

Synthesis of 6-nitrosaccharin

Supplementary Material

Experiments focused on the synthesis of everyday products are often enjoyed and positively received by students. On this work a derivative from saccharin, an artificial sweetener, is prepared. This experiment was introduced and tested by undergraduate second-year chemistry students, as a project involving research and experimental work. No more than 8 students working in pairs have done this work in the same classroom. The experimental procedure is quite simple, although it must be performed on a fume hood. This reaction involves mechanisms of electrophilic aromatic substitution where students can examine the effect of the aromatic ring substituent's orientation on substitution reactions. The presence of nitro group in the aromatic ring avoids the formation of *para* product. For that reason this work is preferable to the synthesis of saccharin that yields a mixture of *orto* and *para*-toluene sulfonyl chloride that is difficult to separate. Oxidation of a methyl group with chromium (VI) oxide in sulfuric acid followed by cyclization to form a five-membered ring is also studied. Alkaline potassium permanganate usually employed as oxidizing agent gives the correspondent carboxylic acid in low yields and requires the addition of hydrochloric acid and temperature to occur cyclization. This experiment also offers the possibility of studying the reduction of the nitro group to amine with ammonium sulfide¹. Recently, a three-step synthetic route for 6-nitrosaccharin was reported, starting from 2,4-dinitrobenzoic acid. However, it involves large reflux periods (of several hours) and the use of gaseous chlorine^{2,3}.

Additional notes for the preparation of 4-nitrotoluene-2-sulfonamide:

A vigorous reaction occurs when the reaction mixture is poured into the beaker containing ice so this step must be done slowly and very carefully. In the liquid-liquid extraction 2 x 40 mL of diethyl ether should be used instead of 2 x 20 mL. When the ammonia solution is added to the ether extracts, the heat of this reaction will cause the diethyl ether to boil, so this addition should also be done slowly.

Recrystallization of 4-nitrotoluene-2-sulfonamide requires a large volume of water due to the low solubility of the compound. The yield is relatively low (20-40%) and the melting point is 185-187°C (186-187°C¹).



SM 12.4.1.1: Reflux apparatus for 4-nitrotoluene-2-sulfonamide



SM 12.4.1.2: Vacuum filtration apparatus

Additional notes for the preparation of 6-nitrosaccharin:

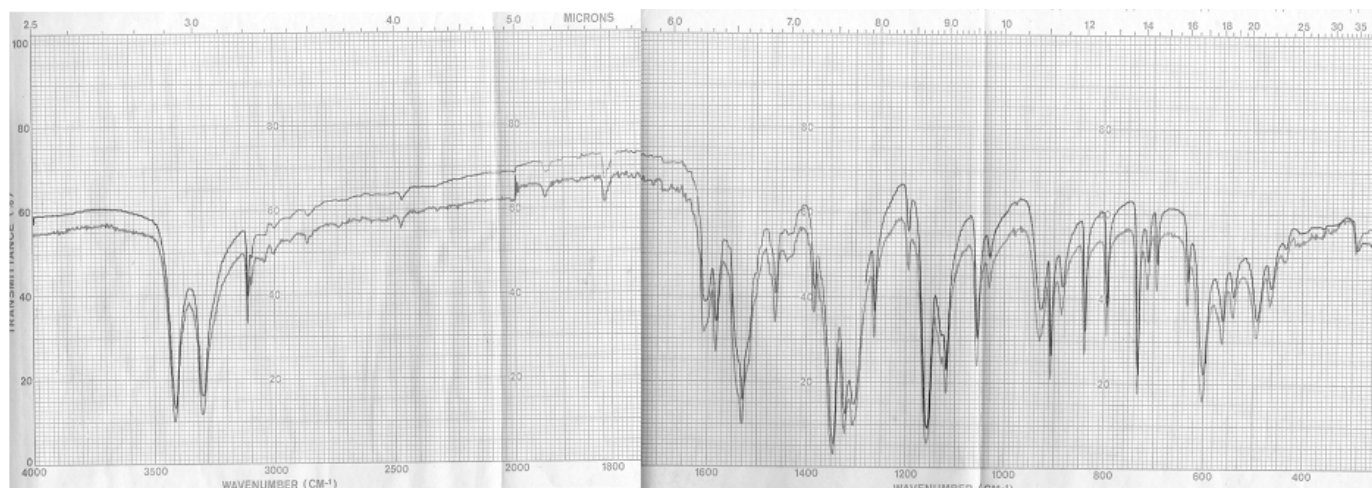
The final product was recrystallized from water on this experiment, and it can also be recrystallized from isopropyl alcohol². Average yield is 50-60% and melting point 210-212°C (209°C¹).



