Lewis Acid Catalyzed Rearrangement of 1,1'-Diphenyl-2,2'-spirobiindane-1,1'-diol

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Abstract: *It is well established that 2,2'-spirobiindane ketones are susceptible to nucleophile-induced retro-Claisen condensations that lead to molecular rearrangements destroying the spiro connectivity. In the course of functionalization of the 2,2'-spirobiindane skeleton, 1,1'-diphenyl-2,2'-spirobiindane-1,1'-diol was prepared as a versatile synthetic intermediate. However, most of the conventional reactions failed because this spirodiol undergoes a facile Lewis-acid catalyzed dehydration. The structure of the rearrangement product was determined and a mechanism for this transformation is proposed.*

Keywords: *Lewis acid, rearrangement, 1,1'-diphenyl-2,2'-spirobiindane-1,1'-diol*

1. INTRODUCTION

As a part of our systematic study of spirobiindane derivatives as potential precursors for reactive intermediates [1] (such as diradicals), we have focused our attention on introduction of groups that would increase the persistency of the diradicals [2]. We have chosen to build the spirocenter early in our synthetic sequence and then to functionalize the 2,2-spirobiindan framework. Work done by Maslak and co-workers [3] clearly indicated the sensitivity of 2,2'-spirobiindan1,1'-dione (**1**) and similar systems to nucleophiles (Figure 1). It is important to keep this in mind in terms of synthetic planning, because once at least two ketones are presen ,one should avoid strong nucleophiles. Preliminary attempts of bis-alkylation of 2,2'-spirobiindan-1,1'-dione, **1**, with phenylmagnesium bromide and phenyllithium resulted in the destruction of the spirosystem. Herein, we would like to report an interesting rearrangement we have encountered of one of the synthetic intermediates (1,1'-diphenyl-2,2'-spirobiindane-1,1'-diol, **2**)

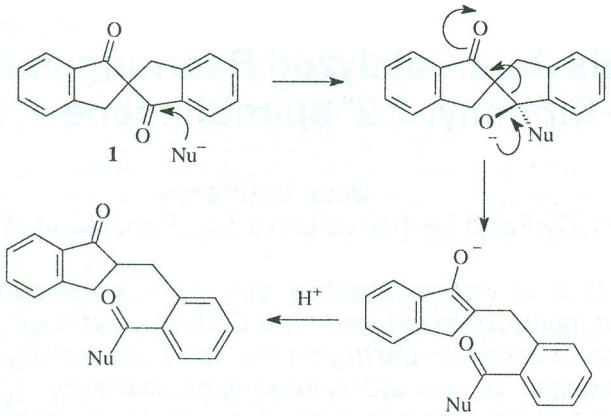

Fig. 1: Nucleophile-induced retro-Claisen condensations of 2,2'-spirobiindan-1,1'-dione that leads to molecular rearrangements destroying the spiro connectivity

2. MATERIALS AND METHODS

The title compounds were purified and characterized using standard procedures. NMR spectra were recorded on Bruker DRX-400 spectrometer (400 MHz for proton) in deuterated chloroform ($CDCl_3$) and were reported in ppm with respect to tetramethylsilane (2 drops per 100 g $CDCl_3$). Infrared spectra were recorded on Perkin Elmer Model 1600. as thin films between sodium chloride plates (reported as film). Gas chromatography was performed on a Varian 3700 with packed columns 1/8" diameter packed with 5% OV-101 on Supelcoport with helium as the carrier gas with a flow rate of 30 mL/min. High resolution mass spectrum was obtained on Waters GC-TOF with Agilent 6890 GC. 1,1'-Dihydroxy-1,1'-diphenyl-2,2'-spirobiindanes were prepared by literature procedure [10].

