Synthesis and Structural Characterization of 3,3'-Dihalo-2,2'-spirobiindan-1,1'-diones

Jane Bogdanov
Sts. Cyril and Methodius University, Republic of Macedonia

Abstract: *Starting from 2,2'-spirobindan-1,1'-dione, 3,3'-dibromo-2,2'-spirobiindan-1,1'-dione, 3,3'-dichloro-2,2'-spirobiindan-1,1'-dione and 3,3'-difluoro-2,2'-spirobiindan-1,1'-dione were prepared using standard chemical transformations. For each of these derivatives six stereoisomers are possible (three pairs of enantiomers). In some cases one or more of the diastereomers were separated and purified and using ^1H NMR and single crystal X-ray crystallography their relative configuration was determined.*

Keywords: *3,3'-Dihalo-2,2'-spirobiindan-1,1'-diones, relative configuration, synthesis*

1. INTRODUCTION

As a part of our systematic study of 2,2'-spirobiindane-1,1'-dione derivatives as potential diradical precursors [1,2], we have focused our attention on introduction of photolabile substituents such as halides. A convenient starting material was the "parent" compound, 2,2'-spirobiindan-1,1'-dione. Its synthesis is well documented in the literature [3] and we had experience with its preparation in our laboratory [4].

Our primary goal was to focus on the preparation of the 3,3'-Dihalo-2,2'-spirobiindan-1,1'-diones (**X(HH)** systems, where X=F, Cl, Br), in order to gain understanding of the stereochemical and reactivity issues and apply it to the more challenging precursors (spirocyclopropane derivatives). The choice of photoremovable **X** substituents was chlorine or bromine, because these are known in the literature to give diradicals either by direct photolysis [5,6] or by photolysis in the presence of amines [7,8], and there are many reliable benzylic halogenation procedures. Once the 1,3-dihalides are prepared they can serve as convenient diradical precursors and synthetic precursors for the spirocyclopropanes.

2. MATERIALS AND METHODS

The title compounds were purified and characterized using standard procedures. All NMR spectra were recorded on Bruker DRX-400 spectrometer (400 MHz for proton) in deuterated chloroform ($CDCl_3$) using TMS as internal standard. The reported X-ray structures were obtained

using X-ray intensity data measured at 98 K (cooled by Rigaku MSC X-Stream 2000) on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a MoKα fine–focus sealed tube (λ = 0.71073 Å) operated at 1600 W (50 kV, 32 mA).

3. RESULTS AND DISCUSSION

3.1 Practical assignment of relative stereochemistry

In the course of this study no optically active spiro compounds or reagents were used, so both enantiomers are always present in equal amounts (all materials are racemates). Since the tetrahedral stereogenic centers on the carbons 3 and 3' are equivalent in terms of their substituents, only six stereoisomers (three pairs of enantiomers) are, in fact, expected for the idealized geometry of these spiro compounds. When one deals with racemic mixtures with several chiral centers, the naming scheme becomes quite cumbersome. However, for racemic compounds only the relative configurations are important. Such relative configurations should be quickly recognizable and be rich in stereochemical content pertinent to the system under study. The crucial stereochemical concern is the relative orientation of the **X** and **H** substituents. To completely state the relations between these substituents, it is sufficient to relate just two (one on carbon 3, and one on carbon 3'). Since one pair (the hydrogens) of the substituents will be the permanent fixture of the spirosystem, while the other will be removed to generate the radical center, it would be desirable to indicate the relative stereochemistry of the "permanent" pair (i.e. in this specific case the hydrogens). The three diastereomeric racemates of the synthetic precursors should in principle have different enough physico-chemical properties, both chromatographically and spectroscopically, to be separable and identifiable. From the point of view of the NMR techniques, inspection of models indicates that there are two symmetrical and one non-symmetrical diastereomers (symmetrical in terms of chemical shift equivalency of the "halves"). The non-symmetrical isomers would yield two sets of signals (the two spiro sub-systems will be non-equivalent). The non-symmetrical isomer (C_1 space group), will always correspond to mixed label, **X(mHH)**. On the other hand, the two symmetrical isomers will have only one set of signals (for both subunits). These isomers are C_2 symmetric, and will always have the designation anti, **X(aHH)** or syn **X(sHH)**. The only method to distinguish between the anti and syn stereoisomers is the one that is unrivaled in structural chemistry-single crystal X-ray crystallography.

