a novel, powerful, eco-friendly reaction medium for various organic transformations [20–25] due to their relatively inexpensive, thermally stable, readily recyclable, and biodegradable. In a continuation of our work [20] to explore PEG as an efficient and eco-friendly reaction medium, we report here a convenient and practical synthesis of sulfonyl azides by using sodium azide in PEG-400 at room temperature (Scheme 1).

Results and discussion

Initially, we examined the effectiveness of PEG-400 for the model reaction of 4-Tosyl chloride and sodium azide (Entry 4, Table 1). In a typical experimental
Scheme 1. Synthesis of sulfonyl azides from sulfonyl chlorides.

procedure, a screening of different solvents (CH3CN, THF, CH2Cl2, toluene, and so on) for the model reaction revealed that PEG-400 was the most active reaction medium.

To investigate the generality and scope of the reaction, various sulfonyl chlorides were subjected to the reaction conditions and no additional catalyst and solvent were required. The results are summarized in Table 1. As presented in Table 1, all aryl and aliphatic sulfonyl chlorides gave sulfonyl azides in excellent yields in 10–40 minutes. Aryl sulfonyl chlorides containing both electron-donating, such as methyl, methoxyl, and electron-withdrawing groups, like nitro, acetamido, underwent the conversion smoothly. Aryl sulfonyl chlorides with electron-withdrawing groups such as NO2 required slightly more time (Entries 8–10, Table 1). With more sterically hindered sulfonyl chlorides, satisfactory yields were still obtained from the nucleophilic substitution (Entries 5, 6, and 10, Table 1).

2-Nitrobenzenesulfonyl chloride took the longest time caused by the electronic and steric hindrance effect (Entry 10, Table 1). The presence of various functional groups such as halides, nitro, acetamido, and methoxyl on the aryl sulfonyl chlorides was tolerated (Entries 7–13, Table 1). Trans-β-styrenesulfonyl chloride and 2-thiophenesulfonyl chloride have also been successfully converted into their corresponding sulfonyl azides in high yields (Entries 14 and 15, Table 1). In short, the products were all formed in excellent yields and no side products were detected. The structures of all products were identified by their physical and spectral data. Infrared spectra of all compounds have strong characteristic band at 2120 cm⁻¹ (N₃), 1310, 1170 cm⁻¹ (PF), and 1100, 1079 cm⁻¹ (SO₂).

Characterization data of selected known compounds and new compound

The products are all known except 3m and were identified by comparing their physical and spectral data with literature values. Spectral data for selected and new compounds are described in the following subsections.

1-Butanesulfonyl azide (3a)

Pale yellow liquid. 1H NMR (CDCl₃); δH 0.99 (t, J = 7.4 Hz, 3H), 1.48–1.57 (m, 2H), 1.88–1.93 (m, 2H), 3.32 (t, J = 7.9 Hz, 2H). 13C NMR (CDCl₃); δC 13.4, 21.3, 25.3, 55.7. IR (KBr), ν/cm⁻¹: 3306, 2965, 2877, 2378, 2136, 1467, 1364, 1242, 1198, 1159, 1100, 1079, 917, 794, 735.

Phenylmethanesulfonyl azide (3b)

Colorless solid, m.p. 53–54 °C. 1H NMR (CDCl₃); δH 4.53 (s, 2H), 7.43–7.48 (m, 5H). 13C NMR (CDCl₃); δC 61.9, 126.6, 129.3, 129.9, 130.9. IR (KBr), ν/cm⁻¹:
Table 1. Synthesis of sulfonyl azides from sulfonyl chlorides using PEG-400 as an efficient reaction medium.\textsuperscript{a}

