Structure of Nitrated Sulfobenzoic Anhydride Obtained from Sulfobenzoic Anhydride or Saccharin

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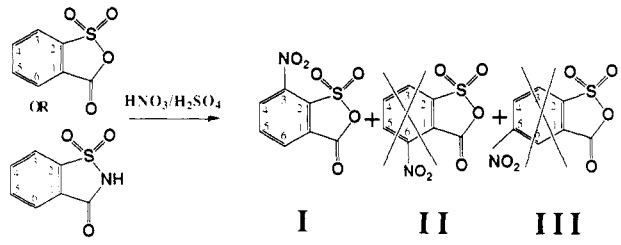
The nitration of either sulfobenzoic anhydride or saccharin has been described previously in the literature to yield 5-nitro-2-sulfobenzoic anhydride.[1-3] We were interested in using nitrated anhydride as a starting material for the preparation of the Bromothymol Blue dye which would contain a functional group capable of covalent attachment to the surface of optical fibers. The optical fibers with immobilized dye molecules can serve as pH sensors for physiological pH measurements.[4,5] To our surprise, we found that the product of nitration, with the same melting point as described in the literature[1-3] (212–218 °C), has a structure of 3-nitro-2-sulfobenzoic anhydride.



I II III

The assignment of the structure of the product of nitration is based on ^1H and ^{13}C NMR spectroscopy. The ^1H NMR spectrum of the anhydride (Figure 1) shows a clean ABC pattern which can correspond to either 3-nitro- (structure I) or 6-nitro-2-sulfobenzoic anhydride (structure II) but not to the earlier claimed 5-nitro-2-sulfobenzoic anhydride (structure III). The ^{13}C NMR spectrum (Figure 2) strongly supports the view that the structure is that of the 3-nitro-2-sulfobenzoic anhydride (I). The most shielded C1 carbon (129.58 ppm) should appear as a doublet for 3-nitro-2-sulfobenzoic anhydride (coupling to H5 ($^3J_{C-H}$ = 9.12 Hz)) but as a triplet or a pair of doublets for 6-nitro-2-sulfobenzoic anhydride (coupling to H3 and H5).[6] The observed doublet indicates 3-nitro-2-sulfobenzoic anhydride. Also, splitting in the carbonyl C atom (155.71 ppm) $^3J_{C-H}$ = 5.12 Hz and $^4J_{C-H}$ = 1.26 Hz is possible only in the 3-nitro-2-sulfobenzoic anhydride and not in the 6-nitro isomer. The additional assigments are given directly on the spectrum.

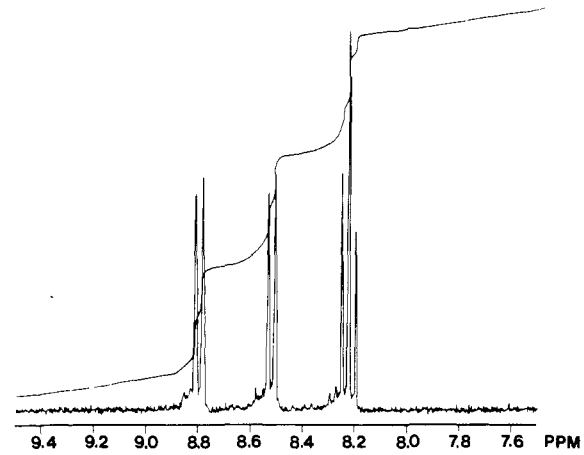


Figure 1. ^1H NMR spectrum of 3-nitro-2-sulfobenzoic anhydride in $CDCl_3$ at room temperature.

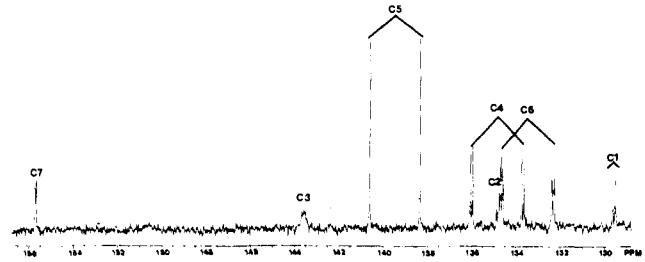


Figure 2. ^{13}C NMR spectrum of 3-nitro-2-sulfobenzoic anhydride in $CDCl_3$ at room temperature.

Carbonyl group has weaker deactivating effect than by the sulfonyl group.[8] Therefore, the nitration in the anhydride as well as in saccharin should occur at position 3. Although it is difficult to neglect steric effects in the substitution at positions 3 and 6, the electronic effects of sulfonyl and carbonyl moieties in terms of σ_m and σ_p parameters suggest the following order of the electron densities: C3 > C6 > C4 > C5 for sulfonamide and amide substituents. Also electron densities estimated from the ^{13}C NMR spectra of anhydride and other sulfobenzoate derivatives[9] indicate the following order of shielding of carbon atoms: C3 > C6 > C5 ≈ C4. Apparently, steric hindrances do not prohibit nitration at position 3 and substitution proceeds at C3.

We found 3-nitro-2-sulfobenzoic anhydride (I) to be the main product of nitration of both sulfobenzoic anhydride and saccharin. This observation corrects the existing erroneous claim of the formation of 5-nitro-2-sulfobenzoic anhydride (III) under identical reaction conditions.