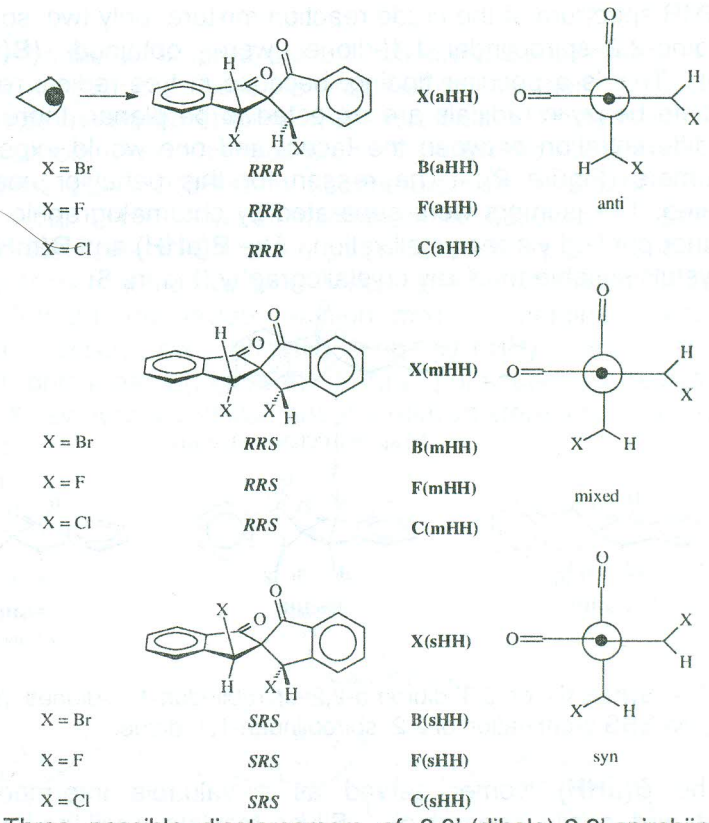

Fig. 1: Three possible diastereomers of 3,3'-(dihalo)-2,2'-spirobiindan-1,1'-dione, **X(HH)** system. Only one enantiomer of each pair is shown.

Additional potential complications arise from the fact that in the non-idealized structures five-membered rings are not flat but adopt a so-called "envelope" conformation This deviation from planarity becomes evident from structural calculations and literature X-ray structure of 2,2'-spirobiindan-1,1'-dione [9] as well as those obtained in our laboratory [4]. In solution, however, there is conformational flexibility. The energy differences between extreme conformers are low [10,11], so the interconversion in solution at 25 ºC is rapid [12,13]. As indeed was observed, the rings rapidly (faster than the NMR time-scale) swing between the extremes, giving "time averaged" signals simplifying the analysis based on the idealized "flat" structures (Fig. 5).

3.2. Synthesis of the 3,3'-Dihalo-2,2'-spirobiindandione Systems

The synthesis of the simplest precursors, **B(HH)**, started with *N*-bromosuccinimide bromination of 2,2'-spirobiindan-1,1'-dione, **2**. Based on

the ^{1}H NMR spectrum of the crude reaction mixture, only two isomers of the 3,3'-dibromo-2,2'-spirobiindan-1,1'-dione were obtained (**B(aHH)** and **B(mHH)**). This is a peculiar finding, because in free-radical reactions the intermediate benzylic radicals are expected to be planar, there should not be any differentiation between the faces, and one would expect all three diastereomers (Figure 2). The reason for this behavior has not been investigated. The isomers were separated by chromatographic means and were further purified via recrystallization. The **B(aHH)** and **B(mHH)** isomers gave crystals suitable for X-ray crystallography (Figure 6) .

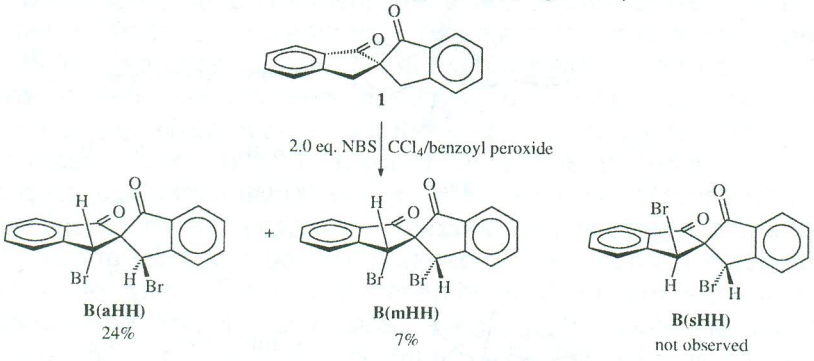

Fig. 2: Synthesis of 3,3'-dibromo-2,2'-spirobiindan-1,1'-diones (**B(aHH)** and **B(mHH)**) via NBS bromination of 2,2'-spirobiindan-1,1'-dione.

