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DTBB-Catalysed lithiation of *cis*- and *trans*-2,3-diphenyloxirane gives the same organolithium intermediate

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Abstract-The reaction of *cis*- or *trans*-2,3-diphenyloxirane with lithium powder and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (DTBB, 5% molar) in the presence of 3-pentanone as electrophile in THF at temperatures ranging between 90 and 50°C gives, after hydrolysis with water, the corresponding 1,3-diol **5** with the same stereochemistry (1*S**,2*R**) independently of the geometry of the starting oxiranes. A mechanistic explanation for this behaviour is given.

Keywords: DTBB-catalysed lithiation; reductive opening of oxiranes.

Introduction

The high reactivity of polar functionalised organolithium compounds¹ makes these species very interesting from a preparative point of view because they can react with electrophiles under very mild reaction conditions, so giving rise very selective processes affording polyfunctionalised molecules in only one synthetic operation. Apart from standard methods for the generation of functionalised organolithium compounds, including halogen-lithium exchange or metal-lithium transmetalation, these intermediates can be generated by reductive opening of different oxygen-, nitrogen- or sulfur-containing heterocycles.² Among them, oxiranes are important synthetic intermediates due to their accessibility and reactivity with nucleophiles,³ such as HO⁻, AcO⁻, Hal⁻, PhNH⁻, MeSe⁻, Me₃Sn⁻, NC⁻, etc., carbon-carbon bonds being produced by reaction with organometallics,⁴ such as organolithium reagents⁵ or Grignard reagents.⁶

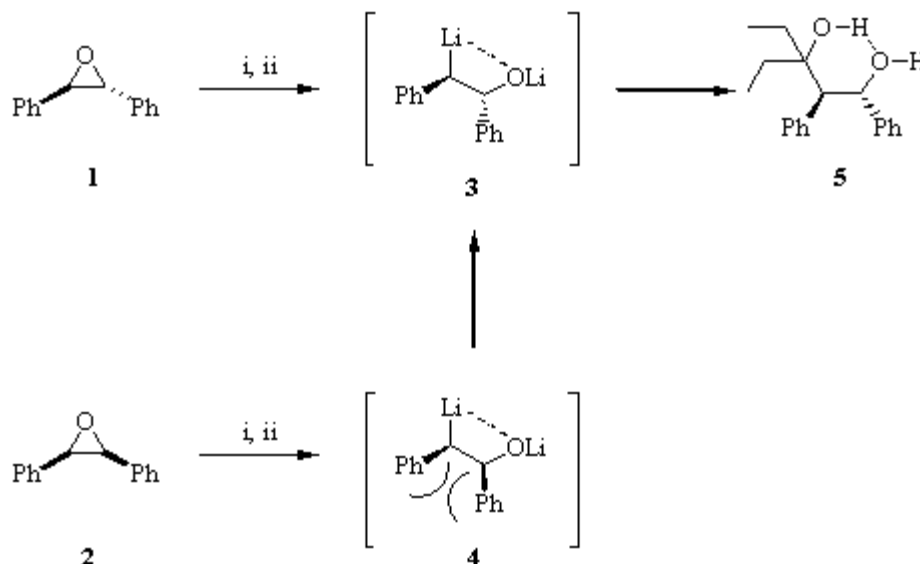
Reductive opening of oxiranes is one of the most efficient and general method for the preparation of β -oxygenated organolithium compounds, which can react with carbonyl electrophiles to give 1,3-diols in a stereoselective manner. Bartmann reported in 1986 that epoxides can be converted to β -metalloalkoxides *via* reductive metallation by lithium naphthalenide and biphenylide.⁷ The reaction must be carried out at low temperature (-78°C) to avoid the decomposition of the organolithic intermediate, so lithium needs to be activated by an arene in order to achieve the lithiation under the required reaction conditions.

In this communication we report our preliminary results on the low temperature DTBB-catalyzed⁸ reductive opening of *trans*- and *cis*-2,3-diphenyloxirane with lithium powder in the presence of 3-pentanone⁹ (Barbier-type reaction conditions¹⁰).

Results and Discussion

The reaction of commercially available *trans*-2,3-diphenyloxirane (**1**) with an excess of lithium powder (1:10 molar ratio) and a catalytic amount of DTBB (1:0.1 molar ratio; 5 mol%) in the presence of 3-pentanone as electrophile in

THF at temperatures ranging between -90 and -50 °C gave, after hydrolysis with water, the corresponding product **5** (60%), in which the stereochemistry of the starting material is kept (Scheme 1). Surprisingly, when the same process was carried out starting from *cis*-2,3-diphenyloxirane (**2**) the same compound **5** (40%) was the only product isolated without any contamination of the corresponding initially expected 2-epimeric product (Scheme 1). As a possible explanation for the results indicated in Scheme 1, we believe that in the case of *cis*-oxirane **2**, the first dianionic specie **4** (which posses a rather rigid structure due to the coordination of the heteroatom to the lithium atom¹¹) undergoes inversion at the carbanionic benzylic center¹² giving the less-hindered intermediate **3**, the same one that results from the direct opening of the *trans*-oxirane **1**. In the reaction of dianion **3** with the electrophile, retention of configuration is observed, this behavior being the normal one in these S_E-type reactions.¹³



Scheme 1. Reagents and conditions: i, Li excess, DTBB (5%), Et₂CO, THF, -90 to -50 °C. ii, H₂O, -50 to 0 °C.