| Entry | Sulfonyl chloride | Sulfonyl azide | Time (mins) | Yield\textsuperscript{b} | Found  | Reported\textsuperscript{c} | m.p. (°C) |
|-------|------------------|----------------|-------------|---------------------------|--------|---------------------------|-----------|
| 1     | CH\(_3\)(CH\(_2\))\(_2\)SO\(_2\)Cl \(1a\) | CH\(_3\)(CH\(_2\))\(_2\)SO\(_2\)N\(_3\) \(3a\) | 10          | 94                        | Oil    | Oil [10]                  |           |
| 2     | \(\text{Ph-SO}_2\)Cl \(1b\) | \(\text{Ph-SO}_2\)N\(_3\) \(3b\) | 10          | 97                        | 53–54  | 53.5–54 [26]              |           |
| 3     | \(\text{Ph-SO}_2\)Cl \(1c\) | \(\text{Ph-SO}_2\)N\(_3\) \(3c\) | 10          | 96                        | 13–14  | 13.5–14.5 [11]            |           |
| 4     | \(\text{Ph-SO}_2\)Cl \(1d\) | \(\text{Ph-SO}_2\)N\(_3\) \(3d\) | 10          | 94                        | 22–23  | 22.5–23.5 [11]            |           |
| 5     | \(\text{Ph-SO}_2\)Cl \(1e\) | \(\text{Ph-SO}_2\)N\(_3\) \(3e\) | 10          | 90                        | Oil    | Oil [7]                   |           |
| 6     | \(\text{Ph-SO}_2\)Cl \(1f\) | \(\text{Ph-SO}_2\)N\(_3\) \(3f\) | 30          | 84                        | 42–43  | 41–43 [14]                |           |
| 7     | H\(_3\)CO\(\text{-SO}_2\)Cl \(1g\) | H\(_3\)CO\(\text{-SO}_2\)N\(_3\) \(3g\) | 10          | 95                        | 50–51  | 51.5–52 [17]              |           |
| 8     | O\(_2\)N\(\text{-SO}_2\)Cl \(1h\) | O\(_2\)N\(\text{-SO}_2\)N\(_3\) \(3h\) | 30          | 90                        | 100–101| 101.5–102 [17]            |           |
| 9     | O\(_2\)N\(\text{-SO}_2\)Cl \(1i\) | O\(_2\)N\(\text{-SO}_2\)N\(_3\) \(3i\) | 30          | 95                        | 78–79  | 80.5–81 [17]              |           |
| 10    | \(\text{Ph-SO}_2\)Cl \(1j\) | \(\text{Ph-SO}_2\)N\(_3\) \(3j\) | 40          | 85                        | 67–68  | 68–71 [15]                |           |
| 11    | Br\(\text{-SO}_2\)Cl \(1k\) | Br\(\text{-SO}_2\)N\(_3\) \(3k\) | 10          | 97                        | 54–55  | 54.5–56 [17]              |           |
| 12    | AcHN\(\text{-SO}_2\)Cl \(1l\) | AcHN\(\text{-SO}_2\)N\(_3\) \(3l\) | 10          | 93                        | 107–108| 108–110 [16]              |           |
### Table 1 (Continued)

| Entry | Sulfonyl chloride | Sulfonyl azide | Time (mins) | Yield | Found | Reported |
|-------|------------------|----------------|-------------|-------|-------|----------|
| 13    | ![Structure 1m](image) | ![Structure 3m](image) | 10 | 92 | 95–97 | – |
| 14    | ![Structure 1n](image) | ![Structure 3n](image) | 30 | 91 | 31–32 | 31.5–33 [26] |
| 15    | ![Structure 1o](image) | ![Structure 3o](image) | 10 | 90 | 30–31 | 30–32 [10] |

*Reaction conditions: sulfonyl chloride (2.0 mmol), sodium azide (2.4 mmol), and PEG-400 (2 mL) at room temperature.*

*Isolated yield.

*The compound reported in the literature.*

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3436, 3294, 2979, 2137, 1599, 1496, 1456, 1407, 1355, 1270, 1179, 1159, 1136, 1031, 884, 793, 748. | 1598, 1462, 1434, 1385, 1378, 1364, 1350, 1261, 1175, 1104, 1059, 889, 802, 740.

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**Benzenesulfonyl azide (3c)**

Colorless solid, m.p. 13–14 °C. 1H NMR (CDCl3): δH 7.63 (t, J = 7.5 Hz, 2H), 7.74 (t, J = 7.5 Hz, 1H), 7.97 (d, J = 7.9 Hz, 2H). 13C NMR (CDCl3): δC 127.5, 129.7, 134.8, 138.5. IR (KBr), ν/cm⁻¹: 3436, 3294, 2979, 2137, 1599, 1496, 1456, 1407, 1355, 1270, 1179, 1159, 1136, 1031, 884, 793, 748.

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**4-Toluenesulfonyl azide (3d)**

Colorless solid, m.p. 22–23 °C. 1H NMR (CDCl3): δH 7.41 (d, J = 8.1 Hz, 2H), 7.84 (d, J = 8.3 Hz, 2H). 13C NMR (CDCl3): δC 21.7, 127.5, 130.3, 135.6, 146.2. IR (KBr), ν/cm⁻¹: 3273, 3067, 2926, 2127, 1595, 1494, 1450, 1371, 1308, 1167, 1211, 1086, 1018, 814, 748.

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**4-Methoxysulfonyl azide (3g)**

Colorless solid, m.p. 50 °C. 1H NMR (CDCl3): δH 3.91 (s, 3H). 13C NMR (CDCl3): δC 23.4, 24.3, 24.7, 29.7, 34.3, 124.1, 124.3, 139.3, 150.4, 150.9, 155.6. IR (KBr), ν/cm⁻¹: 3435, 3055, 2961, 2930, 2870, 2121, 1732, 1583, 1449, 1373, 1313, 1170, 1020, 930, 753.

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**4-Nitrobenzenesulfonyl azide (3h)**

Tan solid, m.p. 100–101 °C. 1H NMR (CDCl3): δH 8.17 (d, J = 8.8 Hz, 2H). 13C NMR (CDCl3): δC 124.9, 143.8, 1318, 1315, 1301, 1178, 1160, 1085, 854, 769, 744.