The **B(aHH)** isomer served as a valuable intermediate (most abundant and easily separable). Silver tosylate assisted hydrolysis in dioxane/water resulted in a mixture of three dialcohol isomers, whose stereochemistry was not determined. Treatment of the dialcohols with thionyl chloride gave a mixture of three dichlorides, of which two were successfully separated and purified (**C(aHH), C(mHH)**) and their relative stereochemistry established by X-ray crystallography (Fig. 3).

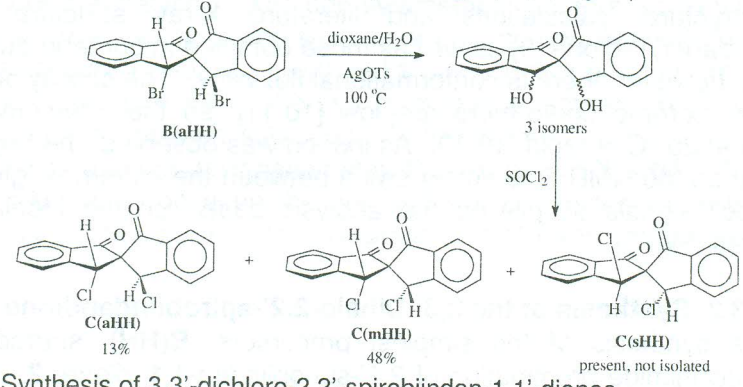

Fig 3.: Synthesis of 3,3'-dichloro-2,2'-spirobiindan-1,1'-diones.

We intetended to prepare the 3,3'-difluoro-2,2-spirobiindan-1,1'-dione, **F(HH)**, and subject it to benzylic bromination in order to obtain system should provide increased stability of the diradical. The synthetic approach was rather simple. We subjected crude 3,3'-dibromo-2,2-spirobiindan-1,1'-dione (~ 84% pure) **B(aHH)** to fluoride-bromide exchange using silver fluoride [14-16]. This kind of exchange is believed to proceed via carbocation mechanism. Since the carbocations are planar and there is no preferential face of attack by the fluoride, one would expect three difluoro isomers. Indeed, the crude reaction mixture contained three difluoro isomers, of which two (**F(sHH)** and **F(mHH)**) were isolated by chromatographic means (Figure 4). Further purification via recrystallization resulted in X-ray quality crystals, and the relative stereochemistry was firmly established.

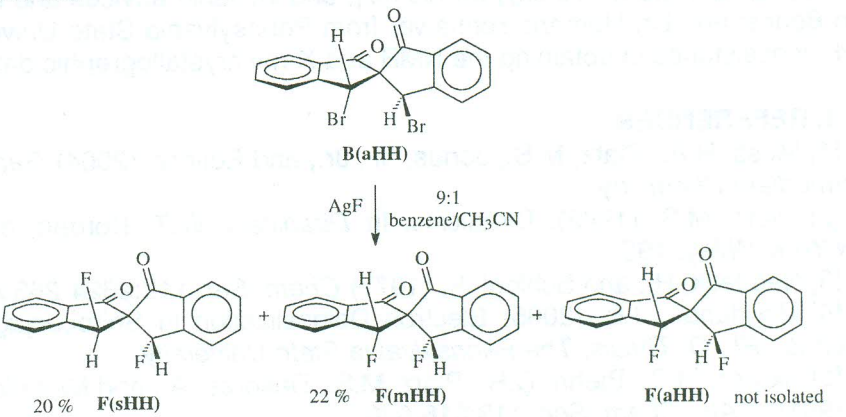

Fig. 4: Synthesis of 3,3'-difluoro-2,2'-spirobiindan-1,1'-diones.

