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2,2′-Dilithiobiphenyl by direct lithiation of biphenylene

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Dedicated to Professor Armin de Meijere on occasion of his 70th birthday.

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ABSTRACT

The reaction of biphenylene (**1**) with an excess of lithium powder (1:14 molar ratio) and a catalytic amount of DTBB (10 mol %) in THF at room temperature leads to the formation of the dilithiated species I by reductive opening of the four-membered ring. Further reaction of this intermediate with different electrophiles [Electrophile = H_2O, D_2O, Me_3SiCl, *t*-BuCHO, Et_2CO, *n*-Pr_2CO, $(CH_2)_5CO$, Ph_2CO and adamantanone] at 0 °C yields the corresponding products **2**, after hydrolysis with water. Cyclisation of some representative examples of compounds **2** with H_3PO_4 gives the corresponding dibenzoxepines **3**.

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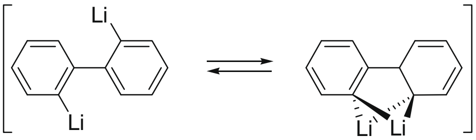
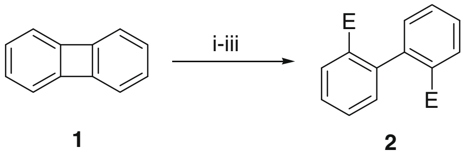
Dilithium compounds are useful intermediates in synthetic organic chemistry because their reaction with two equivalents of an electrophile allows the direct introduction of two electrophilic fragments in the organic skeleton of the organometallic reagent in only one synthetic operation.[1,2] Apart from transmetallation methodologies (mainly mercury- and tin-lithium exchange, only used in some unique cases), the most used procedures for the generation of dilithium intermediates involve deprotonation or halogen–lithium exchange.[3] As an example, in the case of 2,2-dilithiobiphenyl **I**, it has been generated by using the two mentioned methodologies: (a) direct deprotonation of biphenyl with *n*-BuLi/TMEDA,[4] and bromine- or iodine–lithium exchange using *n*-BuLi or *t*-BuLi as lithiating agent.[5] However, and probably due to the general high instability of dilithium intermediates,[1] compound **I** was either obtained with low yield[4] or it was transmetallated into its zinc derivative (by treatment with $ZnCl_2$) in order to perform some further transformations.[4,5] Continuing with our interest in dilithium reagents[6] we report here the generation of 2,2’-dilithiobiphenyl (**I**) by direct lithiation of biphenylene using an arene-catalyst, a methodology that has been extensively used in our group in the last few years.[7]



I

The reaction of commercially available biphenylene **1** with an excess of lithium (1:14 molar ratio) and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB; 1:0.2 molar ratio, 10% molar) in THF at room temperature led, after 2 h, to a solution containing the intermediate **I**, which was then treated with an electrophile [1:2.2 molar ratio; Electrophile = H_2O, D_2O, Me_3SiCl, *t*-BuCHO, Et_2CO, *n*-Pr_2CO, $(CH_2)_5CO$, Ph_2CO, adamantanone] at 0 °C for 30 min. After hydrolysis with water at temperatures ranging between 0 and 20 °C for 1 h the expected products **2** were isolated (Scheme 1 and Chart 1).[8]



Scheme 1. Reagents and conditions: (i) Li (1:14 molar ratio), DTBB (10% molar), THF, rt, 2 h; (ii) electrophile = H_2O, D_2O, Me_3SiCl, *t*-BuCHO, Et_2CO, *n*-Pr_2CO, $(CH_2)_5CO$, Ph_2CO, adamantanone (2.2 equiv), 0 °C, 30 min; (iii) H_2O, 0 °C to rt, 1 h.

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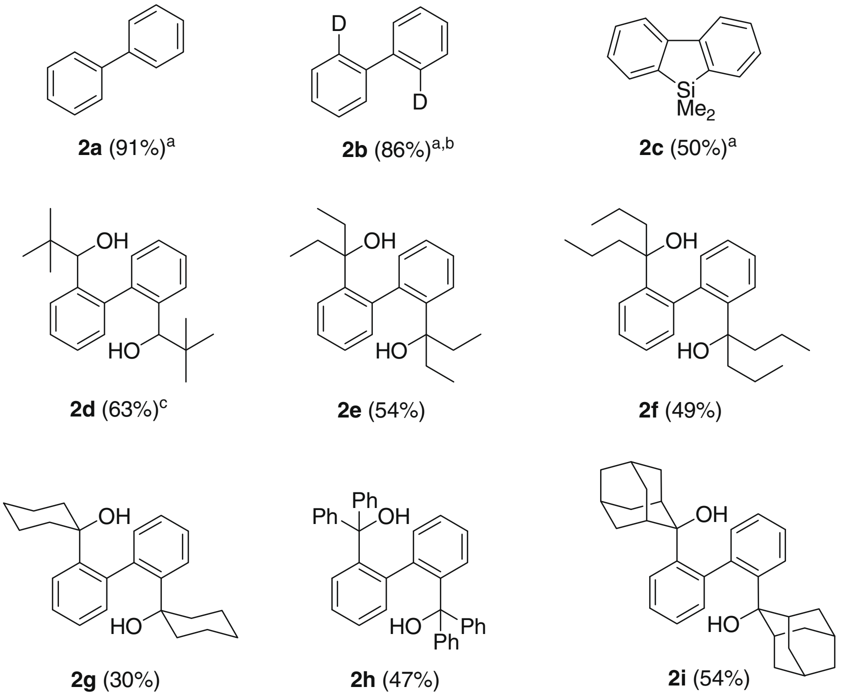


