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# Polyphenylene as an electron transfer catalyst in lithiation processes

Miguel Yus,* Cecilia Gómez and Pablo Candela

*Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, Apdo. 99, E-03080 Alicante, Spain*

Dedicated to Professor Dieter Hoppe on the occasion of his 60th birthday

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**Abstract**—The lithiation of different functionalised chlorinated materials (**1a**–**c**), dichlorinated compounds (**1d**–**f**) and benzofused cyclic ethers (**1g**,**h**) with lithium powder in the presence of catalytic amounts of either linear (LPP) or crosslinked (CPP) polyphenylene, in THF at temperatures ranging between −78 and 20°C, leads to the expected organolithium intermediates (**Ia**–**h**), which by reaction with electrophiles [Bu$^t$CHO, PhCHO, $Et_2CO$, $(CH_2)_5CO$, PhCOMe, $Me_3SiCl$] gives, after hydrolysis with water, the expected products **2aa**–**hf**. © 2002 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

Organolithium intermediates are important reagents in synthetic organic chemistry as a versatile source of carbanionic species.[1] Their use, especially in carbon–carbon formation reactions, has been increased in the last years by using functionalised organolithium compounds.[2] In this case, the reaction of these intermediates bearing a functionality with electrophilic reagents allows the direct preparation of polyfunctionalised molecules. Apart from problems concerning the compatibility between the functional group and the carbon–lithium bond, one inherent problem associated with the preparation of very reactive functionalised organolithium compounds is the lithiation at low temperatures. In many cases, this process does not work using lithium metal and it is necessary to activate the metal[3] in order to get the desired lithiation. During the last few years, two methodologies have been developed in order to activate lithium: (a) the use of a stoichiometric amount of an arene,[4] what is called lithium-arene or lithium arenide;[5] (b) the use of a substoichiometric (catalytic) amount of the same arene,[6,7] naphthalene and 4,4′-di-*tert*-butylbiphenyl (DTBB) being in both cases the most commonly used arenes. We have extensively applied the second (b) methodology in the following areas: (1) to prepare organolithium reagents from non-halogenated materials;[8] (2) to prepare functionalised organolithium compounds (by halogen–lithium exchange[2] or by ring opening of heterocycles[9]); (3) to generate polylithiated synthons;[10] and (4) to activate other metals, especially nickel.[3c] In some cases, it is necessary to work under Barbier-type reaction conditions,[11] that is, in the presence of the electrophile in order to avoid decomposition of the corresponding organolithium intermediates. One further improvement of the arene-catalysed lithiation is the use of a naphthalene- or biphenyl-supported polymer as a catalyst.[12] In this case, the insoluble electron transfer agent can be removed at the end of the reaction by simple filtration. In this paper, we report on the use for the first time of oligomers of polyphenylene, very easily available, as catalysts in lithiation processes. In this case, the polymeric catalyst contains only aromatic rings without any spacer between them, being prepared by a polycondensation method instead of by an olefin polymerisation.[12]

## 2. Results and discussion

Linear polyphenylene (LPP) was prepared according to the procedure described by Yamamoto[13] as a yellow powder by reaction of 1,4-dibromobenzene with magnesium under THF reflux, followed by treatment with a catalytic amount of $NiCl_2(PPh_3)_2$. From its elemental analysis $[(C_{1.2}H)_n]$[14] and its IR data, this compound seems to be an oligomer of ca. four aromatic rings per two bromine atoms. In order to change the properties of this oligomer, we also prepared another polymer using a 5% of 1,3,5-tribromobenzene as crosslinking agent, so crosslinked polyphenylene (CPP) was also isolated as a yellow solid. In this case, the elemental analysis $[(C_{1.4}H)_n]$[14] and IR data correspond to the existence of ca. 12 aromatic rings per two bromine atoms. This second compound seems to be more similar than polyphenylene of high molecular weight.[14]

