



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

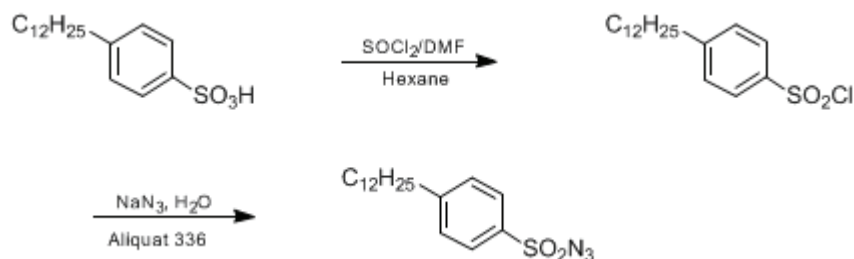
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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4-DODECYLBENZENESULFONYL AZIDES

[Benzenesulfonyl azides, 4-dodecyl-]



Submitted by G. G. Hazen, F. W. Bollinger, F. E. Roberts, W. K. Russ, J. J. Seman, and S. Staskiewicz¹.

Checked by Mark Spaller and Stephen F. Martin.

1. Procedure

Caution! Although the mixture of dodecylbenzenesulfonyl azides is the safest of a group of diazo transfer reagents,² one should keep in mind the inherent instability, shock sensitivity, and explosive power of azides. All users should exercise appropriate caution.

4-Dodecylbenzenesulfonyl chlorides. A 250-mL, three-necked, round-bottomed flask, equipped with a mechanical overhead stirrer, a Claisen adapter bearing an immersion thermometer, a pressure-equalizing addition funnel, and reflux condenser, is charged with a solution of 60.00 g (0.184 mol) of dodecylbenzenesulfonic acids (Note 1) and 8.64 mL of dimethylformamide (DMF) in 60 mL of hexane. Stirring is initiated while the mixture is heated to 70°C using a heating mantle, and 22.1 mL (36.24 g, 0.304 mol) of thionyl chloride (Note 2) is added at a rate to maintain controlled reflux (Note 3). The required addition time is about 1 hr. The dark solution is heated an additional 2 hr at 70°C and cooled to 40°C (Note 4). While still warm (~40°C), the mixture is transferred to a 250-mL separatory funnel, and the dark lower layer is separated from the hexane solution (Note 5). The hexane layer is cooled to 25°C and washed with 60 mL of aqueous 5% sodium bicarbonate solution (Note 6). The bicarbonate wash is back extracted with 36 mL of hexane and the combined hexane layers are treated with 3 g of carbon (Note 7), (Note 8) and stirred for 2 hr at 25°C. The carbon is removed by filtration and the cake is washed with three portions (12-mL each) of hexane. The combined hexane layers plus the hexane washes are used to prepare the azide.

4-Dodecylbenzenesulfonyl azides. A 500-mL, three-necked, round-bottomed flask fitted with a mechanical overhead stirrer is charged with the hexane solution from step A. To this solution is added a solution of 11.6 g (0.178 mol based on the total solids from the sulfonyl chlorides above) of sodium azide (NaN₃) in 100 mL of water and 2.0 g of phase transfer catalyst (Aliquat 336) (Note 9). Stirring is initiated, and the reaction progress is monitored by thin layer chromatography (Note 10). Approximately 4 hr at 25°C is required to complete the reaction. The two-phase mixture is transferred to a 500-mL separatory funnel and the aqueous layer is removed. The hexane layer is washed with 100 mL of aqueous 5% sodium bicarbonate solution and dried over 28 g of anhydrous sodium sulfate. The drying agent is removed by suction filtration, and the cake is washed with 20 mL of hexane. The concentration and purity of the 4-dodecylbenzenesulfonyl azides are best determined by evaporation of a small sample to an oil of constant weight with visible spectrophotometric assay for the azide (Note 11). The hexane solution of dodecylbenzenesulfonyl azides, when standardized as above (Note 11), can be used as obtained for most applications. However, if desired, careful concentration of the hexane solution under reduced pressure at room temperature affords 58.2–61.4 g (90–95%) of the oily mixture of dodecylbenzenesulfonyl azides; corrected for the assay of the azides the yield is usually 95% (Note 12) and (Note 13).