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**2-Nitrobenzenesulfonyl azide (3j)**

Tan solid, m.p. 68–71 °C. 1H NMR (CDCl3): δH 7.88 (dd, 1H), 7.92 (dd, 1H), 8.20 (dd, 1H). 13C NMR (CDCl3): δC 134.2, 131.7, 132.7, 133.0, 148.3. IR (KBr), ν/cm⁻¹: 3320, 3100, 2923, 2381, 2157, 1594, 1550, 1438, 1363, 1315, 1261, 1194, 1145, 1120, 967, 853, 755, 737.

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**2-Nitrobenzenesulfonyl azide (3j)**

Tan solid, m.p. 68–71 °C. 1H NMR (CDCl3): δH 7.88 (dd, 1H), 7.92 (dd, 1H), 8.20 (dd, 1H). 13C NMR (CDCl3): δC 134.2, 131.7, 132.7, 133.0, 148.3. IR (KBr), ν/cm⁻¹: 3320, 3100, 2923, 2381, 2157, 1594, 1550, 1438, 1363, 1315, 1261, 1194, 1145, 1120, 967, 853, 755, 737.
4-Acetamidobenzensulfonyl azide (3l)

White solid, m.p. 107–108 °C. $^1$H NMR (CDCl$_3$): $\delta$H 2.25 (s, 1H), 7.78 (d, $J$ = 9.0 Hz, 2H), 7.79 (bri, 1H), 7.89 (d, $J$ = 8.8 Hz, 2H). $^{13}$C NMR (CDCl$_3$): $\delta$C 24.7, 119.6, 129.6, 129.0, 132.7, 143.9, 168.9. IR (KBr), v/cm$^{-1}$: 3303, 3264, 3185, 3112, 2130, 2120, 1676, 1585, 1534, 1405, 1365, 1315, 1265, 1165, 1086, 839, 752, 707.

7.89 (d, $J$ = 8.8 Hz, 2H). $^{13}$C NMR (CDCl$_3$): $\delta$C 24.7, 119.6, 129.6, 129.0, 132.7, 143.9, 168.9. IR (KBr), v/cm$^{-1}$: 3303, 3264, 3185, 3112, 2130, 2120, 1676, 1585, 1534, 1405, 1365, 1315, 1265, 1165, 1086, 839, 752, 707.

3-Chloro-4-acetamidobenzensulfonyl azide (3m)

White solid, m.p. 95–97 °C. $^1$H NMR (CDCl$_3$): $\delta$H 2.32 (s, 3H), 7.85 (dd, $J$ = 2.2, $J$ = 9.0 Hz, 1H), 7.87 (bri, 1H), 7.97 (d, $J$ = 2.2 Hz, 1H), 8.74 (d, $J$ = 8.8 Hz, 1H). $^{13}$C NMR (CDCl$_3$): $\delta$C 25.1, 120.9, 122.6, 127.5, 128.0, 134.7, 135.1, 138.2. IR (KBr), v/cm$^{-1}$: 3292, 3065, 2345, 2130, 1754, 1601, 1504, 1392, 1375, 1306, 1171, 1098, 857, 837, 778, 745.

Trans-$\beta$-styrenesulfoyl azide (3n)

White solid, m.p. 115–117 °C. $^1$H NMR (CDCl$_3$): $\delta$H 6.94 (d, $J$ = 15.3 Hz, 1H), 7.45–7.47 (m, 2H), 7.50 (m, 1H), 7.53–7.55 (m, 2H), 7.70 (d, $J$ = 15.3 Hz, 1H). $^{13}$C NMR (CDCl$_3$): $\delta$C 123.2, 126.8, 128.9, 129.4, 129.6, 129.8, 131.3, 132.2. IR (KBr), v/cm$^{-1}$: 3292, 3065, 2345, 2130, 1725, 1610, 1576, 1495, 1450, 1368, 1180, 1154, 1107, 1074, 975, 863, 821, 749.

2-Thiophenesulfonyl azide (3o)

Pale yellow, m.p. 30–31 °C. $^1$H NMR (CDCl$_3$): $\delta$H 7.21 (dd, $J$ = 3.9, $J$ = 4.9 Hz, 1H), 7.80 (dd, $J$ = 1.4, $J$ = 4.9 Hz, 1H), 7.21 (dd, $J$ = 1.4, $J$ = 3.9 Hz, 1H). $^{13}$C NMR (CDCl$_3$): $\delta$C 128.0, 134.7, 135.1, 138.2. IR (KBr), v/cm$^{-1}$: 3271, 3101, 2129, 1754, 1601, 1504, 1400, 1378, 1345, 1167, 1094, 1019, 857, 757, 746.

Conclusion

In summary, we have disclosed a simple, mild, and efficient method for the synthesis of sulfonyl azides. Compared to the previously reported methods, this protocol offers several advantages including exceedingly mild conditions, operational simplicity, more environmentally benign, short reaction time, and higher reaction yield. Further investigations on the application of PEG-400 on other catalytically synthetic reactions will be reported in due course.

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