The stereochemistry of product **5** was determined by NMR studies and was confirmed by X-Ray (Figure 1).

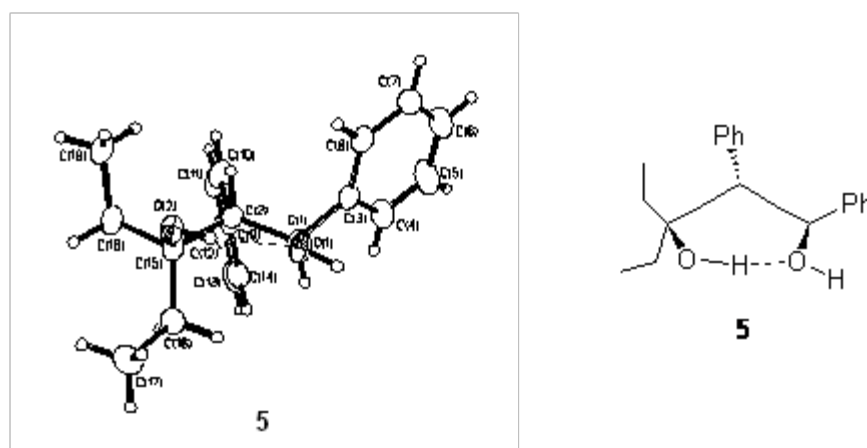


Figure 1. X-Ray structure of compound **5**

Conclusion

In this paper we have described a new behavior of intermediate **4** (obtained from the *cis*-epoxide **2**), which due to its rigid structure shows a high steric hindrance suffering benzylic inversion to yield the same intermediate **3** than the one coming from the epimeric *trans*-epoxide **1**. Studies are in due course in order to know the scope and applications of the preliminary results shown here.

Experimental Part

Preparation of 3-ethyl-1,2-diphenyl-1,3-pentanediol (5). To a cooled green suspension of lithium (7 mmol, 49 mg) and DTBB (0.05 mmol, 13 mg) in dry THF (3 mL) at -90°C was slowly added (*ca.* 30 min) a solution of 3-pentanone (1.5 mmol, 180 mL) and the *cis*- or *trans*-2,3-diphenyloxirane (1 mmol, 200 mg) in THF (2 mL). The resulting mixture was stirred for 2 h allowing the temperature to rise to -50°C and then it was hydrolysed with water (5 mL). The resulting mixture was extracted with ethyl acetate (3 \times 10 mL). The organic layer was dried over anhydrous MgSO_4 and evaporated (15 Torr). The resulting residue was then purified by flash chromatography (silica gel, hexane/ethyl acetate). Yields are given in text and physical, analytical and spectroscopic data follow. R_f (hexane: ethyl acetate 8:2) = 0.76; m.p. 141°C ; n (film) 3261 (OH), 3080, 3066, 3026, 1602 cm^{-1} (C=CH); d_H 0.76 (3H, t, $J = 7.3$, CH_3), 0.99 (3H, t, $J = 7.3$, CH_3), 1.09, 1.57, 1.76, 2.12 (4H, 4m, 2 \times CH_2), 3.23 (1H, d, $J = 10.2$, PhCHCOH), 3.82 (2H, br s, 2 \times OH), 5.24 (1H, d, $J = 10.2$, PhCHOH), 7.08 (10H, br s, ArH); d_C 7.3, 7.6 (CH_3), 27.9, 30.0 (CH_2), 59.8 (PhCHCOH), 77.4 (Et_2COH), 78.2 (PhCHOH), 126.4, 126.9, 127.1, 127.8 (ArCH), 139.2, 143.6 (ArC); m/z 266 ($\text{M}^+ - \text{H}_2\text{O}$, 1%), 181 (15), 180 (100), 179 (32), 178 (13), 165 (16), 160 (51), 131 (15), 107 (10), 105 (13), 91 (24), 79 (14), 77 (18), 57 (30); HRMS: $\text{M}^+ - 2 \times \text{H}_2\text{O}$, found 248.1580. $\text{C}_{19}\text{H}_{20}$ requires 248.1565. Crystal data: $\text{C}_{19}\text{H}_{24}\text{O}_2$, $M = 284.38$; orthorhombic, $a = 9.8420(7)$, $b = 10.5542(8)$, $c = 15.8826(12)$ Å, $a = 90^{\circ}$, $b = 90^{\circ}$, $g = 90^{\circ}$; $U = 1649.8(2)$ Å³; space group P 2(1) 2(1) 2(1); $Z = 4$; $D_c = 1.145\text{ Mg cm}^{-3}$; $\rho = 0.71073\text{ g cm}^{-3}$; $m = 0.072\text{ mm}^{-1}$; $F(000) = 616$; $T = -100 \pm 1^{\circ}\text{C}$.

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