Acid induced rearrangement of 2a. A 100 mg sample of **2a** was dissolved in 0.7 mL of deuterated chloroform, transferred into an NMR tube and allowed to stand for a week on a bench top. The traces of acid in the deuterated chloroform induced a rearrangement (that could be conveniently monitored via ^1H NMR) to phenyl-[2-(3-phenyl-1-*H*-indene-2-ylmethyl)-phenyl]-methanone, **3**: (400 MHz, $CDCl_3$): 7.77 (d, J = 8.0 Hz, 2 H), 7.56 (t, J = 7.4 Hz, 1 H), 7.42 (t, J = 7.9 Hz, 4 H), 7.38 (m, 11 H), 7.38 (s, 2 H), 3.33 (s, 2 H). The sample was evaporated to dryness, dried *in vacuo* to give analytically pure **3** as yellow oil; GC R_t = 14.12 min (Varian temp. program: 160 °C, 3 min, 8 °C/min 280 °C); HRMS ($C_{29}H_{22}O$): Calc. 386.1671, found 386.1672 ^1H NMR (400 MHz, C_6D_6): 7.79 (m, 2 H), 7.36 – 6.96 (m, 15 H), 6.88 (dt, J = 7.3 Hz, J = 1.5 Hz, 1 H), 3.98 (s, 2 H), 3.20 (s, 2 H); IR (liquid film): 1665 cm^{-1} (C=O).

3. RESULTS AND DISCUSSION

After careful inspection of the reaction conditions, we found that in all cases the Grignard or phenyllithium was added to **2** (i.e normal addition). We speculated that once the phenyl adds to the ketone, the resulting tetrahedral intermediate collapses in analogous manner to that illustrated in Figure 1, resulting in ring opening. To remedy this problem, we decided to do a "reverse addition" i.e. slowly add a solution of the dione to a slight excess (2.1-2.3 equivalents) of a pre-cooled phenyllithium solution. If the ring opening is slower than the second addition of phenyllithium, then we have a chance to obtain the elusive diphenylspirodiol. We assumed that the dilithium dialkoxide should be stable under the reaction conditions and protonation should yield the desired product.

Indeed, the reverse addition gave the desired product, **2** in 69% yield (mixture of two diastereomers, **2a** : **2b** = 2.5 : 1.0). Several attempts of obtaining X-ray quality crystals of **2a** have failed. The stereochemistry of **2a** and **2b** was established based on ^{1}H NMR data and via structural correlation with the 1,1'-dimethoxy-1,1'-diphenyl-2,2'-spirobiindane, for which we have obtained single crystal X-ray crystallographic data.

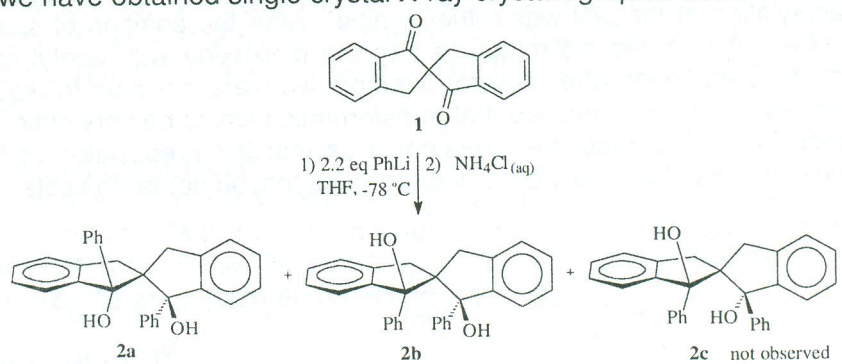

Fig. 2: Synthesis of 1,1'-diphenyl-2,2'-spirobiindane-1,1'-diols (**2a** and **2b**).

We have come to a conclusion, based on the spectral data, that the spirodiol, **2**, is sensitive to the acidic impurities in the deuterated chloroform. The ^{1}H NMR spectroscopy indicated quantitative conversion of **2a** (or **2b**) to **3**. The proposed rearrangement mechanism of this acid-catalyzed dehydration of 1,3-spirodiols is depicted in Figure 3.