With these two polymers in hand we studied their use as

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* Corresponding author. Tel.: +34-9-6590-3548; fax: +34-9-6590-3549; e-mail: yus@ua.es

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electron transfer catalysts in the following three lithiation reactions:

*Preparation of functionalised organolithium compounds by chlorine–lithium exchange* catalysed by LPP or CPP, starting from chloroacetals **1a** and **1b** or the chloroether **1c** (Chart 1) in THF at −78°C. The corresponding intermediates **Ia–c** (Chart 2) reacted with carbonyl compounds [$Et_2CO$, $(CH_2)_5CO$, PhCHO, PhCOMe] to give, after hydrolysis, the expected hydroxyacetals **2aa–bc** (Chart 3 and Table 1, entries 1–4) and hydroxyethers **2cc**,**cd** (Chart 3 and Table 1, entries 5 and 6).

*In situ generation of dilithiated synthons* by LPP- or CPP-catalysed lithiation of dichlorinated materials **1d–f** (Chart 1) under Barbier-type reaction conditions, in the presence of the corresponding electrophiles [$Et_2CO$, $(CH_2)_5CO$, $Me_3SiCl$] in THF at −78°C, so the expected products

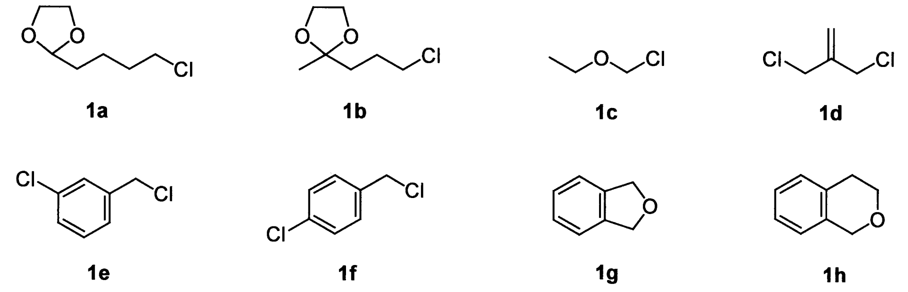

**Chart 1.** Starting materials used in the LPP- and CPP-catalysed lithiation.

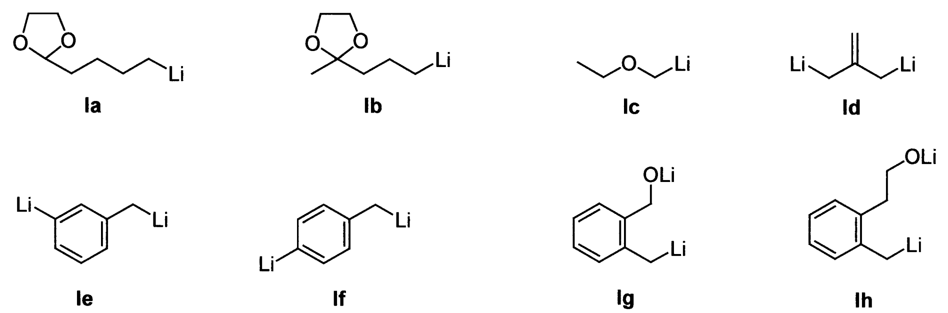

**Chart 2.** Intermediates involved in the lithiation of compounds **1**.

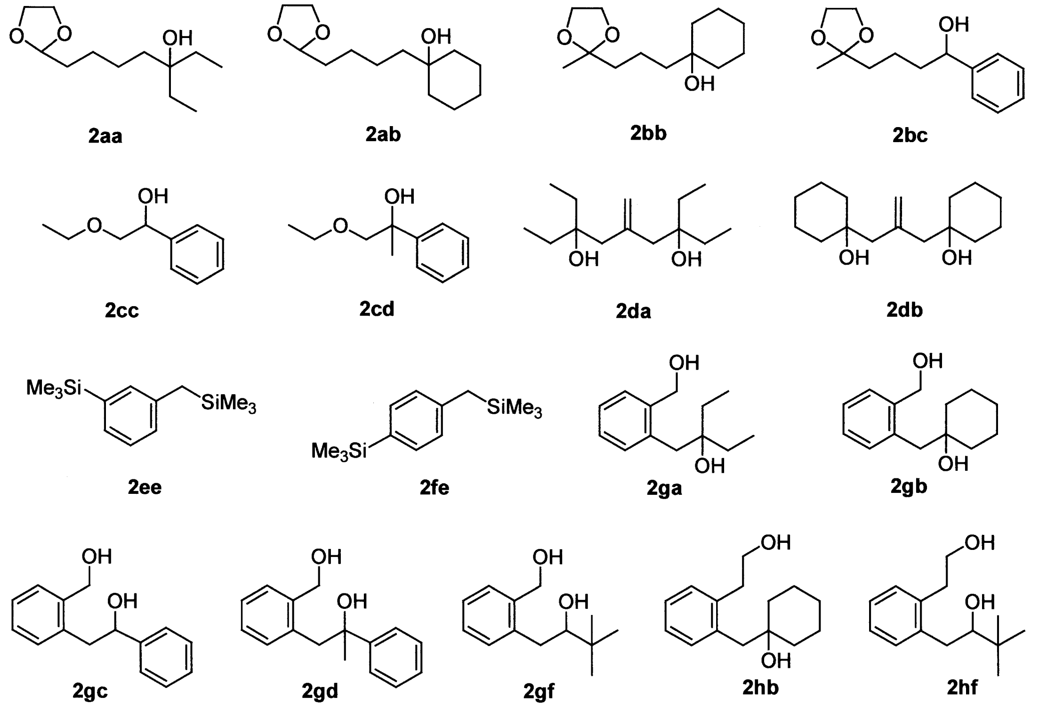