SM 12.4.1.3: Copper funnel (previously heated by flame) for hot filtration

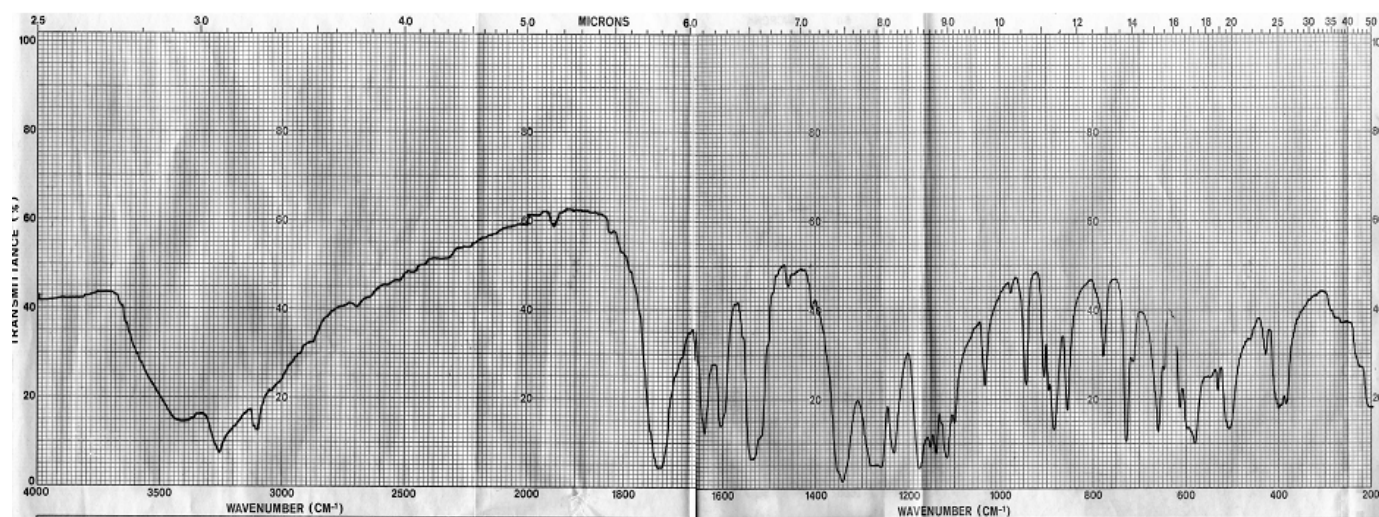
IR and NMR spectra:

Students easily identify in **SM 12.4.1.4** the two strong bands at 3420 and 3220 cm^{-1} due to the N-H stretching vibrations. Strong absorption can be observed at 1350 and 1150 due to S=O stretching vibrations.



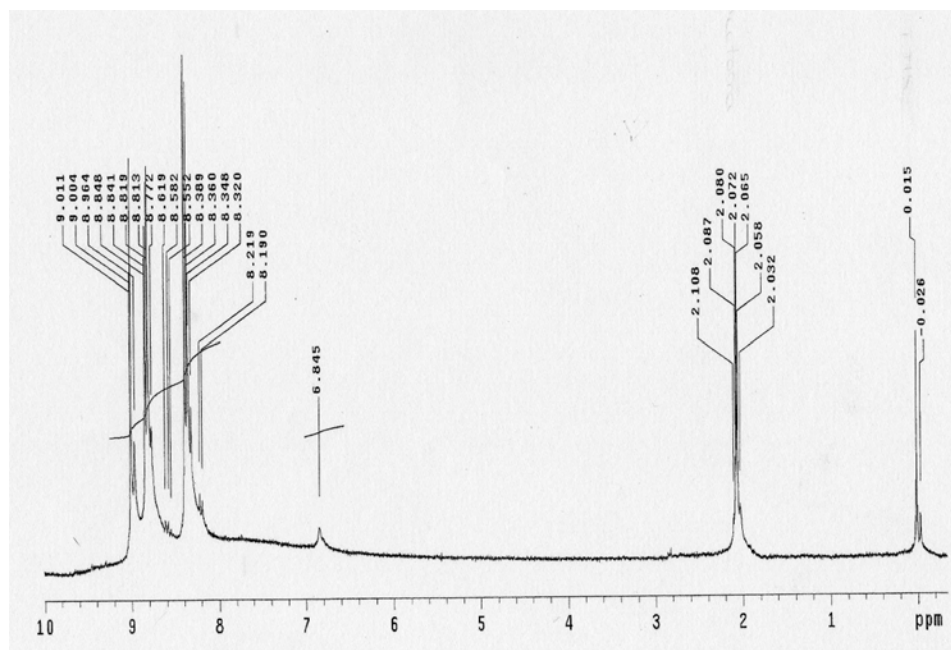
SM 12.4.1.4: IR (KBr) of 4-nitrotoluene-2-sulfonamide

In **SM 12.4.1.5** students can observe additionally a strong band at 1730 cm⁻¹ due to the C=O group.



SM 12.4.1.5: IR (KBr) of 6-nitrosaccharin

NMR spectrum in **SM 12.4.1.6** was obtained with student's samples and doesn't present the best resolution; nevertheless students easily identify the three signals corresponding to the aromatic protons and NH proton absorption.



SM 12.4.1.6: ^1H NMR $[(\text{CD}_3)_2\text{CO}]$ of 6-nitrosaccharin

Spectroscopic data for 6-nitrosaccharin can be found in literature² (^1H NMR in DMSO-d_6 and mass spectral data).

¹ N. C. Rose, S. Rome, *J. Chem. Educ.*, 1970, 47, 649.

² E. A. Serebryakov, P. G. Kisilitsin, V. V. Semenov, S. G. Zlotin, *Synthesis*, 2001, 1659.

³ A. I. Gerasyuto, S. G. Zlotin, V. V. Semenov, *Synthesis*, 2000, 300.