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Polymer Supported Arene-Catalysed Lithiation Reactions[†]

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Abstract

The reaction of functionalised mono or dichlorinated materials **1a-6a** with an excess of lithium and a catalytic amount of a naphthalene (P_N) or biphenyl (P_B) supported polymer (eassily prepared by radical copolymerisation of 2-vinylnaphthalene or 4-vinylbiphenyl with vinylbenzene and divinylbenzene) in THF either in the presence or not of different electrophiles [Me_3SiCl, ^iPrCHO, PhCHO, Et_2CO, $(CH_2)_4CO$, $(CH_2)_5CO$, $(c\text{-}C_3H_5)_2CO$, $^iPr_2CO$, PhCOMe, PhCH=NPh] at -78 or -50°C leads, after hydrolysis with water, to the expected functionalised products **1ca-6ck**. The polymeric catalyst is quantitatively recovered and can reused several times without any loss of activity.

Keywords: lithiation; catalysis; lithium and compounds; polymers

I. Introduction

The most common methodology for the preparation of organolithium compounds [1] involves lithium metal and a halogenated compound. In general, this procedure does not need any activation of the metal unless the lithiation has to be performed at low temperatures. Thus, when unstable organolithium intermediates [2-6][1] have to be prepared at -78°C or even below, it is necessary to use a solution of stoichiometric amounts of lithium and an arene (the so called lithium-arene or lithium arenide [7-9]) in tetrahydrofuran in order to get effective halogen-lithium exchange. Recently, we were able to improve the former procedure by using a catalytic amount (<10%) of the arene, naphthalene and 4,4'-di-

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[†] This paper is dedicated to the memory of Prof. Joaquin de Pascual Teresa.

[1] This is the case of functionalised organolithium compounds [2,3] or polylithiated synthons [4]. For the last paper on these topics from our laboratory, see references [5] and [6], respectively.

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tert-butylbiphenyl (DTBB) being the most commonly used [10] [11].[2] This version is not only interesting because it is not necessary to remove a large amount of the arene during the work-up, but also because this mixture is more active than the corresponding stoichiometric one. For instance, using the above mentioned arene-catalysed lithiation, it is possible to generate organolithium reagents starting from non-halogenated materials [12,13][3] and heterocyclic compounds [5,14], these processes being in general not realizable using the stoichiometric version. The ideal situation, using a catalytic amount of the arene for the lithiation reaction, would be the use of a polymer supported arene, which could be filtered at the end of the process without contaminating the final product with the electron carrier. In this paper we report the preparation and use of such as polymeric catalyst for the generation of very reactive organolithium intermediates [15] [16].[4]

II. Results and discussion

The preparation of the polymers containing naphthalene (P_N) and biphenyl (P_B) was carried out using the Itsuno methodology [17] to give cross-coupling polymers. Thus, a solution of 2-vinylnaphthalene (VNP) or 4-vinylbiphenyl (VBP) (1 mmol scale), vinylbenzene (VBZ) and divinylbenzene (DVB) (for molar ratios, see Scheme 1) in a mixture of benzene and tetrahydrofuran containing a catalytic amount of azoisobutyronitrile (AIBN, 30 mol %) was treated with a solution of poly(vinyl alcohol) in water and the mixture was heated at reflux to give the corresponding polymeric catalyst P_N or P_B, respectively (Scheme 1). A different type of polymerisation to give P'_B-9·0·1 was performed by refluxing VNP and DVB in tetrahydrofuran in the presence of a catalytic amount of AIBN.

