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4,4'-Di-*tert*-butylbiphenyl-Catalysed Lithiation of 2,3-Dichloropropene: A Barbier-Type Practical Alternative to 2,3-Dilithiopropene

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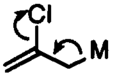
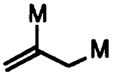
Abstract: The reaction of 2,3-dichloropropene (1) and different carbonyl compounds (2) with an excess of lithium powder (1:7 molar ratio) in the presence of a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (5 mol %) in tetrahydrofuran at 0°C leads, after hydrolysis with aqueous hydrochloric acid, to the corresponding 1,4-diols in a Barbier-type process.

The reaction of 2,3-dichloropropene with zero valent metals is a known procedure for obtaining pure allene gas[1]; in this process a β-elimination reaction[2] from the first formed β-functionalized organometallic intermediate of the type **I** is supposed to occur, being a very fast process even at low temperatures, which inhibits the second metalation to **II**. Another possible route for dianions of the type **II** could be the direct metalation of propene; however, for instance in the case of M=Li, the lithiation of propene with *n*-butyllithium/tetramethylethylenediamine affords the corresponding 1,3- instead of the 2,3-dilithiated system[3,4]; this result is consistent with the observation that 2,3-dilithiopropene is not formed by further lithiation of allyllithium[5]. On the other hand, and following our continous interest on functionalized organolithium compounds and their application in synthetic organic chemistry[6], we have recently developed a new procedure for the lithiation of different substrates at low temperature, which involves the use of an excess of lithium powder and a catalytic amount of an arene, naphthalene being the most used[7]. Employing this methodology is possible to prepare very reactive functionalized organolithium compounds by chlorine-lithium[7,8] or sulphur-lithium[7,9] exchange and other related processes, such as reductive cleavage of tetrahydrofuran[10a], sulfonates[10b], sulfates[10c], aziridines[10d], and the obtention of *C,O*-dilithiated diarylmethanols[10e]. In the present paper we describe a solution to the problem of using the dianion **II** for M=Li by combining the above described arene-catalytic lithiation[7] of 2,3-dichloropropene with a Barbier-type process[8b,11] in the presence of a carbonyl compound as electrophile[12].

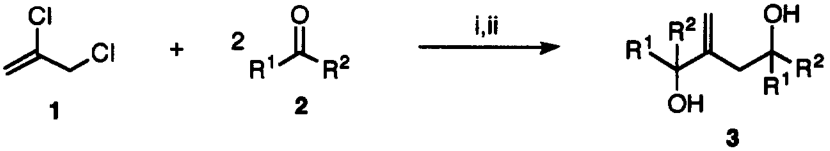


I



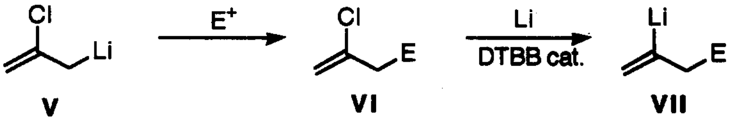
II

The reaction of 2,3-dichloropropene **1** and a carbonyl compound **2** (1:2 molar ratio) with an excess of lithium powder (1:7 molar ratio) in the presence of a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (DTBB, 5 mol %) in tetrahydrofuran at 0°C led, after hydrolysis with hydrochloric acid to the corresponding methylenic 1,4-diols **3** (Scheme 1 and Table 1). In the case of using aromatic carbonyl compounds, such as benzaldehyde or propiophenone (Table 1, entries 3 and 7, respectively) the reaction has to be performed at -40°C in order to avoid undesirable by-processes. The use of naphthalene as the arene catalyst led to poorer results; thus, the same reaction as above but using naphthalene instead of DTBB[13] afforded compounds **3b** and **3f** in 54% and 21% (GLC), respectively (Table 1, entries 2 and 6, and footnotes e and h, respectively).



