



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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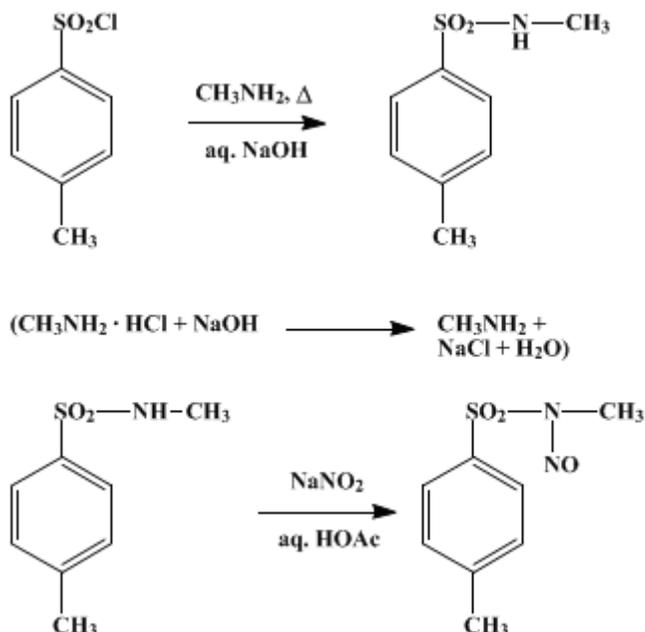
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.943 (1963); Vol. 34, p.96 (1954).

***p*-TOLYLSULFONYLMETHYLNITROSAMIDE**

[*p*-Toluenesulfonamide, N-methyl-N-nitroso-]



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1. Procedure

A total of 320 g. (1.68 moles) of *p*-toluenesulfonyl chloride (Note 1) is divided into three portions of 190, 90, and 40 g.; and a solution of alkali is prepared by dissolving 70 g. of sodium hydroxide in 70 ml. of water with cooling. The 190-g. portion of the sulfonyl chloride is added with swirling during about 5 minutes to 210 ml. (2.1 moles) of 33% aqueous methylamine (or 174 ml. of the 40% solution) contained in a 1-l. round-bottomed flask. The mixture is allowed to heat up to 80–90° in order to maintain the sulfonmethyamide (m.p. 78°) in a molten condition (Note 2). After all this portion of the sulfonyl chloride has been added, the mixture is shaken vigorously. Boiling is prevented by mild cooling with water in order to avoid an excessive loss of methylamine.

As soon as the mixture has become acidic (Note 3), as indicated by testing a drop on litmus paper, 50 ml. of the 50% sodium hydroxide solution is added carefully with swirling. This is followed immediately by gradual addition of the 90-g. portion of the sulfonyl chloride as before. When the mixture has again become acidic (Note 3), 25 ml. of the sodium hydroxide solution is added, followed by the final 40 g. of the sulfonyl chloride. After the mixture has again become acidic, the remainder of the sodium hydroxide solution is added. The liquid phase of the final mixture should be alkaline (Note 4).

After the walls of the flask have been rinsed with a little water, the reaction is completed by heating the mixture, consisting of two layers and a precipitate of sodium chloride, on a steam bath for 15 minutes with vigorous mechanical stirring. The hot reaction mixture (Note 2) and (Note 5) is then poured into 1.5 l. of glacial acetic acid contained in a 5-l. round-bottomed flask, and the smaller flask is rinsed clean with 250 ml. of acetic acid (Note 6). The solution is cooled in an ice bath to about 5° (Note 7) and stirred mechanically as a solution of 124 g. (1.8 moles) of sodium nitrite in 250 ml. of water is added from a dropping funnel during about 45 minutes. The temperature of the mixture is kept below 10°, and stirring is continued for 15 minutes after addition is complete. During the reaction, the nitroso

compound separates as a yellow crystalline product.

One liter of water is added to the mixture; then the precipitate is separated by suction filtration, pressed on the funnel, and washed with about 500 ml. of water. The product is transferred to a beaker, stirred well with about 500 ml. of cold water, then filtered and washed again on the funnel. This process is again repeated if necessary to remove the odor of *acetic acid*. After drying to constant weight in a vacuum desiccator over *sulfuric acid*, the product melts in the range between 55° and 60° (Note 8). The yield is 306–324 g. (85–90%) (Note 9) and (Note 10).

2. Notes

1. The *p*-toluenesulfonyl chloride used by the submitters was a product recrystallized from a 1:20 mixture of *benzene*: 60–80° petroleum ether, and it melted at 67.5–69°. The checkers employed material obtained from Distillation Products Industries. Sulfonic acid may be removed from old samples of the sulfonyl chloride by thorough washing with cold water followed by immediate drying in a vacuum desiccator over *sulfuric acid*.