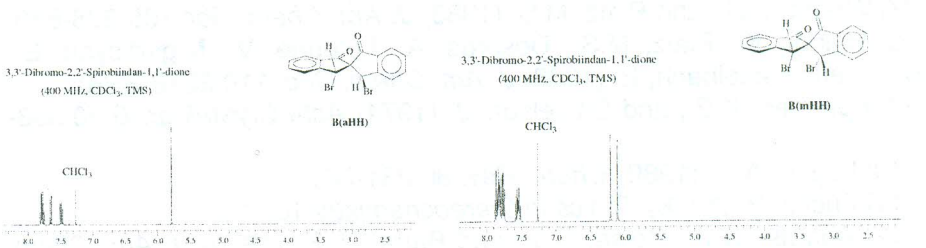

Fig. 5: ^{1}H NMR spectra of two diastereomers of 3,3'-dibromo-2,2'-spirobiindane-1,1'-dione, **B(aHH)** (left) and **B(mHH)** (right) in $CDCl_3$ (400 MHz).

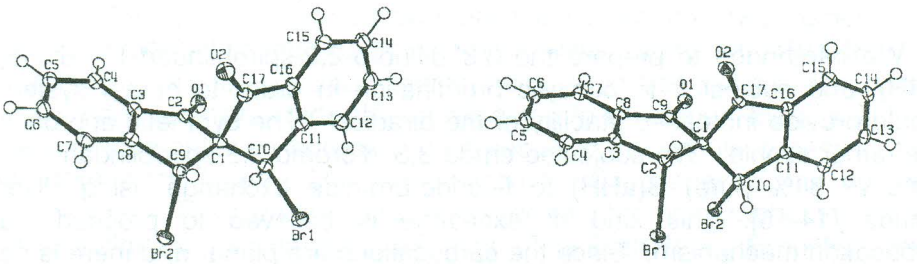

Fig. 6: ORTEP drawings of **B(aHH)** (left) and **B(mHH)** (right). Displacement ellipsoids are drawn at 50% probability level.

ACKNOWLEDGEMENT

The author expresses deep gratitude to Dr. Pshemak Maslak (Pennsylvania State University) for his help and valuable advices and to Dr. Alan Benesi and Dr. Hemant Yennawar from Pennsylvania State University for their assistance in obtaining the NMR and X-ray crystallographic data.

4. REFERENCES

[1] Moss, R.A., Platz, M.S., Jones, M., Jr., and Editors. (2004) *Reactive Intermediate Chemistry.*

[2] Platz, M.S. (1982). Diradicals. In *Diradicals.* W.T. Borden, editor. New York: Wiley. 195.

[3] Neudeck, H., and Schlogl, K. (1977) *Chem. Ber.* 110:2624-2639.

[4] Bogdanov, J.B. (2005) Electron Delocalization in Spiroconjugated Systems. *Ph. D. Thesis, The Pennsylvania State University.*

[5] Biewer, M.C., Biehn, C.R., Platz, M.S., Despres, A., and Migirdicyan, E. (1991) *J. Am. Chem. Soc.* 113:616-620.

[6] Goodman, J.L., and Berson, J.A. (1985) *J. Am. Chem. Soc.* 107:5409-5424.

[7] Wright, B.B., and Platz, M.S. (1983) *J. Am. Chem. Soc.*105:628-630.

[8] Haider, K., Platz, M.S., Despres, A., Lejeune, V., Migirdicyan, E., Bally, T., and Haselbach, E. (1988) *J. Am. Chem. Soc.* 110:2318-2320.

[9] Petersen, K.B., and Danielsen, J. (1974) *Acta Crystalogr. B* 30:338-341.

[10] Legon, A.C. (1980) *Chem. Rev.* 80:231-262.

[11] Fuchs, B. (1978) *Topics in Stereochemistry* 10:1-23.

[12] Adams, W.J., Geise, H.J., and Bartell, L.S. (1970) *J. Am. Chem. Soc.* 92:5013-5019.

[13] Lambert, J.B., Papay, J.J., Khan, S.A., Kappauf, K.A., and Magyar, E.S. (1967) *J. Am. Chem. Soc.* 89:7036-7044.

[14] Bhandari, K.S., and Pincock, R.E. (1974) *Synthesis*:655-656.

[15] Heumann, A. (1979) *Synthesis*:53-54.

[16] Ruzziconi, R., and Sebastiani, G.V. (1980) *J. Heterocyc. Chem.* 17:1147-1148.