The reaction of the functionalised chlorinated materials **1a**-**3a** with an excess of lithium powder and a catalytic amount of the corresponding polymer (*ca.* 10 mol %)[5] in tetrahydrofuran at -78°C for 1 h led to a solution of the corresponding lithium intermediates **1b**-**3b**, which upon treatment with different electrophiles [^{i}PrCHO, PhCHO, Et_2CO, $(CH_2)_4CO$, $(CH_2)_5CO$, $^iPr_2CO$, PhCOMe, PhCH=NPh] at temperatures ranging between -78 and 20°C led, after hydrolysis with water, to the expected products **1c**-**3c** (Chart 1 and Table 1). At the end of the work-up the solid polymer was filtered off, washed and dried, being quantitatively recovered and reused two or three times without apparent loss of efficiency (Table 1, entries 7, 23, 25, 28, 29, 41 and 49, and footnote d).

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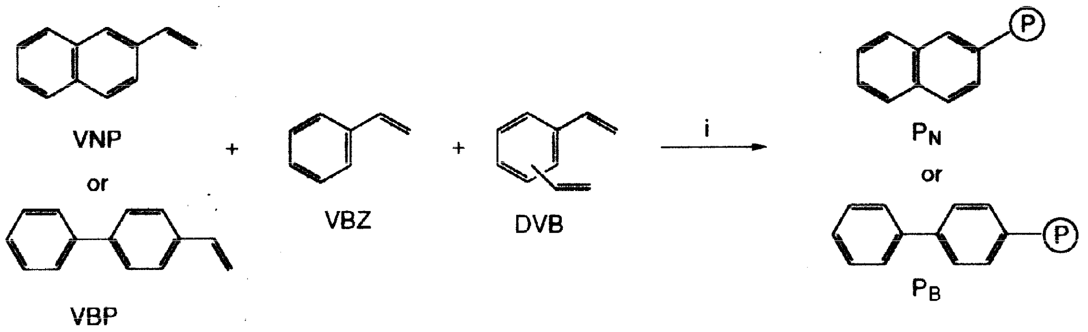
[2] For the first account on this methodology and a recent review, see references [10] and [11], respectively.

[3] For the last paper on this topic from our laboratory and a recent review see, respectively, the corresponding references indicated in the text.

[4] For a preliminary communication, see reference [15]. For a recent account on the use of a polymer supported lithium naphthalenide with a silicon mediated junction between the arene and the polymeric structure, see reference [16]; in this case a drawback of the starting polymer is that it does not react with lithium powder, necessitating use of lithium biphenyl as lithiating agent and also that the polymer has to be used in stoichiometric amounts.

[5] This percent is calculated from the relative molar proportions of VNP or VBP in the polymer considering that the stoichiometric amount would need 2 eq of the arene per chlorine atom in the starting material **1a**-**3a** according to the equation:

$$RCl + 2\,LiArH \rightarrow RLi + LiCl + 2\,ArH$$



VNP or VBP	VBZ	DVB	P
1	5	2	P-1·5·2
19	0	1	P-19·0·1
9	0	1	P'-9·0·1

Scheme 1. *Reagents and conditions*: i, AIBN, THF, PhH, poly(vinyl alcohol), H_2O, for polymer P or AIBN, THF for P'.