2a (91%)[a] **2b** (86%)[a,b] **2c** (50%)[a]

2d (63%)[c] **2e** (54%) **2f** (49%)

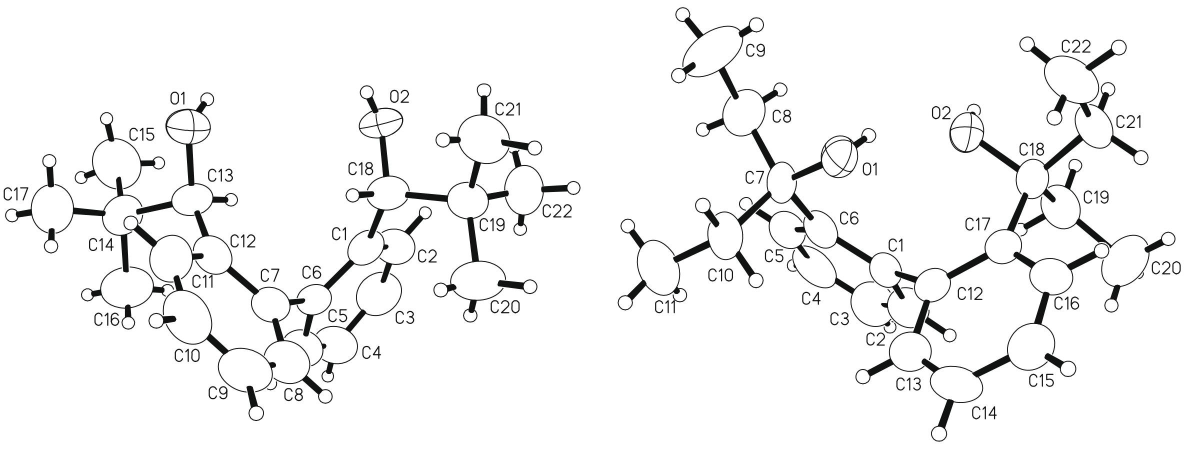
2g (30%) **2h** (47%) **2i** (54%)

Chart 1. Structures and isolated yields of pure compounds **2** (>95%, from GLC and/or 300 MHz ^{1}H NMR), after column chromatography unless otherwise stated; (a) GLC yield; this compound was impurified by small amounts of DTBB (<15%); (b) >95% Deuterium incorporation (tandem GLC–MS); (c) A 2:1 mixture of diastereomers was obtained, which were separated by column chromatography.

Since the starting material **1** can act as electron carrier in the lithiation step,[7] the same process was performed in the absence of DTBB as external arene: in this case we observed total conversion of biphenylene in about the same reaction time. However, the reaction is not clean and several by-products were obtained together with the expected ones **2**, some of them resulting from the partial reduction of the aromatic ring, which would be an indirect proof of the participation of the arene **1** as electron transfer agent. In addition, when the reaction shown in Scheme 1 was carried out at lower temperatures (or removing the excess of lithium at the end of the lithiation step), worst results were obtained, the corresponding monosubstituted ones being the major products.[9] Actually, in all cases compounds **2** were obtained together with small amounts of the mentioned monosubstituted compounds (<10%), which were easily separated from the desired product **2** by column chromatography during the final isolation.

