1,2-Benzisothiazole 1,1-Dioxide: a Convenient Synthesis. The Question of the Possible Aromaticity of 1,2-Benzothiazepine 1,1-Dioxides

Rudolph A. Abramovitch,* Babu Mavunkel, and James R. Stowers

Department of Chemistry and Geology, Clemson University, Clemson, South Carolina 19631, U.S.A.

A convenient synthesis of 1,2-benzisothiazole 1,1-dioxide from toluene-*o*-sulphonamide is reported, and this allows the preparation of a number of 1,2-benzothiazepine 1,1-dioxides bearing hydrogen atoms in the seven-membered ring; ^{1}H n.m.r. spectroscopy suggests that the latter is not aromatic.

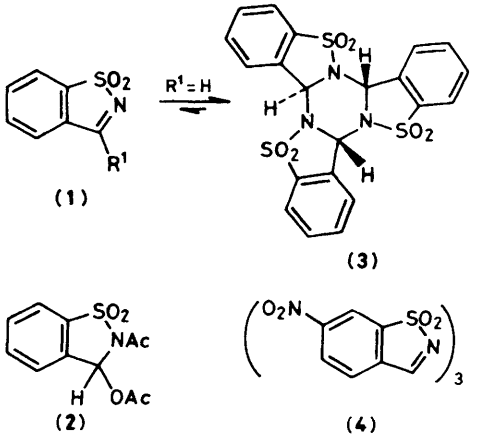
3-Alkyl- and 3-aryl-1,2-benzisothiazole 1,1-dioxides (**1**) are now readily available.[1] There is, however, only one reported[2] synthesis of the parent compound (**1**; R^1 = H) (in extremely poor yield) from *o*-chloramine T by a two-step process, each step leading to complex mixtures. The product so formed was thought to be either the monomer or the dimer. We now report a convenient synthesis of (**1**; R^1 = H) and discuss the possible aromaticity of its ring expansion products, the 1,2-benzothiazepine 1,1-dioxides.

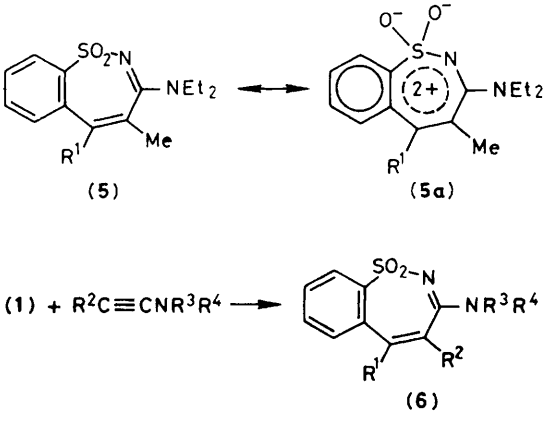
Numerous attempts to reduce saccharin *pseudo*chloride (**1**; R^1 = Cl) or to dehydrogenate 2,3-dihydro-1,2-benzisothiazoline 1,1-dioxide to (**1**; R^1 = H) failed. For example, oxidation of the dihydro-compound with $(PhSeO)_2O$ gave *N*-phenylselenylsaccharin. Similarly, treatment of benzenesulphonamide with Bu^{n}Li and then trimethylorthoformate did not give the desired dimethylformamide (DMF) [which could have been cyclized to (**1**) in acid]. On the other hand, oxidation of toluene-*o*-sulphonamide with chromium trioxide in acetic anhydride gave the *N*,*O*-diacetyl derivative (**2**) (50%), m.p. 152—154 °C.† When (**2**) was dissolved in conc. H_2SO_4 at room temp., and the solution was stirred for 3 h and then poured onto crushed ice, (**1**; R^1 = H) was formed (30%), m.p. 230—232 °C. The compound initially formed was the monomer (soluble in chloroform). Following one recrystallization (EtOH or DMF) it was totally insoluble in chloroform. An ebullioscopic molecular weight determination in DMF gave a value of 531 (calc. for trimer 501). On the other hand, a freezing point depression study (camphor) gave a value of 166.5 (calc. for monomer 167). The mass spectrum of the trimer had no peak at *m/z* 501, but peaks at 437 (trimer $-SO_2$), 334 (dimer), 270 (dimer $-SO_2$), 269 (100%), and 167 (monomer) were present. The ^{1}H n.m.r. spectrum of the trimer in dimethyl sulphoxide (DMSO) exhibited three singlets at δ 7.2, 6.5, and 6.0, suggesting that it existed in a *cis–cis–trans* arrangement (**3**) of the triazine.[3] The product was identical to that obtained by the earlier procedure.[2]