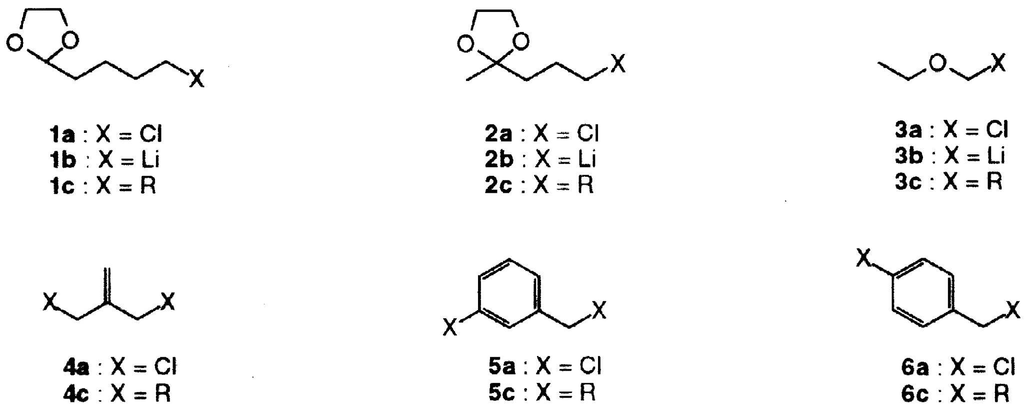


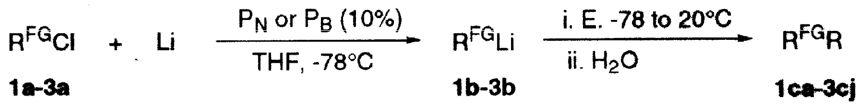
Chart 1.

From the results summarised in Table 1 can be deduced the following conclusions:

(1) In general, yields are higher using polymeric catalysts in the case of starting materials **1a** and **2a**, compared to the same reactions performed in solution (Table 1, entries 1, 5, 9, 13, 21, 25, 28 and 32) using catalytic (Table 1, footnotes c and f) or stoichiometric (Table 1, footnote e) amounts of the arene.

(2) In the case of the starting material **3a**, the yields are higher working in solution than with the polymeric catalyst, either working in a two-step process (Table 1, entries 43, 47 and 49, and footnote h) or under Barbier-type conditions (Table 1, entries 40, 41 and 45, and footnote g).

Table 1
Polymer supported arene-catalysed lithiations in a two-step process



$$\underset{\textbf{1a-3a}}{R^{FG}Cl} + Li \xrightarrow[\text{THF, -78°C}]{P_N \text{ or } P_B \text{ (10\%)}} \underset{\textbf{1b-3b}}{R^{FG}Li} \xrightarrow[\text{ii. } H_2O]{\text{i. E. -78 to 20°C}} \underset{\textbf{1ca-3cj}}{R^{FG}R}$$

Entry	Starting material	Catalyst	Intermediate	Electrophile E	Product[a] No.	Product[a] R	Product[a] Yield (%)[b]
1	**1a**	P_N-1·5·2	**1b**	^{i}PrCHO	**1ca**	^{i}PrCHOH	52 (62)[c]
2		P_B-1·5·2					70
3		P_N-19·0·1					79
4		P'_B-9·0·1					63
5	**1a**	P_N-1·5·2	**1b**	PhCHO	**1cc**	PhCHOH	85 (52)[c]
6		P_B-1·5·2					91
7		P_N-19·0·1					66[d]
8		P'_B-9·0·1					75
9	**1a**	P_N-1·5·2	**1b**	Et_2CO	**1cd**	Et_2COH	66 (46)[c]
10		P_B-1·5·2					66
11		P_N-19·0·1					64
12		P_B-19·0·1					99
13	**1a**	P_N-1·5·2	**1b**	$(CH_2)_5CO$	**1cg**	$(CH_2)_5COH$	90 (79)[c]
14		P_B-1·5·2					73
15		P_N-19·0·1					92
16		P'_B-9·0·1					88
17	**1a**	P_N-1·5·2	**1b**	$^iPr_2CO$	**1ch**	$^iPr_2COH$	70
18		P_B-1·5·2					67
19		P_N-19·0·1					65
20		P_B-19·0·1					90
21	**1a**	P_N-1·5·2	**1b**	PhCOMe	**1ci**	PhC(OH)Me	83 (44)[c]
22		P_B-1·5·2					87
23		P_N-19·0·1					67[d]
24		P_B-19·0·1					93
25	**2a**	P_N-1·5·2	**2b**	^{i}PrCHO	**2ca**	^{i}PrCHOH	41[d] (52)[e]
26		P_N-19·0·1					62
27		P_B-19·0·1					60

Table 1 (cont.)

