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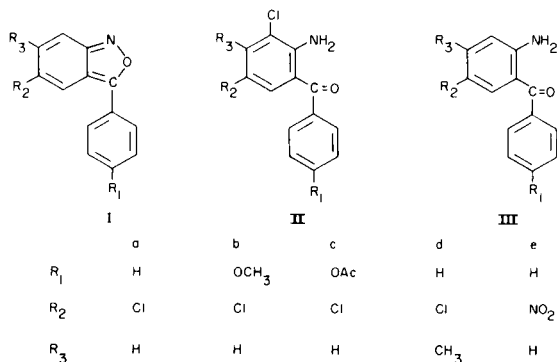
Novel reductive chlorination of 3-aryl-2,1-benzisoxazoles with thionyl chloride is described. The chlorinated aminobenzophenones have been characterised.

J. Heterocyclic Chem., 16, 1087 (1979).

Sir:

The isoxazole ring in benzisoxazoles and their quaternary salts is readily cleaved by metallic hydrides, metal-acid combinations and catalytic hydrogenations. A variety of amino and alkylaminobenzophenones have been produced through these reductive procedures and several extensions and modifications claimed (1). Since amino and alkylaminobenzophenones are key intermediates in the synthesis of clinically employed benzodiazepines such as Diazepam, Nitrazepam, Oxazepam and Flurazepam, and continue to attract much attention (2), easier and more economical ways of producing these compounds are still of interest and importance. We wish to describe here a facile and novel procedure for the production of aminobenzophenones from 3-aryl-2,1-benzisoxazoles.

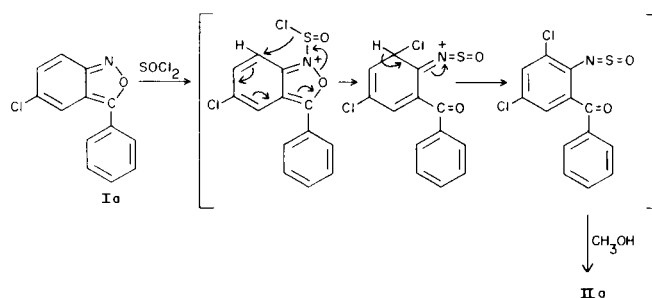
When 3-phenyl-5-chloro-2,1-benzisoxazole (3) (Ia) was mixed with excess of thionyl chloride to obtain a clear solution and allowed to stand at room temperature for 12 hours, removal of thionyl chloride gave brown pasty material. Trituration with methanol produced a yellow crystalline solid, m.p. 94° (from benzene-petroleum ether 1:1), in 80% yield. This product, assigned structure IIa, is supported by elemental analysis and spectral data and confirmed by comparison with an authentic sample.



The ir spectrum of IIa in potassium bromide showed ν C=O 1635 cm⁻¹ (s), ν NH₂ 3350 cm⁻¹ and 3450 cm⁻¹. Nmr showed a complex pattern of aromatic protons and two exchangeable hydrogen atoms (NH₂). The major mass fragments were M⁺ 265, M⁺ -1 264, and M⁺ -C₆H₅CO 160. The molecular weight determination indicated IIa to be

dichloroaminobenzophenone and the position of the halogen at C₇ was fixed by comparison with an authentic sample. The mixture m.p. of IIa with 3,5-dichloroaminobenzophenone was undepressed and their spectra were superimposable. Similarly were prepared IIb to IIe.

The quaternary salts, methiodide and methyl methosulphate of Ia underwent no change when treated with thionyl chloride under identical conditions. No reaction occurred when Ia was kept with hydrogen chloride-saturated absolute methanol for several weeks. These observations suggest an initial attack of thionyl chloride on the basic nitrogen atom, and a tentative mechanism is proposed below. All attempts to isolate the sulfinylamine



were unsuccessful; however, the ir spectrum did indicate the presence of N=S=O unit. The formation of IIIa appears to be the result of competing electronic reorganisation in the isoxazole ring only and thereby forming unhalogenated *N*-sulfinylamine without the transfer of halogen into the benzenoid ring system and subsequent hydrolysis in the work up. Further studies are in progress to understand the mechanism and extend the applicability of the reaction.

Acknowledgement.

We are thankful to Dr. A. J. Boulton of East Anglia for helpful suggestions and Dr. G. S. Sidhu, Director, Regional Research Laboratory, Hyderabad, for some of the mass spectra.

REFERENCES AND NOTES

(1a) K. W. Gopinath, J. S. Sandhu, D. Mago and A. K. Sharma,

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British Patent 1,460,141 (1975); *Chem. Abstr.*, 87, 22781d (1977); (b) G. N. Walker, *J. Org. Chem.*, 27, 1929 (1962) and references cited therein; (c) G. E. Hardtmann and N. J. Florham, U. S. Patent 3,642,897 (1972); *Chem. Abstr.*, 76, 153341f (1972).

(2) R. B. Moffett in "Lectures in Heterocyclic Chemistry", Vol. III, R. N. Castle and M. Tisler, Eds., HeteroCorporation,

170 South State Street, Orem, Utah 84057 USA, 1976, pp. S-123-S-130 and references cited therein.

(3) All benzisoxazoles described were prepared by established procedures and they gave satisfactory elemental as well as spectral analyses.