2. Notes

1. Dodecylbenzenesulfonic acids, a 97% mixture of branched chain isomers, was purchased from Spectrum Chemical Mfg. Corp.
2. Reagent grade **thionyl chloride** from Fisher Scientific Co. was used.
3. An excess of **thionyl chloride–dimethylformamide** catalyst is used to prevent formation of sulfonic anhydrides. A stoichiometric amount of **thionyl chloride** gives a much reduced yield.
4. The progress of the reaction is monitored by thin layer chromatography. A 0.1-mL sample is removed, evaporated to dryness and dissolved in 2 mL of **hexane**. The solution is spotted on an Analtech silica GF plate (8 cm × 2.5 cm) and developed in **hexane/methylene chloride** (4/1). Visualization by UV light shows $R_f = 0.4$ for the sulfonyl chlorides.
5. If allowed to cool to 25°C, the dark layer may solidify, hampering the separation. This very acidic layer is the excess **thionyl chloride/DMF** complex. It should be handled with proper protection in a ventilated area. To facilitate visual identification of the layers, the checkers added about 25 mL of **hexane**.
6. The pH of the bicarbonate wash is a reflection of the efficiency with which the dark lower layer has been removed. In the course of a dozen runs, this pH ranged from 5.5 to 7.1. If the pH of the wash is below 5.5, a second wash with bicarbonate is necessary.
7. Nuchar SA **carbon** from Westvaco Co. was used.
8. It is essential that the **carbon** treatment be carried out within a few hours. Experiments where this treatment was delayed for 16 hr invariably produced an azide mixture of lower purity (85%) and lower yield (80%). Although the sulfonyl chlorides hydrolyze only slightly (1–2%) in wet **hexane** in 24 hr, that amount of sulfonic acids in the presence of the phase transfer agent catalyzes the hydrolysis of sulfonyl chlorides. After treatment with **carbon**, the **hexane** solution of sulfonyl chlorides can be stored for several weeks in the refrigerator with little or no adverse effect on the next step.
9. Aliquat 336 (tri-n-alkylmethylammonium chloride) was obtained from Aldrich Chemical Company, Inc. The material is a mixture of C₈ and C₁₀ chains with C₈ predominating. There is a slight initial exothermic reaction on adding the phase transfer catalyst. Intermittent cooling with a cold water bath is required to keep the temperature below 35°C.
10. A sample of the **hexane** layer from the reaction mixture is diluted 10 fold with **hexane**, spotted and developed as described in (Note 4). Visualization by UV light shows $R_f = 0.3$ for sulfonyl azides.
11. The assay for sulfonyl azides is adapted from the method of Siewinski, et al.³ The **azide** content of the **hexane** solution was assayed as follows to determine the contained yield:

1. Standard Curve:

Stock solution: 80 mg of NaN₃ diluted to the mark in a 100-mL volumetric flask with 0.1 N NaOH-MeOH.

Procedure: Into a series of four, 100-mL volumetric flasks, transfer 5, 7, 10 and 15 mL respectively of the stock solution. Into a 100-mL volumetric labelled blank, pipet 10 mL of 0.1 N NaOH-MeOH solution. To all add 2 drops of 0.1% ethanolic phenolphthalein indicator solution, and 20 mL of aqueous 1.5% **sodium sulfate** (Na₂SO₄). Acidify each, in turn, to the **phenolphthalein** end point with 1 N **hydrochloric acid** and immediately add 25 mL of 1 M **ferric ammonium sulfate** [Fe(NH₄)(SO₄)₂] solution. Dilute to the mark with 1.5% Na₂SO₄. Let stand 10 min, then read absorbance at 458 nm. Plot absorbance vs. concentration.

2. Sample:

Pipet 5 mL of the **hexane** solution containing 4-dodecylbenzenesulfonyl azides into a 100-mL volumetric flask and dilute to the mark with **methanol**. Pipet 5 mL of this solution into a small stoppered flask. Add 2 mL of aqueous 1 N **potassium hydroxide** solution and heat at 75°C for ~20 min. Allow to cool to room temperature, add 2 drops of 0.1% **phenolphthalein** solution, and 10 mL of 1.5% Na₂SO₄. Shake, then transfer quantitatively to a 60-mL separatory funnel. Add 10 mL of **butanol** (or **isoamyl alcohol**) to the sample flask, shake, then transfer to the separatory funnel. Shake the funnel, let the layers separate, then remove the bottom (H₂O) layer into a 100-mL volumetric flask. Add an additional 10 mL of 1.5% Na₂SO₄ to the alcohol layer in the separatory funnel, shake, let the layers separate, then transfer the water layer to the volumetric flask. Neutralize the combined water layers to the **phenolphthalein** end point with 1 N **hydrochloric acid**, then immediately add 25 mL of Fe(NH₄)(SO₄)₂.

Dilute to the mark with 1.5% Na₂SO₄ solution, let stand 10 min, then read absorbance at 458 nm. Read azide concentration against the NaN₃ calibration curve.

12. The checkers determined the yield by evaporation of the [hexane](#) solution to constant weight (3–10 hr at 0.1 mm). The yields cited are based on the assumption that the 3% impurity in the starting sulfonic acids is not present in the final product. The checkers found the material obtained upon concentration, to be sufficiently pure for use without further purification.