28	**2a**	P_{N}-1·5·2	**2b**	PhCHO	**2cc**	PhCHOH	49^{d} (51)^{e}
29		P_{B}-1·5·2					57^{d}
30		P_{N}-19·0·1					92
31		P_{B}-19·0·1					84
32	**2a**	P_{N}-1·5·2	**2b**	$(CH_2)_5CO$	**2cg**	$(CH_2)_5COH$	64 (60-72)^{f}
33		P_{B}-1·5·2					83
34		P_{N}-19·0·1					87
35		P_{B}-19·0·1					62
36	**2a**	P_{N}-1·5·2	**2b**	$^{i}Pr_2CO$	**2ch**	$^{i}Pr_2COH$	87
37		P_{B}-1·5·2					60
38		P_{N}-19·0·1					78
39		P_{B}-19·0·1					64
40	**3a**	P_{N}-1·5·2	**3b**	^{n}BuCHO	**3cb**	^{n}BurCHOH	59 (87)^{g}
41	**3a**	P_{N}-1·5·2	**3b**	PhCHO	**3cc**	PhCHOH	66^{d} (84)^{g}
42		P_{B}-19·0·1					81
43	**3a**	P_{N}-1·5·2	**3b**	$(CH_2)_4CO$	**3cf**	$(CH_2)_4COH$	78 (90)^{h}
44		P_{B}-19·0·1					73
45	**3a**	P_{N}-1·5·2	**3b**	$^{i}Pr_2CO$	**3ch**	$^{i}Pr_2COH$	69 (75)^{g}
46		P_{B}-19·0·1					48
47	**3a**	P_{N}-1·5·2	**3b**	PhCOMe	**3ci**	PhC(OH)Me	79 (91)^{h}
48		P_{B}-19·0·1					65
49	**3a**	P_{N}-1·5·2	**3b**	PhCH=NPh	**3cj**	PhCHNHPh	58^{d} (85)^{h}

[a] All products **1ca-3cj** were 90-95% pure (GLC and/or 300 MHz ^{1}H NMR).

[b] Isolated crude yield based on the starting material **1a-3a**.

[c] Yield corresponding to the same reaction using naphthalene (8 mol %) as the electron carrier catalyst (reference [18]).

[d] The catalyst was reused twice.

[e] Yield corresponding to the same reaction using a stoichiometric amount of naphthalene as the electron carrier catalyst (reference [19]).

[f] Yields corresponding to the same reaction using naphthalene (1-20 mol %) as the electron carrier catalyst (reference [10]).

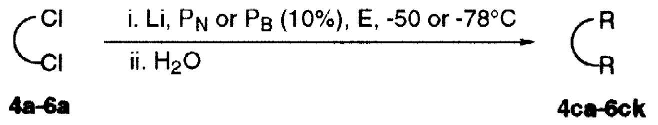
[g] Yield corresponding to the same reaction using DTBB (5 mol %) as the electron carrier catalyst, but under Barbier-type reaction conditions (reference [20]).

[h] Yield corresponding to the same reaction using DTBB (5 mol %) as the electron carrier catalyst (reference [20]).

(3) Although difficult to generalise, because all assayed polymers worked nicely, we observed that polymers P-19·0·1 worked better than P-1·5·2, especially P_{B}-19·0·1 (compare, for instance, in Table 1 entries 12, 20, 24, 27 and 31). On the other hand, polymer P'_{B}-9·0·1, more easily to be prepared than the other polymers of series P, can also be used with similar results (Table 1, entries 4, 8 and 16).

In the second part of this study we apply the use of an arene-containing polymer catalyst to carry out lithiations under Barbier-type reaction conditions (lithiation in the presence of the electrophile) [22,23]. This variant is particulary interesting when the intermediates are too unstable to be able to survive under the conditions of the two-step process (Table 1). This is the case with polylithiated synthons [4], which can be generated by lithiation of the corresponding polychlorinated materials. Thus, treatment of compounds **4a**-**6a** under the above mentioned conditions (-78°C for **4a** and -50°C for **5a** and **6a**), but in the presence of the electrophile [Me_3SiCl, ^iPrCHO, Et_2CO, $(c\text{-}C_3H_5)_2CO$, $(CH_2)_4CO$, $(CH_2)_5CO$, $^iPr_2CO$], lithium and the polymer catalyst (10 mol %)[5] led, after hydrolysis with water, to the expected products **4c**-**6c** (Chart 1 and Table 2).