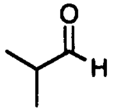
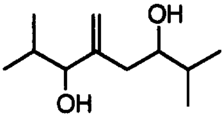
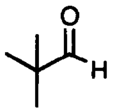
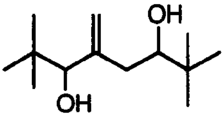
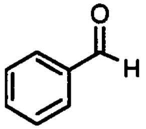
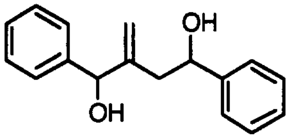
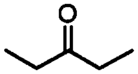
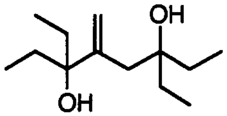
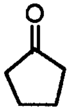
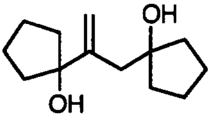
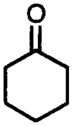
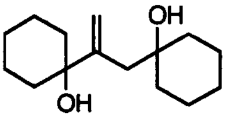
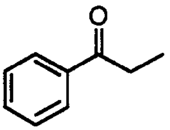
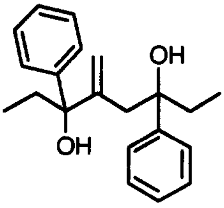
Scheme 1. *Reagents and conditions*: i, Li excess (1:7 molar ratio), DTBB (5 mol %), THF, 0°C; ii, H_2O-HCl.

From a mechanistic point of view, we think that the first lithiation takes place at the allylic position giving the intermediate **V**; this species has two possibilities of reacting, (a) in absence of the electrophile suffers β-elimination to yield allene, or (b) in the presence of the electrophile reacts rapidly to the corresponding intermediate **VI**, which is lithiated also in a fast process to give the functionalized organolithium derivative **VII**. This is the last species before the obtention of compound **3**, by reaction with other molecule of the electrophile (Scheme 2). We find this way more probable than the formation of the very unstable dilithiated species **II** (with M=Li)[4,5]; on the other hand, we could not isolate compounds of the type **VI**, even performing the reaction at -110°C. In general, we always obtain products **3** contaminated with variable amounts of the product resulting from the abstraction by the intermediate **VII** of a proton from the reaction media[14]. In addition, the temperature plays an important role: at low temperature (<-78°C) the reaction works worse than at 0°C because the transformation **V**→**VI** is a slow process and the β-elimination competes adventageously giving allene as the main product.



Scheme 2.

Table 1. Obtention of 1,4-Diols **3**

		Product[a]		
Entry	Carbonyl compound (**2**)	Structure (no.)	Yield (%)[b]	M.p. (°C)[c]
1		 (**3a**)	71 (1:1)	-[d]
2		 (**3b**)	82[e] (8:7)	-[d,f]
3[g]		 (**3c**)	73 (5:4)	-[d]
4		 (**3d**)	52	50-51
5		 (**3e**)	70	83-84
6		 (**3f**)	56[h]	101-102
7[g]		 (**3g**)	30 (1:1)	-[d]

[a] All products **3** were fully characterized by their analytical (for **3d**-**3f**) and spectroscopic data (IR, ^{1}H and ^{13}C NMR, and mass spectra). [b] Isolated yield after flash chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1**; in parenthesis the diastereoisomer ratio from ^{1}H (entries 1 and 7), ^{13}C NMR (entry 3), or after chromatographic separation (entry 2). [c] From hexane/ethyl acetate. [d] Syrup. [e] A 54% yield (GLC) was obtained by using naphthalene instead of DTBB under the same reaction conditions. [f] M.p.'s for the pure separated diastereo-isomers: 66-67°C and 81-82°C. [g] The reaction was performed at -40°C. [h] A 21% yield (GLC) was obtained by using naphthalene instead of DTBB under the same reaction conditions.

Finally, 1,4-diols **3** can be easily transformed into the corresponding substituted methylenetetrahydrofurans. As an example, compound **3d** was intramolecularly dehydrated with 8 M HCl in THF to yield 2,2,5,5-tetraethyl-3-methylenetetrahydrofuran in 95% isolated yield[15,16].

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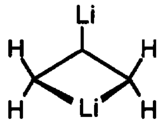
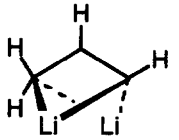


III



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