**Chart 3.** Compounds **2** prepared from starting materials **1**.

**Table 1.** Preparation of compounds **2**

| Entry | Starting material[a] | Catalyst[b] | Intermediate[c] | Electrophile | Product **2**[d] | | |
|---|---|---|---|---|---|---|---|
| | | | | | No. | Yield (%)[e] | Reference[f] |
| 1 | **1a** | LPP | **Ia** | Et$_2$CO | **2aa** | 64 [46] | 15 |
| 2 | **1a** | CPP | **Ia** | (CH$_2$)$_5$CO | **2ab** | 65 [70–79] | 15 |
| 3 | **1b** | CPP | **Ib** | (CH$_2$)$_5$CO | **2bb** | 46 [61] | 16 |
| 4 | **1b** | CPP | **Ib** | PhCHO | **2bc** | 64 [51] | 16 |
| 5 | **1c** | CPP | **Ic** | PhCHO | **2cc** | 91 [84] | 17 |
| 6 | **1c** | CPP | **Ic** | PhCOMe | **2cd** | 75 [91] | 17 |
| 7 | **1d** | LPP | **Id** | Et$_2$CO | **2da** | 66 [72] | 18 |
| 8 | **1d** | LPP | **Id** | (CH$_2$)$_5$CO | **2db** | 92, 79[g] [67] | 18 |
| 9 | **1e** | CPP | **Ie** | Me$_3$SiCl | **2ee** | 44 [78] | 19 |
| 10 | **1f** | CPP | **If** | Me$_3$SiCl | **2fe** | 65 [83] | 19 |
| 11 | **1g** | CPP | **Ig** | Et$_2$CO | **2ga** | 60 [74] | 20 |
| 12 | **1g** | CPP | **Ig** | (CH$_2$)$_5$CO | **2gb** | 66 [51] | 20 |
| 13 | **1g** | CPP | **Ig** | PhCHO | **2gc** | 61 [68] | 20 |
| 14 | **1g** | CPP | **Ig** | PhCOMe | **2gd** | 56 [63] | 20 |
| 15 | **1g** | CPP | **Ig** | Bu$^t$CHO | **2gf** | 66 [56] | 20 |
| 16 | **1h** | CPP | **Ih** | (CH$_2$)$_5$CO | **2hb** | 49 [53] | 21 |
| 17 | **1h** | CPP | **Ih** | Bu$^t$CHO | **2hf** | 53 [59] | 21 |

[a] See Chart 1.