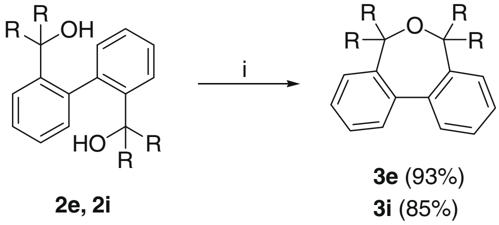
As Chart 1 shows, in the case of using Me_3SiCl as electrophiles, the expected product resulting from the incorporation of two silicon fragments was not obtained: instead, silafluorene **2c** was the only reaction product isolated. This behaviour was already described in the literature[5c] and can be explained accepting the participation of pentacoordinated organosilicon intermediates.[10]

When pivalaldehyde was used as electrophile the expected mixture of diastereomers (**2d**, 2:1 after chromatographic isolation) was obtained and separated by column chromatography. The structure of the major diastereomer (R^*,R^*) was established by X-ray analysis (Chart 2), the same technology being used for confirming the structure of the diol **2e** (Chart 2).

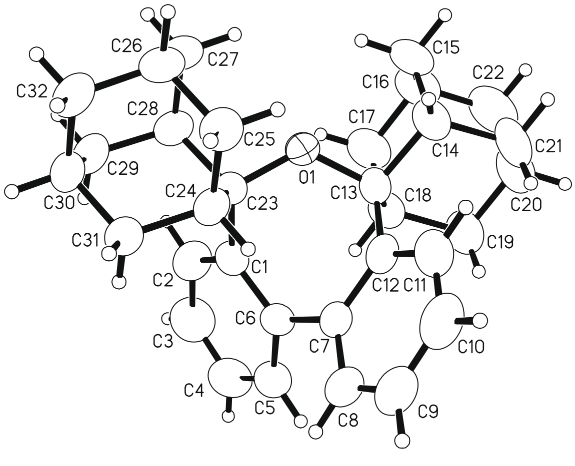


2d (major R^*,R^*) **2e**

Chart 2. X-ray structures of diols **2d** (major) and **2e**, derived from pivalaldehyde and 3-pentanone, respectively.



Scheme 2. Reagents and conditions: (i) 85% H$_3$PO$_4$, Et$_2$O, rt, 1d (for **2e**) or 4 h (for **2i**).



3i

Chart 3. X-ray structure of oxepine **3i**.

In the second part of this study we carried out the dehydration of some diols **2** in order to get the corresponding oxygen-containing heterocycles. Thus, treatment of diols **2e** and **2i** with 85% phosphoric acid in ether at room temperature gave the expected dibenzoxepines **3e** and **3i**, respectively (Scheme 2).[11,12]

The structure of compound **3i** was confirmed by X-ray analysis (Chart 3).

In summary, we have described herein the easy generation of a 2,2′-dilithiobiphenyl using a very simple methodology, the DTBB-catalysed lithiation of commercially available biphenylene. This dianion has been trapped with different electrophiles, especially carbonyl compounds affording interesting diols that were easily cyclised under acidic conditions to yield the expected oxepines. Compared to other possible methodologies (transmetallation, deprotonation or halogen–lithium exchange), the here reported generation of the dilithiated species **I** is the most convenient one concerning the atom-economy philosophy.[13]

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Supplementary data

Supplementary data (analytical, physical and spectroscopic data for compounds **2** and **3**, as well as the corresponding literature references for known compounds) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.02.216.

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8. *General procedure for compounds* **2**: To a dark green suspension of lithium powder (49 mg, 7 mmol) and DTBB (13 mg, 0.05 mmol) in THF (1 mL) was added dropwise a solution of biphenylene (77 mg, 0.5 mmol) in THF (2 mL) and the mixture was stirred for 2 h at rt. The corresponding electrophile (1.1 mmol, except for compound **2a** and **2b**, where direct work-up or 0.5 ml of D$_2$O was used, respectively) was then added at 0 °C and it was stirred at the same temperature for 30 min. The resulting mixture was hydrolysed with water (5 mL) allowing the temperature to rise to rt. The mixture was extracted with EtOAc (3 × 10 mL), the organic layer dried with MgSO$_4$ and solvents were evaporated in vacuo to yield a residue that was purified by column chromatography (silica gel, hexane–EtOAc) to afford the title products.
9. The monosubstituted products (**2**, with one E = H) would be formed by abstraction of one hydrogen from the reaction medium (probably from THF at the α-position; see, for instance: Clayden, J.; Yasin, S. A. *New J. Chem.* **2002**, *26*, 191–192), before or after quenching with one molecule of the electrophile.
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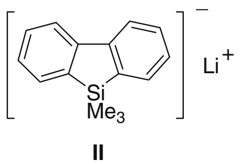

II

11. *General procedure for compounds* **3**: A solution of the pure diol **2** (0.1 mol) in ether (1 mL) was treated with 85% H_3PO_4 (1 mL) and it was stirred at rt until the starting material was consumed (TLC; 1 d for **2e** and 4 h for **2i**). Then it was extracted with EtOAc (3×10 mL), the organic layer dried with $MgSO_4$ and evaporated in vacuo to afford the pure oxepines **3**.
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