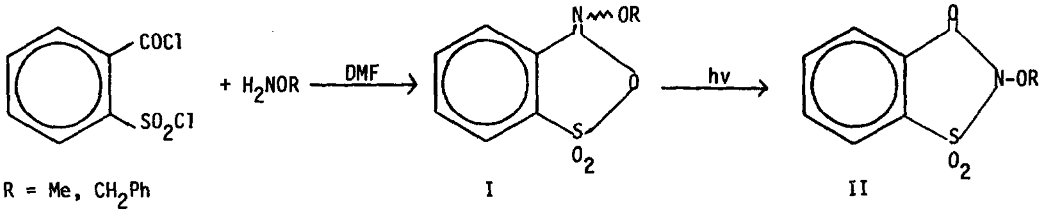
Tetrahedron Letters No. 32, pp 3289 - 3291, 1972. Pergamon Press. Printed in Great Britain.

PHOTOCHEMICAL ISOMERIZATION OF N-ALKOXYISOSULFOBENZIMIDES

Louis A. Levy
Analytical and Synthetic Chemistry Branch
National Institute of Environmental Health Sciences
P. O. Box 12233
Research Triangle Park, N. C. 27709

(Received in USA 19 May 1972; received in UK for publication 30 June 1972)

As part of a study concerned with the chemistry and possible metabolic fate of saccharin it was necessary to prepare some N-oxygenated derivatives of the parent benzisothiazalone S,S-dioxide nucleus. Reaction of 2-chlorosulfonylbenzoyl chloride[1] with methoxyamine in dimethylformamide solution gave in 40% yield, as the only isolated product, a mixture of syn and anti N-methoxyisosulfobenzimide I[2], m.p. 110-112°, rather than the desired N-methoxysulfobenzimide II[2], (N-methoxysaccharin). That the reaction products had structure I rather than II was apparent from the spectral data.

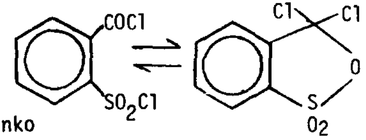


The material had no absorption in the infrared assignable to a carbonyl function. However, a peak of moderate intensity at 1630 cm^{-1} was suggestive of an imino group. In the nmr spectrum there were two peaks attributable to the syn and anti methoxyl groups at 4.05 ppm and 4.08 ppm. Warming to 70° did not bring the two peaks into coalescence thereby establishing the existence of two distinct methoxyl groups. Further corroboration of structure I was the determination of the molecular weight by high resolution mass spectrometry as 213.0093 ($C_8H_7O_3NS$ requires 213.0094). The mass spectrum of I was of continuing value in addition to providing confirmation of the elemental composition. The fragmentation pattern was more easily interpretable on the basis of structure II suggesting that isomerization of I to II is occurring in the mass spectrometer.[3] On the basis of this observation and the proposal that processes observable in the mass spectrometer correlate with photochemical reactions[4] the preparation of II by photochemical isomerization of I was attempted. Irradiation of I in acetonitrile solution with unfiltered ultraviolet light[5], while monitoring the course of the reaction by nmr spectrometry, resulted in the rapid disappearance of the two methoxyl peaks of I and the concomittant appearance of a single peak at 4.22 ppm attributable to II. The structure of II, m.p. 87-89^{0}, as written is substantiated by its infrared spectrum, carbonyl absorption at 1740 cm^{-1}, its nmr spectrum and a mass spectrum identical to I. Compound I is recovered after refluxing for 2.5 hours in dioxane. Several investigators have explored the thermal isomerization of isoimides to the corresponding imides[6]. These isomerizations occur only slowly at reasonably high temperatures, suggesting that the isomerization observed in the mass spectrometer is a good model for the photochemical process as opposed to a thermally induced rearrangement occurring in the relatively cool[7] inlet of the spectrometer.

A similar sequence of reactions can be carried out using benzyloxyamine to produce the corresponding benzyl derivatives of I and II. So far all attempts to remove the benzyl moiety from II and so to make available N-hydroxysaccharin have not been successful, leading either to recovered starting material or hydrogenolysis of the nitrogen oxygen bond resulting in the formation of saccharin. This reaction offers further confirmation of the structure of photoproduct II.

REFERENCES AND FOOTNOTES

1. This compound was prepared by refluxing a mixture of o-sulfobenzoic anhydride and phosphorous pentachloride and purified by passing the crude product through a column of silicic acid. The possibility of the equilibrium and the question as to which isomer is which as been investigated. (D. Sh. Rozina, L. T. Nesterenko and Yu. I. Vainshtein, Zhur. Obshchei, Khim., **28**, 2878 (1958). Material used in this study has intense carbonyl absorption at 1790 cm^{-1}.



2. This compound is so named to emphasize the analogy with the imide-isoimide nomenclature used for the compounds derived from dicarboxylic acids and its relationship to o-sulfobenzoic anhydride. Reaction of o-phthaloyl dichloride with methoxyamine results in formation of the isoimide.
3. For example the major peaks at m/e 109 and 104 attributable to the SO_2NOMe and PhCO fragments

seem more likely to derive from II than I. A metastable peak at 55.6 (calcd. 55.8) for the process $C_8H_7O_3NS \longrightarrow C_7H_4O + (SO_2NOMe)^+$ is observed.

4. A. L. Burlingame, C. Fenselau, W. J. Richter, W. G. Dauben, G. W. Shutter and N. D. Vietmayer, J. Am. Chem. Soc., 89, 3346 (1967).
5. No reaction is observed if a pyrex filter is used.
6. M. Narita, M. Akiyama and M. Okawara, Bull. Chem. Phar. Soc. Japan, 44, 437 (1971) report that isomerization of N-benzyloxyisomaleimides to the corresponding imide occurred in 40% yield after 10 hours reflux in DMF.
7. The inlet temperature was 100°C.