Table 2
Polymer supported arene-catalysed lithiations under Barbier-type reaction conditions



Entry	Starting material	Catalyst	Electrophile E	Product[a]		
				No.	R	Yield (%)[b]
1	**4a**	P_N-1·5·2	^iPrCHO	**4ca**	^iPrCHOH	56[c] (64)[d]
2		P_B-1·5·2				76[c]
3		P_N-19·0·1				49[c]
4		P_B-19·0·1				47[c]
5	**4a**	P_N-1·5·2	Et_2CO	**4cd**	Et_2COH	82[e] (72)[d]
6		P_B-1·5·2				77
7		P_N-19·0·1				89[f]
8		P_B-19·0·1				93
9	**4a**	P_N-1·5·2	$(c\text{-}C_3H_5)_2CO$	**4ce**	$(c\text{-}C_3H_5)_2COH$	76[f] (81)[d]
10		P_B-1·5·2				79
11		P_N-19·0·1				89
12		P_B-19·0·1				76
13	**4a**	P_N-1·5·2	$(CH_2)_4CO$	**4cf**	$(CH_2)_4COH$	69 (79)[g] (89)[d]
14		P_B-1·5·2				91
15		P_N-19·0·1				92
16		P_B-19·0·1				50

Table 2 (cont.)

17	**4a**	P_N-1·5·2	$(CH_2)_5CO$	**4cg**	$(CH_2)_5COH$	96 (67)[d]
18		P_B-1·5·2				67
19		P_N-19·0·1				92
20		P_B-19·0·1				96
21	**4a**	P_N-1·5·2	$^iPr_2CO$	**4ch**	$^iPr_2COH$	94 (75)[d]
22		P_B-1·5·2				81
23		P_N-19·0·1				99
24		P_B-19·0·1				99
25	**5a**	P_N-1·5·2	Me_3SiCl	**5ck**	Me_3Si	70 (78)[h]
26		P_B-1·5·2				85
27		P_N-19·0·1				82
28		P_B-19·0·1				97
29	**6a**	P_N-1·5·2	Me_3SiCl	**6ck**	Me_3Si	98 (83)[h]
30		P_B-1·5·2				82
31		P_N-19·0·1				88
32		P_B-19·0·1				99

[a] All products **4ca-6ck** were >90% pure (GLC and/or 300 MHz ^1H NMR).

[b] Isolated crude yield based on the starting material **4a-6a**.

[c] *ca.* 1:1 Mixture of diastereoisomers (300 MHz ^1H NMR).

[d] Yield of the same reaction using naphthalene (6 mol %) as the electron carrier catalyst under Barbier-type reaction conditions (reference [21]).

[e] The catalyst was reused four times.

[f] The catalyst was reused three times.

[g] The catalyst was reused twice.

[h] Yield of the same reaction using DTBB (4 mol %) as the electron carrier catalyst uner Barbier-type reaction conditions (reference [6).

Also in the case of the results included in Table 2, the catalyst could be recovered quantitatively at the end of the reaction and reused two, three or four times (Table 2, entries 5, 7, 9 and 13) without appreciable loss of activity, according to the yields obtained. Looking at the results of Table 2 it can be concluded that in general the yields observed for the process in solution or under solid phase conditions are of the same order. In this case the main advantage of the heterogeneous reactions is the easy removal of the electron transfer catalyst at the end of the reaction.

III. Conclusion

As a conclusion, we present in this paper a new type of electron transfer reagent based on arene supported polymers, which work nicely in lithiation reactions under very mild reaction conditions, in two-step processes or under Barbier-type conditions, giving very reactive functionalised organolithium compounds or dilithiated synthons, interesting intermediates for the direct synthesis of polyfunctionalised molecules.