[b] LPP: linear polyphenylene; CPP: crosslinked polyphenylene.

[c] See Chart 2.

[d] See Chart 3.

[e] Isolated crude yield (>90% pure from 300 MHz $^1$H NMR and/or GLC) for entries 1–10 and isolated yield (>95% pure from 300 MHz $^1$H NMR and/or GLC) after column chromatography (silica gel, hexane/ethyl acetate) for entries 11–17, based on the starting material **1**; in square brackets, isolated yields corresponding to the reaction performed with the arene (naphthalene or DTBB) in solution.

[f] Literature reference for the same reaction using the arene catalyst in solution.

[g] Yield after reusing the same polymeric catalyst.

**2da–fe** were obtained after hydrolysis (Chart 3 and Table 1, entries 7–10). In this case we really do not know if dilithiated species **Id–f** are involved in the process (the process can also take place following a double sequence of lithiation–S$_E$-reaction), but at the end we can introduce as many electrophilic fragments as chlorine atoms are present in the starting material, giving the corresponding products **2da–fe**.

*Ring opening of benzofused cyclic ethers* such as phthalan (**1g**) and isochroman (**1h**) (Chart 1). The CPP-catalysed lithiation of these systems in THF at 0°C (for **1g**) or room temperature (for **1h**) give the corresponding intermediates **Ig**,**h** (Chart 2), which upon treatment with different electrophilic reagents [Et$_2$CO, (CH$_2$)$_5$CO, PhCHO, PhCOMe, Bu$^t$CHO] and final hydrolysis gave the expected compounds **2ga–hf** (Chart 3 and Table 1, entries 11–17).

Some general comments can be done from the results shown in Table 1. First of all, yields using LPP or CPP are comparable to the reaction carried out in solution (Table 1, footnotes e and f). Secondly, both catalysts (LPP and CPP) work with similar yields, being possible to reuse then in a second catalysed lithiation (Table 1, footnote g). One possible reason for the slight loose of catalyst activity can be attributed to the presence of the bromine atoms in the catalyst structure, which can give undesirable by-reactions (lithiation followed by S$_E$ or condensation reactions).[22] One general advantage of the procedure described here, common to the use of other insoluble polymer supported catalysts,[12] is that the catalyst can be easily removed at the end of the reaction by simple filtration. Finally, this is the first time wherein a polymeric electron transfer catalyst is used in the reductive opening of heterocyclic precursors.

## 3. Conclusion

From the results included in this paper we conclude than polyphenylene, either in a linear (LPP) or crosslinked (CPP) form, is an adequate electron transfer catalyst in lithiation reactions, both by chlorine–lithium exchange or by ring opening of oxygen-containing heterocycles, its efficiency being comparable to the reaction using an arene in catalytic amount but in solution or other polymer supported arene catalysts.

## 4. Experimental

### 4.1. General

For general information, see Ref. 23.

### 4.2. Preparation of linear (LPP) and crosslinked (CPP) polyphenylene[13]

To a suspension of magnesium (0.29 g, 12 mmol) in THF (2 mL) was added 1,2-dibromoethane (50 μL). Then, a solution of 1,4-dibromobenzene (2.95 g, 12 mmol) in THF (5 mL) was added and the resulting mixture was refluxed for 2 h. A solution of NiCl$_2$(PPh$_3$)$_2$ (10 mg) in THF (5 mL) was added dropwise and the polymerisation was completed after refluxing 1 h. The reaction mixture was hydrolysed with 2 M HCl (10 mL) and the precipitated polymer was collected over a glass filter and dried in vacuo to yield linear polyphenylene (LPP, 0.94 g) as a yellow powder.