2. At lower temperatures, the *sulfonylmethylamide* is likely to form a hard cake. In smaller runs, e.g. 0.2 mole, the mixture heats up considerably less; therefore, the reaction mixture should be warmed on a steam bath after the first addition of sulfonyl chloride and thereafter as necessary.

3. The reaction mixture may not become acidic after a given addition of sulfonyl chloride, especially the first one. If such is the case, no more than 5 minutes need be allowed between successive sulfonyl chloride and alkali additions. The whole procedure requires about 30 minutes.

4. If the final mixture is acidic, indicating excessive loss of *methylamine*, sufficient *methylamine* should be added to render the mixture basic. This situation is more likely to occur in smaller runs (0.1–0.2 mole).

5. The precipitate of *sodium chloride* need not be removed before nitrosation; it dissolves when the final product is washed with water.

6. The total amount of 1750 ml. of *acetic acid* is necessary to dissolve the amide completely at lower temperatures. With less *acetic acid*, it is difficult to secure complete nitrosation, even with very efficient stirring of the suspension.

In one experiment with 750 ml. of *acetic acid*, the resulting impure product was washed first with water to remove *acetic acid* and then with 1*N* *sodium hydroxide* to remove *p*-tolylsulfonylmethylamide (the nitroso compound is not attacked by cold aqueous *sodium hydroxide*). The yield of *p*-tolylsulfonylmethylnitrosamide was 76%, m.p. 58–60°. Acidification of the alkaline wash yielded (9% recovery) the *p*-tolylsulfonylmethylamide, m.p. 77.5–78.5°.

7. An ice-salt mixture may be used for more efficient cooling, but reaction temperatures below 0° should be avoided because the total amount of *acetic acid* is just sufficient to keep the *sulfonylmethylamide* in solution above 0°.

8. A melting point in the lower part of this range generally indicates contamination with *p*-tolylsulfonylmethylamide, which may be removed as described in (Note 6); however, this purification is not necessary since the presence of this amide does not interfere in the preparation of *diazomethane*.

9. **Caution!** Although this material has been kept at room temperature for years without significant change, there has been reported one instance in which a sample stored for several months detonated spontaneously. For long periods of storage, it is recommended that the material be recrystallized and placed in a dark bottle. Recrystallization is best accomplished by dissolution in boiling *ether* (1 ml. per g.), addition of an equal volume of low-boiling petroleum ether (technical *pentane*), and cooling over night in a refrigerator. Other solvents (*benzene*, *carbon tetrachloride*, *chloroform*) may be used for recrystallization, but the maximum temperature should not exceed 45°.

10. *p*-Tolylsulfonylmethylnitrosamide is a useful substance for the preparation of *diazomethane* (p. 250). It is apparently of low toxicity. Its properties afford advantages over other nitroso compounds which have been used for preparation of *diazomethane*.

3. Discussion

p-Tolylsulfonylmethylnitrosamide has been prepared previously by adding *sodium nitrite* to an acid aqueous suspension of *p*-tolylsulfonylmethylamide.^{2,3,4} The present method is more rapid and gives higher yields.⁵

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 4, 221](#)
- [Org. Syn. Coll. Vol. 4, 250](#)
- [Org. Syn. Coll. Vol. 5, 842](#)

References and Notes

1. De Rijks-Universiteit, Groningen, the Netherlands.
 2. Friedlander, *Fortschritte der Teerfarbenfabrikation*, **10**, 1216 (1910); Bayer Co. D.R.P. 224,388 [*Chem. Zentr.*, **1910 II**, 609].
 3. Takizawa, *J. Pharm. Soc. Japan*, **70**, 490 (1950) [*C. A.*, **46**, 454 (1952)].
 4. Tomita, Kugo, and Hirai, *J. Pharm. Soc. Japan*, **73**, 1247 (1953) [*C. A.*, **48**, 13616 (1954)].
 5. de Boer and Backer, *Rec. trav. chim.*, **73**, 229 (1954).
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Appendix

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

sulfonyl chloride

petroleum ether

sulfonic acid

p-tolysulfonylmethylamide

[sulfuric acid \(7664-93-9\)](#)

[acetic acid \(64-19-7\)](#)

[Benzene \(71-43-2\)](#)

[ether \(60-29-7\)](#)

[sodium hydroxide \(1310-73-2\)](#)

[chloroform \(67-66-3\)](#)

[sodium chloride \(7647-14-5\)](#)

[carbon tetrachloride \(56-23-5\)](#)

[sodium nitrite \(7632-00-0\)](#)

[Pentane \(109-66-0\)](#)

[methylamine \(74-89-5\)](#)

Diazomethane (334-88-3)

sulfonylmethylamide

p-Toluenesulfonyl chloride (98-59-9)

p-Tolylsulfonylmethylnitrosamide

p-Toluenesulfonamide, N-methyl-N-nitroso- (80-11-5)

p-tolylsulfonylmethylamide