Experimental Section

Commercially available saccharin and sulfobenzoic anhydride from Aldrich Chemical Co. were used without purification. Melting points were determined using a Mel-Temp open capillary melting point apparatus. IR spectra were recorded on a Nicolet FTIR Model 5DXB type spectrometer. A 300-MHz GE Model 300 spectrometer was used to obtain ^1H and ^{13}C NMR spectra.

Nitration of Sulfobenzoic Anhydride or Saccharin. Nitration was carried out using a mixture of concentrated nitric acid and sulfuric acid according to the procedure in the literature.[1-3] Compound I was obtained as a white solid product by pouring the reaction mixture onto crushed ice, filtration, washing with cold water, and drying.[1,2,3] Compound I was formed in 15% yield

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with a melting point of 215–217 °C (lit. mp 210–212 °C,[1] 212–218 °C,[2] 212 °C[3]). IR (KBr, cm^{-1}): 1800, 1530, 1340, 1190, 1040, 1010. ^1H NMR ($CDCl_3$, δ ppm): 8.80 (d), 8.53 (d), 8.22 (t). ^{13}C NMR ($CDCl_3$, δ ppm): 129.58 (C1), 133.49, 134.86 (C4 or C6), 134.80 (C2), 139.49 (C5), 143.60 (C3), 155.71 (C7).

Registry No. I, 127472-56-4; III, 22952-25-6; sulfobenzoic anhydride, 81-08-3; saccharin, 81-07-2.

Convenient General Method for the Preparation of Primary Alkyllithiums by Lithium–Iodine Exchange

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The metathesis between an organic halide and an organolithium known as the lithium–halogen interchange was discovered some 50 years ago by the groups of Wittig and Gilman.[1,2] The reaction, which is a reversible process leading to an equilibrium mixture favoring the more stable organolithium,[3] has been used extensively to prepare relatively stable organometallics such as aryl-,[4-10] vinyl-,[5-9,11,12] and cyclopropyllithiums[6-9,13] by treatment of the corresponding organohalide with a more reactive alkyllithium, but the use of the interchange for the generation of an alkyllithium has, with a few notable exceptions,[14-16] met with less success.[4-9] The difficulties commonly encountered in the formation of simple alkyllithiums by lithium–halogen interchange are a consequence of the reversible nature of the reaction and the capricious behavior of alkyl halides when treated with an organolithium. Competing reactions such as β-elimination,[4-9] α-metalation,[17] and Wurtz-type coupling to produce symmetrical and mixed hydrocarbons[3,6-9] can seriously compromise the interchange as an efficient route to alkyllithiums. Recent mechanistic investigations of the lithium–halogen exchange[18-21] have revealed that many of these difficulties can be circumvented by judicious choice of experimental conditions. Herein we report a simple, convenient, and efficient method for the preparation of primary alkyllithiums by low-temperature lithium–iodine interchange that is based on the results of these mechanistic studies.

Primary alkyllithiums are readily prepared at −78 °C (dry ice/acetone bath) under an atmosphere of dry, deoxygenated argon (or nitrogen) by addition of 2.1–2.2 molar equiv of commercial *tert*-butyllithium (*t*-BuLi) in pentane to an approximately 0.1 M solution of primary alkyl iodide in dry *n*-pentane–diethyl ether (3:2 by volume). Neither the temperature nor the concentration of the alkyl iodide is critical to the success of the reaction: the interchange is exothermic, and for this reason the reaction should be run well below ambient, but the exchange proceeds rapidly and cleanly at temperatures ranging from −131 °C (N_2/pentane bath) to −23 °C (CCl_4/dry ice bath). The interchange is complete within a few min at −78 °C (or −131 °C), and the alkyllithium may be used at this temperature; however, the excess *t*-BuLi remaining in solution may complicate product isolation if an electrophile is added to the cold reaction mixture. Residual *t*-BuLi is easily removed by simply allowing the reaction mixture to stand at room temperature for ca. 1 h: the *t*-BuLi is consumed by rapid proton abstraction from diethyl ether,[22] leaving a clean solution of the less reactive primary alkyllithium. As demonstrated by the results summarized in Table I, addition of any of a variety of electrophiles to the alkyllithium solution delivers essentially pure product in good to excellent isolated yield. Significantly, the only byproduct generated by this procedure is a small quantity (typically 2–10%) of easily removed hydrocarbon derived, as detailed below, from formal reduction of the iodide during the interchange reaction.[18,23]

$$RCH_2I \xrightarrow[n\text{-}C_5H_{12}/Et_2O,\ -78\ ^\circ C,\ 5\ min]{t\text{-BuLi}} RCH_2Li \xrightarrow{E^+} RCH_2E$$

The success of the interchange reaction depends critically on the choice of halide, alkyllithium, and solvent. Under the conditions outlined above, the mechanism of the interchange reaction between a primary alkyl iodide and *t*-BuLi most likely involves rapid, reversible attack of the alkyllithium on the iodine atom of the substrate.[18,20,24,25] Primary alkyl bromides, in contrast, react with *t*-BuLi predominantly by a process involving single-electron transfer.[18-21,26] This pronounced halogen effect on the mechanism of the interchange has a practical consequence: alkyl iodides rather than bromides should be used in the exchange reaction for the preparation of primary alkyl-

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