Crosslinked polyphenylene (CPP, 1.07 g) was prepared as described above for LPP but adding 1,3,5-tribromobenzene

(0.193 g, 0.6 mmol) as crosslinking agent together with 1,4-dibromobenzene.

**4.2.1. Linear polyphenylene (LPP).** $\nu$ (KBr) 3026, 1585, 1479, 810 (C=C–H), 1072 cm$^{-1}$ (C–Br). HRMS (EI), Found: 76.0323 (1%), $C_6H_4^+$ requires 76.0313; 152.0618 (7%), $C_{12}H_8^+$ requires 152.0626; 230.9856 (15%), $C_{12}H_8Br^+$ requires 230.9808; 304.1247 (8%), $C_{24}H_{16}^+$ requires 304.1252. Anal. found: C, 60.60; H, 4.23; calcd for $(C_{24}H_{16}Br_2)_n$: C, 62.10; H, 3.45.

**4.2.2. Crosslinked polyphenylene (CPP).** $\nu$ (KBr) 3027, 1592, 1479, 807 (C=C–H), 1074 cm$^{-1}$ (C–Br). HRMS (EI), Found: 152.0601 (45%), $C_{12}H_8^+$ requires 152.0626; 226.0804 (42%), $C_{18}H_{10}^+$ requires 226.0783; 228.0956 (34%), $C_{18}H_{12}^+$ requires 228.0939; 230.9856 (34%), $C_{12}H_8Br^+$ requires 230.9808; 300.0912 (33%), $C_{24}H_{12}^+$ requires 300.0939; 380.1599 (7%), $C_{30}H_{20}^+$ requires 380.1565; 461.9640 (100%), $C_{24}H_{16}Br_2^+$ requires 461.9619. Anal. found: C, 80.77; H, 4.84; calcd for $(C_{72}H_{48}Br_2)_n$: C, 80.61; H, 4.48.

### 4.3. LPP- or CPP-catalysed lithiation of starting materials 1. Isolation of compounds 2

*Two-step preparation of compounds* **2aa**–**cd**,**2ga**–**gf**,**2hb**,**hf**: *general procedure*. To a suspension of lithium powder (0.125 g, 18 mmol) and the corresponding polymer, LPP or CPP (30 mg), in THF (4 mL) was added 2 mmol of the corresponding starting material at different temperatures [−78°C (**1a**–**c**), 0°C (**1g**) and 20°C (**1h**)] and the mixture was stirred for 1 h at the same temperature. Then, the corresponding electrophile (2.2 mmol) was added at −78°C, the mixture was stirred 1 h at the same temperature and hydrolysed with water (5 mL). The polymer was filtered off and the solution neutralised with 2 M HCl and extracted with ethyl acetate (3×10 mL). The organic layer was dried over anhydrous $Na_2SO_4$ and evaporated at reduced pressure (15 Torr) to obtain the expected products with the yields indicated in Table 1. Compounds **2aa**,**ab**,[15] **2bb**,**bc**,[16] **2cc**,**cd**,[17] **2ga**–**gf**,[20] and **2hb**,**hf**,[21] previously prepared in our laboratory, were identified by comparison of their spectroscopic data with authentic samples.

*Preparation of compounds* **2da**–**fe** *under Barbier-type reaction conditions*: *general procedure*. To a suspension of lithium powder (0.125 g, 18 mmol) and the corresponding polymer, LPP or CPP (30 mg), in THF (4 mL) was added a solution of the corresponding electrophile (2.2 mmol) and the dichlorinated starting material **1d**–**f** (1 mmol) at −78°C and the resulting mixture was stirred allowing the temperature to rise to 20°C. Then, it was hydrolysed and worked up, as it was described above for the two-step procedure, to obtain the expected products with the yields indicated in Table 1. Compounds **2da**,**db**,[18] and **2ee**,**fe**,[19] previously prepared in our laboratory, were identified by comparison of their spectroscopic data with authentic samples.

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