Reductive Metallation of Substituted Isobenzofurans. Further Evidence concerning Stereoselective *cis*-Reactions

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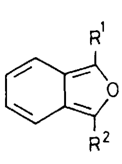
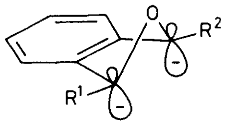
The monoanion formed by the reductive metallation of 1-t-butyl-3-phenylisobenzofuran shows *cis*-stereochemistry in its reaction products as does the known dianion of 1,3-diphenylisobenzofuran.

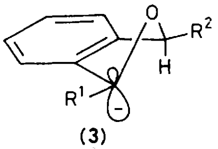
Earlier we reported[1] that the dianion formed by reductive metallation of 1,3-diphenylisobenzofuran (**1a**) reacted in a highly stereoselective manner with water, methyl iodide, or carbon dioxide to form *cis* products. In rationalizing this behaviour, it was suggested that the most stable conformation of the dianion would be one in which the steric interactions of the phenyl groups would be minimized and orbital overlap of the anionic centre with the benzene ring would be optimized[2] [*i.e.* (**2a**)]. Rapid reaction at the anionic sites would provide products reflecting this geometry. Alternatively, the mono-



(1)



(2)



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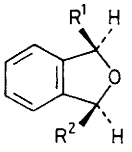

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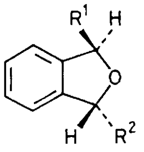

(5)

a; $R^1 = R^2 = Ph$
b; $R^1 = Ph, R^2 = Bu^t$

reacted intermediate monoanion, for the reasons already mentioned, would have as its most stable conformation that shown in (**3a**) and again *cis* products would be expected.

In this communication evidence is presented which supports the latter hypothesis that a monoreacted monoanion can react in a stereoselective *cis* manner.

The compound (**1b**), 1-t-butyl-3-phenylisobenzofuran[3] reacted readily with sodium in tetrahydrofuran (THF) to form a deep red anion. Titration of water quenched aliquot samples showed that the reaction was complete in 8 h and two g-atoms of Na per mol of (**1b**) had reacted.

Quenching a sample of the anion with methanol and column chromatography of the organic products gave an 80% yield of *cis*-1-t-butyl-1,3-dihydro-3-phenylisobenzofuran, (**4b**)† and a trace of the *trans*-isomer, (**5b**). The stereochemistry of (**4b**) was established in two ways. First, treatment of (**4b**) with potassium t-butoxide readily isomerized it to (**5b**).† Second, hydrogenation of (**1b**) formed, *via cis* addition of hydrogen, (**4b**).

The anion formed on reductive metallation of (**1b**) was treated with D_2O. The isolated product was monodeuteriated; a single proton was detected by ^1H n.m.r. spectroscopy‡ and the mass spectrum showed a molecular ion at m/z 253. Clearly, the radical anion (or dianion) of (**1b**) reacted with the solvent (THF) to form the monoreacted monoanion (**3b**). Obviously, ample time was available for isomerization of (**3b**) to occur if this were preferred. That *cis* stereochemistry was still predominant in the products supports our earlier rationale for the preferred conformation of the monoanion (**3a**) [or (**3b**)].

These investigations of the reactions of (**1b**) were complicated by the facile oxidation of the products§ and by the tendency of the anionic species initially generated to react with the solvents used.¶

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References

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2 Analogous to other anionic systems. See M. Malessard, M. P. Mazaleyrat, and Z. Welvart, *J. Am. Chem. Soc.*, 1977, **99**, 6933; M. Davey, R. Lapouyade, and H. Bouas-Laurent, *Tetrahedron Lett.*, 1978, 783, and references cited therein and those cited in ref. 1.
3 J. G. Smith and R. T. Wikman, *J. Org. Chem.*, 1974, **39**, 3648.

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† Compound (**4b**): oil, ^1H n.m.r. ($CDCl_3$) 1.07 (s, 9H), 4.97 (d, *J* 3.5 Hz, 1H), 5.98 (d, *J* 3.5 Hz, 1H), 6.8—7.5 (m, 9H). Satisfactory analytical data were obtained. Compound (**5b**): oil, ^1H n.m.r. ($CDCl_3$) 1.03 (s, 9H), 5.18 (d, *J* 3.5 Hz, 1H), 6.18 (d, *J* 3.5 Hz, 1H), 6.8—7.6 (m, 9H).

‡ An oil, ^1H n.m.r. ($CDCl_3$) 1.07 (s, 9H), 4.97 (s, 1H), 6.8—7.6 (m, 9H); i.r. (neat) 1950 cm^{-1} (C–D stretch).

§ A sample of (**4b**), exposed to the air for 6 weeks, was treated with a 1 : 1 mixture of diethyl ether–hexane. A crystalline hydroperoxide precipitated (positive test with acidified aqueous KI): ^1H n.m.r. ([$^2H_6$]benzene) 0.95 (s, 9H), 5.10 (s, 1H), 7.0—8.1 (m, 9H). Satisfactory analytical data were obtained.

¶ Reductive metallation of (**1b**) in diethyl ether using Schlenk tubes resulted in gas evolution (increase in pressure). The ^1H n.m.r. spectrum of the crude reaction products (protonation) showed that ethyl groups were present. This had also been observed (ref. 1) for (**1a**).