13. The spectroscopic data for the mixture of four isomeric secondary dodecylbenzenesulfonyl azides (2.5:1.6:1.6:1.0) is as follows: ¹H NMR (400 MHz, CDCl₃) δ: 0.70–1.00 (m, 6 H), 1.00–1.50 (m, 12 H), 1.50–1.80 (m, 6 H), 2.90–2.50 (m, 1H), 7.25–7.45 (m 2 H), 7.87 (m 2 H); ¹³C NMR (100 MHz, CDCl₃) δ: 12.07, 13.94, 14.02, 14.05, 14.07, 14.10, 20.63, 21.89, 22.50, 22.61, 22.63, 22.65, 22.69, 27.18, 27.48, 27.52, 27.58, 29.15, 29.26, 29.30, 29.32, 29.44, 29.46, 29.49, 29.51, 29.57, 29.61, 29.72, 31.69, 31.82, 31.83, 31.88, 31.91, 36.21, 36.34, 36.60, 36.61, 36.64, 38.06, 38.85, 40.24, 46.11, 46.38, 48.15, 127.55, 127.66, 128.33, 128.93, 129.01, 135.82, 135.85, 154.56, 154.82, 154.87, 156.09; IR (film) 2126 cm⁻¹.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

4-Dodecylbenzenesulfonyl chlorides have been prepared from the corresponding acids using [chlorosulfonic acid](#),⁴ [phosphorus oxychloride](#),² and [thionyl chloride](#).⁵ The use of catalytic amounts of DMF in conjunction with [thionyl chloride](#) is based on the work of H. Bosshard, et al.⁶ The insolubility of the [DMF/thionyl chloride](#) complex in the reaction solvent permits easy removal at the end of reaction. Extraction with dilute base removes the last trace of acids and the solution is pure enough for the next step.

The method described above for the preparation of the mixture of 4-dodecylbenzenesulfonyl azides is new and based on the work of Bollinger and Hazen.^{5,7} Sulfonyl azides have been prepared by diazotizing substituted sulfonyl hydrazides,⁸ and treating sulfonyl halides in methanol-water,⁹ ethanol-water,¹⁰ [acetone](#),^{2,5,7} or [acetone](#)-water solutions¹¹ with aqueous or solid [sodium azide](#).^{5,7,12} Use of phase transfer catalysis for the preparation of sulfonyl azides is new, simple and effective. It avoids solvent changes and permits isolation of a [hexane](#) solution of sulfonyl azides without concentration.

The use and advantages of 4-dodecylbenzenesulfonyl azides as a diazo transfer agent are fully discussed by Hazen, Weinstock, Connell, and Bollinger.⁷ In contrast to [p-toluenesulfonyl azide](#), that has the shock sensitivity of tetryl (N-methyl-N-2,4,6-trinitroaniline) and the explosiveness of TNT, the mixture of 4-dodecylbenzenesulfonyl azides exhibits no shock sensitivity at the highest test level (150 kg cm) and 24% of the heat of decomposition measured in cal/g. [p-Toluenesulfonyl azide](#) appears as a diazo transfer agent in *Org. Synth., Coll. Vol. V* **1973**, 179; *VI*, **1988**, 389, 414 and its preparation is reported in the first of these. Two explosions during its preparation have been reported.^{13,14}

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 9, 197](#)

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

sulfonyl chlorides

H₂O

4-DODECYLBENZENESULFONYL AZIDES

Benzenesulfonyl azides, 4-dodecyl-

dodecylbenzenesulfonyl azides

4-Dodecylbenzenesulfonyl chlorides

dodecylbenzenesulfonic acids

sulfonyl azides

ethanolic phenolphthalein

tetryl (N-methyl-N-2,4,6-tetranitroaniline

[hydrochloric acid \(7647-01-0\)](#)

[methanol \(67-56-1\)](#)

[chlorosulfonic acid \(7790-94-5\)](#)

[thionyl chloride \(7719-09-7\)](#)

[sodium bicarbonate \(144-55-8\)](#)

[sodium sulfate \(7757-82-6\)](#)

[butanol \(71-36-3\)](#)

acetone (67-64-1)

carbon (7782-42-5)

Phosphorus Oxychloride (21295-50-1)

potassium hydroxide (1310-58-3)

sodium azide (26628-22-8)

methylene chloride (75-09-2)

phenolphthalein (77-09-8)

isoamyl alcohol (123-51-3)

azide

dimethylformamide,
DMF (68-12-2)

hexane (110-54-3)

p-toluenesulfonyl azide (941-55-9)

ferric ammonium sulfate