IV. Experimental section

IV.1. General

For general information see reference [24]. Retention times (t_r) were measured with a Hewlet Packard HP-5890 instrument equipped with a flame ionisation detector and a 12 m capillary column (0.2 mm diam, 0.33 mm film thickness), using nitrogen (2 mL/min) as carrrier gas under the following conditions: $T_{injector}$ = 275°C, T_{column} = 60°C (3 min) and 60-270°C (15°C/min). Monomers VBZ, DVB (80% mixture of isomers), VNP and VBP (Aldrich), as well as AIBN (Fluka), poly(vinyl alcohol) (98-99% hydrolysed; Average M_w 85,000-146,000) and the electrophiles (Aldrich) were commercially available and used without any further purification except in the case of monomer DVB, which was successively washed twice with a 1% aqueous solution of sodium hydroxide and then with water in order to remove the stabiliser (see reference [25]).

IV.2. Preparation of polymeric catalysts P_N and P_B. General procedure [17,25] .- Poly(vinyl alcohol (80 mg for P-1·5·2 or 54 mg for P-19·0·1) was dissolved in water (20 mL for P- 1·5·2 or 14 mL for P-19·0·1), heated at 40°C for 30 min and filtered. The resulting solution was mixed with another solution of VNP or VBP (1 mmol scale), VBZ, DVB (for the corresponding proportions see Scheme 1) and AIBN (50 mg, 0.3 mmol) in a mixture of benzene (5 mL) and THF (1.5 mL) and it was heated at 80°C under an argon atmosphere for *ca.* 36 h. The resulting suspension was filtered and the solid obtained was successively washed with methanol, water, THF and ether (2 x 2 mL in each case) and dried under vacuum (1 Torr) to give the title polymers in practically quantitative yield.

P_N-1·5·2: pale yellow solid [Found: C, 90.3; H, 7.8. $(C_{12}H_{10})\cdot(C_8H_8)_5\cdot(C_{10}H_{10})_2$ requieres C, 92.5; H, 7.5].

P_B-1·5·2: pale yellow solid [Found: C, 91.5; H, 7.7. $(C_{14}H_{12})\cdot(C_8H_8)_5\cdot(C_{10}H_{10})_2$ requieres C, 92.5; H, 7.5].

P_N-19·0·1: pale yellow solid [Found: C, 89.2; H, 7.0. $(C_{12}H_{10})_{19}\cdot(C_{10}H_{10})$ requieres C, 93.4; H, 6.6].

P_B-19·0·1: pale yellow solid [Found: C, 90.7; H, 7.3. $(C_{14}H_{12})_{19}\cdot(C_{10}H_{10})$ requieres C, 93.3; H, 6.7].

IV.3. Preparation of polymeric catalyst P'-9·0·1 [26].- A solution of VBP (720 mg, 4 mol), DVB (71 µm, 0.4 mmol) and AIBN (75 mg, 0.45 mmol) in THF (5 mL) was refluxed for 6 h under an argon atmosphere. After cooling at room temperature the resulting suspension was worked up as described above for polymeric catalysts P_N and P_B to give the title product in quantitative yield: pale yellow solid [Found: C, 90.9; H, 6.7. $(C_{14}H_{12})_9{\cdot}(C_{10}H_{10})$ requieres C, 93.2; H, 6.8].