A variable-temperature n.m.r. study[4] of (**1**) ⇌ (**3**) in [$^2H_6$]DMSO, showed the appearance of a band at δ 9.3, attributed to the monomer (**1**; R^1 = H), as the temperature was raised, with a concurrent decrease in the intensities of the bands at δ 7.2, 6.5, and 6.0. Even after the solution had been heated to 190 °C and then cooled to 30 °C some monomer (*ca.* 30%) still persisted in solution. Such a procedure allowed us to carry out cycloadditions on the monomer at room temperature.

6-Nitro-1,2-benzisothiazole 1,1-dioxide (**4**), m.p. 256—258 °C, was prepared similarly (30% yield) from 4-nitrotoluene-2-sulphonamide and also existed as the trimer (δ 7.5, 6.7, and 6.3).

It was shown earlier that (**1**) could be ring-expanded to give 1,2-benzothiazepine 1,1-dioxides (**5**) on treatment with ynamines.[5] These benzothiazepines exhibited remarkable chemical stability and the possibility was raised that the seven-membered ring in (**5**) might have aromatic character, as implied by structure (**5a**). The availability of (**1**; R^1 = H) allowed an examination of this possibility. A number of 3-dialkylamino-1,2-benzothiazepine 1,1-dioxides (**6**) (particularly with R^1 and/or R^2 = H) were synthesized and their ^{1}H and ^{13}C n.m.r. spectra were studied. The ^{1}H n.m.r. spectra of compounds in (**6a**—**c**) were particularly informative. C-5–H in (**6a**) and (**6c**) resonated at δ 6.2 and 6.3, respectively. C-4–H in (**6b**) and (**6c**) resonated at δ 7.1 and 7.2, respectively. These values may be compared with those for the vinyl protons of cinnamic acid, for instance: δ 6.3 and 7.7.[6] A structure such as (**5a**; R^1 = H) would have been expected to deshield strongly protons bonded to the positively charged aromatic seven-membered ring. Also $J_{4,5}$ in (**6c**) was found to be 12.7 Hz, much larger than expected for an aromatic system; vicinal proton couplings in aromatic rings are generally in the range 6—9.5 Hz, but in the range of 2—12.5 Hz for *cis*-olefins.[7] These results suggest that the seven-membered ring in (**6**) is not aromatic and that its relative chemical inertness requires another explanation.





a; R^1 = H, R^2 = Me
b; R^1 = Me, R^2 = H
c; R^1 = R^2 = H

† All new compounds gave appropriate microanalytical and spectral (i.r., n.m.r., and mass) data.

This research was supported by grants from NINCDS, National Institutes of Health, and the U.S.–Israel Binational Foundation. The last permitted useful discussions with Dr. D. Ben Ishai which are acknowledged.

Received, 26th January 1983; Com. 125

References

1 R. A. Abramovitch, E. M. Smith, M. Humber, B. Purtschert, P. C. Srinivasan, and G. M. Singer, *J. Chem. Soc., Perkin Trans.* 1, 1974, 2589.
2 J. Koetschet and P. Koetschet, *Helv. Chim. Acta*, 1929, **12**, 669; J. Koetschet, P. Koetschet, and P. Viaud, *ibid.*, 1930, **13**, 587.
3 W. L. F. Armarego and S. C. Sharma, *J. Chem. Soc. C*, 1970, 1600.
4 H. Fritz and P. Pfaender, *Chem. Ber.*, 1965, **98**, 989.
5 R. A. Abramovitch, K. M. More, I. Shinkai, and P. C. Srinivasan, *Heterocycles*, 1976, **5**, 95.
6 C. J. Pouchert and J. R. Campbell, 'The Aldrich Library of NMR Spectra. Volume VI,' Aldrich Chemical Co., Milwaukee, Wisconsin, U.S.A., 1974, p. 132.
7 L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd Edn, Pergamon Press, Oxford, 1969.