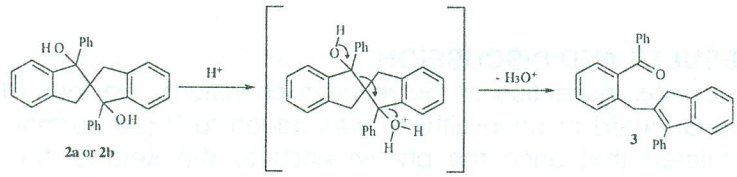

Fig. 3: Lewis-acid catalyzed rearrangement of 1,1'-diphenyl-2,2'-spirobiindane-1,1'-diol to give

We decided to proceed to find alternative protective groups for the tertiary alcohols, possibly such that could serve as radical precursor (Barton-type deoxygenation chemistry[4]). If we use acetyl chloride directly on the dialcohol, **2**, the liberated hydrogen chloride would promote rearrangement to **3**. An example from the literature supported this claim: Schonberg and co-workers refluxed a mixture of the spirodiol and excess of acetyl chloride [5] and after work-up they obtained 5,11-diphenylbenzo[b]fluorene, **4**. They rationalized its formation by the mechanism described in Figure 4 where the protonated **3** (**3H**$^+$) was involved as an intermediate. Our approach to diacetylation of the diol was rather simple. After the addition of spirodione to phenyllithium, we attempted to trap the dialkoxide with acetyl chloride. Unfortunately, even after several attempts we were not able to isolate the diacetate. This result implied that transformation would be very difficult if not impossible. This outcome revealed to us that the preparation of Barton-type esters would be very difficult or perhaps maybe not be feasible.

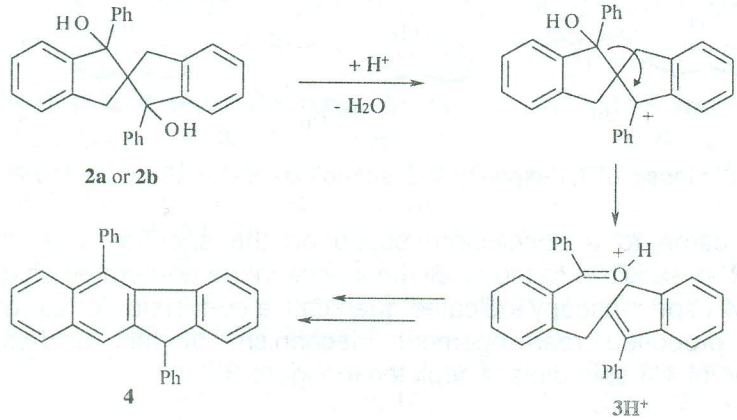

Fig. 4: Schonberg's proposed mechanisam for rearrangement of **2** to 5,11-diphenylbenzo[b]fluorene, **4**.

We have attempted preparation of the cyclopropane derivative using the methodology developed by Walborsky [6] involving reductive coupling of 1,3-diols using low valent titanium (McMurry reagent,[7,8] $TiCl_3/LiAlH_4$) to afford the cyclopropane. Subjecting **2a** to these conditions resulted in rearrangement product **3**. The presence of traces of Lewis acid, (we suspect unreacted $TiCl_3$) was sufficient to trigger the rearrangement. Additionally, we have attempted to deoxygenate **2a** using the procedure by Lau and co-workers [9], utilizing $NaCNBH_3$ in presence of ZnI_2, and instead the desired product we obtained the rearrangement product **3**. In this case the Lewis acid, ZnI_2, was responsible for the rearrangement. The dialcohols (**2a** and **2b**) were found to be too sensitive for the desired synthetic manipulations.

4. CONCLUSION

Functionalization of 1,1'-diphenyl-2,2'-spirobiindane-1,1'-diols are severely limited using standard reactions because this spirodiol undergoes a facile Lewis-acid catalyzed dehydration. Based on the identity of the rearrangement product, phenyl-[2-(3-phenyl-1-*H*-indene-2-ylmethyl)-phenyl]-methanone, a mechanism for this transformation was proposed. The dialcohols (**2a** and **2b**) were found to be too sensitive for the desired synthetic manipulations, which severely limits their usefulness as synthetic precursors.

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