IV.4. Two-step preparation of compounds **1ca-3cj**. *General procedure*.- To a suspension of lithium powder (112 mg, 16 mmol) and the corresponding polymer (0.2 mmol; 10 mol %) in THF (5 mL) was added the starting material **1a-3a** at -78°C and the mixture was stirred for 1 h at the same temperature. Then, the corresponding electrophile (2.2 mmol) was added and the resulting mixture was stirred overnight allowing the temperature to rise to 20°C. The resulting mixture was hydrolysed with water (10 mL), the polymer was filtered off, washed and dried as described above (section IV.2), and the solution neutralised with 2M HCl and extracted with ethyl acetate (3 x 10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated at reduced pressure (15 Torr) to give a residue, which contained essentially pure title compounds (90-95%) but could be purified by column chromatography (silica gel, hexane/ethyl acetate). Yields are included in Table 1. Compounds **1ca** [18], **1cc** [18], **1cd** [18], **1cg** [18], **1ci** [18], **2ca** [19], **2cc** [19], **2cg** [10], **3cb** [20], **3cc** [20], **3cf** [20], **3ch** [20], **3ci** [20] and **3cj** [20] were characterised by comparison of their physical (GLC) and spectroscopic data (NMR) with authentic samples prepared by us [10,18-20].

2-(5-Hydroxy-5-isopropyl-6-methylheptyl)-1,3-dioxolane (1ch): colourless oil; t_r 12.59 min; R_f 0.54 (hexane/ethyl acetate: 3/2); ν (liquid film) 3220 (OH), 1190, 1140 cm^{-1} (C-O); δ_H (300 MHz $CDCl_3$) 0.91, 0.94 (12 H, 2 d, *J* 6.7 Hz, $\underline{Me}_2CH$), 1.35-1.45, 1.46-1.56 [7 H, 2 m, $(C\underline{H}_2)_3CO\underline{H}$], 1.64-1.71 (2 H, m, $C\underline{H}_2CO_2$), 1.83-1.97 (2 H, septet, *J* 6.7 Hz, $Me_2C\underline{H}$), 3.79-4.01 (4 H, 2 m, $OC\underline{H}_2C\underline{H}_2O$), 4.85 (1 H, t, *J* 4.6 Hz, $OC\underline{H}O$); δ_C (75 MHz $CDCl_3$) 17.2 (2 C), 17.5 (2 C), 24.2, 21.5, 33.7 (2 C), 33.9 (2 C), 64.8 (2 C), 77.1, 104.5; *m/z* (EI) 226 (M^+ - H_2O, <1), 115 (14), 99 (11), 95 (12), 81 (10), 73 (100), 71 (72), 69 (48), 67 (20), 57 (26), 55 (42), 45 (63), 44 (10), 43 (97), 42 (10), 41 (55%); HRMS (EI): M^+, found 226.1912. $C_{14}H_{26}O_2$ requires 226.1933.

2-(4-Hydroxy-4-isopropyl-5-methylhexyl)-2-methyl-1,3-dioxolane (2ch): colourless oil; t_r 11.76 min; R_f 0.54 (hexane/ethyl acetate: 3/2); ν (liquid film) 3220 (OH), 1196 cm^{-1} (C-O); δ_H (300 MHz $CDCl_3$) 0.93. 0.95 (12 H, 2 d, *J* 7.2 Hz, $\underline{Me}_2CH$), 1.26-1.52, 1.59-1.64 [5 H, 2 m, $(C\underline{H}_2)_2CO\underline{H}$], 1.31 (3 H, s, $\underline{Me}$), 1.58-1.65 (2 H, m, $C\underline{H}_2CO_2$), 1.92 (2 H, septet, *J* 7.0, $Me_2C\underline{H}$), 3.91-3-95 (4 H, m, $OC\underline{H}_2C\underline{H}_2O$); δ_C (75 MHz $CDCl_3$) 17.0 (2 C), 17.3 (2 C), 18.4, 23.4, 33.6, 33.7 (2 C), 39.8, 64.2 (2 C), 77.2, 109.6; *m/z* (EI) 226 (M^+ - H_2O, 1), 139 (13), 124 (33), 109 (36), 99 (19), 97 (28), 95 (15), 87 (84), 83 (10), 81 (14), 71 (41), 69 (33), 67 (14), 59 (18), 57 (11), 55 (34), 53 (10), 45 (12), 44 (11), 43 (100), 42 (10%); HRMS (EI): M^+, found 226.1914. $C_{14}H_{26}O_2$ requires 226.1933.

IV.5. Preparation of compounds **4ca-6ck** *under Barbier-type reaction conditions. General procedure.*- To a suspension of lithium powder (112 mg, 16 mmol) and the corresponding polymer (0.2 mmol, 10 mol %) in THF (5 mL) was added a solution of the electrophile (2.2 mmol) and the dichlorinated starting material **4a-6a** (1 mmol) at -78°C and the resulting mixture was stirred overnight allowing the temperature to rise to 20°C. Then it was hydrolysed and worked up as was described above for compounds**1ab-3cj** (section IV.4) to afford the expected compounds **4ca-6ak**. Yields are included in Table 2. Compounds **4ca** [21], **4cd** [21], **4ce** [21], **4cf** [21], **4cg** [21], **4ch** [21], **5ck** [6], **6ck** [6] were characterised by comparison of their physical (GLC) and spectroscopic data (NMR) with authentic samples prepared by us [6,21].

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VI. References

[1] Wakefield BJ. Organolithium Methods. London: Academic Press, 1988.
[2] Nájera C, Yus M. Trendes Org. Chem. 1991;2:155-181.
[3] Nájera C, Yus M. Recent Res. Devel. Org. Chem. 1997;1:67-96.
[4] Foubelo F, Yus M. Trends Org. Chem. 1998;7:1-26.
[5] Soler T, Bachki A, Falvello LR, Foubelo F, Yus M. Tetrahedron:Asymmetry 1998;9:3939-3943.
[6] Gómez C, Huerta FF, Yus M. Tetrahedron 1998;54:1853-1866.
[7] Holy NL. Chem. Rev. 1974;74:243-277.
[8] Screttas CG, Micha-Screttas M. J. Org. Chem. 1978;43:1064-1071.
[9] Cohen T, Bhupathy M. Acc. Chem. Res. 1989;22:152-161.
[10] Yus M, Ramón DJ. J. Chem. Soc., Chem. Commun. 1991:398-400.
[11] Yus M. Chem. Soc. Rev. 1997:155-161.
[12] Bachki A, Foubelo F, Yus M. Tetrahedron Lett. 1998;39:7759-7762.
[13] Guijarro D, Yus M. Recent Res. Devel. Org. Chem., in press.
[14] Yus M, Foubelo F. Rev. Heteroatom Chem 1997;17:73-107.
[15] Gómez C, Ruiz S, Yus M. Tetrahedron Lett. 1998;39:1397-1400.
[16] van der Ancker TR, Hanson GR, Lee F-C, Raston CL. J. Chem. Soc., Chem. Commun. 1997:125-126.
[17] Itsuno S, Sakurai Y, Ito K, Murayama T, Nakahama S, Fréchet JMJ. J. Org. Chem. 1990;55:304-310.
[18] Gil JF, Ramón DJ, Yus M. Tetrahedron 1993;49:4923-4938.
[19] Ramón DJ, Yus M. J. Org. Chem. 1991;56:3825-3831.
[20] Guijarro A, Mancheño B, Ortiz J, Yus M. Tetrahedron 1996;52:1643-1650.
[21] Gómez C, Ramón DJ, Yus M. Tetrahedron 1993;49:4117-4126.
[22] Blomberg C. The Barbier Reaction and Related One-Step Processes. Berlin: Springer Verlag, 1993.
[23] Alonso F, Yus M. Recent Res. Devel. Org. Chem. 1997;1:397-436.
[24] Choudhury PK, Almena J, Foubelo F, Yus M. Tetrahedron 1997;53:17373-17382.
[25] Seebach D, Marti RE, Hintermann T. Helv. Chim. Acta 1996;79:1710-1740.
[26] Calmes M, Daunis J, Ismaili H, Jacquer R, Koudou J, Nkusi G, Zouanato A. Tetrahedron 1990;46:6021-6032.