

# Selective catalytic carbanionic ethylation of methylphenols: influence of catalyst and substitution pattern

Barry R. Steele,\* Carolina Villalonga-Barber, Maria Micha-Screttas and Constantinos G. Screttas

*Institute of Organic and Pharmaceutical Chemistry, National Hellenic Research Foundation, Vas. Constantinou Ave. 48, Athens 116 35, Greece*

Received 22 December 2005; revised 19 January 2006; accepted 26 January 2006

**Abstract**—Addition of ethylene to the carbanions formed by the metallation of the lithium salts of di- and trimethylphenols by the strongly basic system, *n*-BuLi–LiK(OCH<sub>2</sub>CH<sub>2</sub>NMe<sub>2</sub>)<sub>2</sub> provides a useful synthetic route to a range of alkylphenols. The ease of alkylation of the methyl groups decreases in the order *ortho*>*meta*>*para* while the inclusion of Mg(OCH<sub>2</sub>CH<sub>2</sub>OEt)<sub>2</sub> in the catalyst restricts alkylation to the methyl groups *ortho* to the hydroxy group. Dialkylation occurs only at the *ortho*-methyl groups and only if the adjacent *meta*-position is unsubstituted. The potential of these products for the synthesis of sterically hindered ligands is outlined.

© 2006 Elsevier Ltd. All rights reserved.

## 1. Introduction

Bulky aromatic molecules are of interest in view of the possibility they offer for the stabilisation of low oxidation states and unsaturated compounds, as well as for the construction of sterically demanding ligands, which in recent years have played an important role in coordination chemistry and homogeneous catalysis.<sup>1</sup> Metal complexes with bulky phenoxide and anilide substituents, and imine ligands derived from bulky aniline or salicylaldehyde derivatives feature prominently in these areas.<sup>2</sup> These molecules also have potential applications in other areas of chemistry, not only because of their bulk but by virtue of the highly enhanced lipophilicity which they are able to confer. We have reported a method for the facile preparation of a series of bulky aromatic hydrocarbons containing 1-ethylpropyl substituents,<sup>3</sup> and we are now studying the synthesis and properties of their functionalised derivatives.<sup>4,5</sup> Here we describe a particularly simple preparation of some sterically hindered phenols.

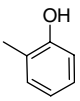
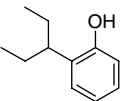
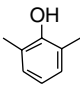
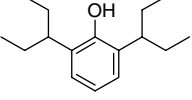
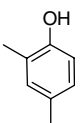
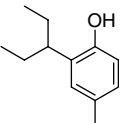
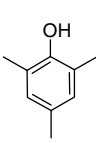
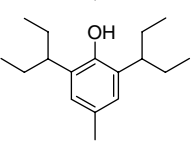
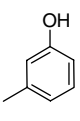
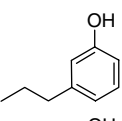
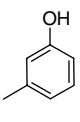
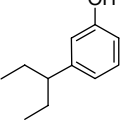
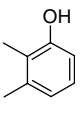
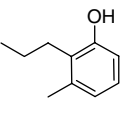
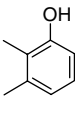
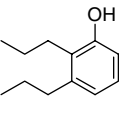
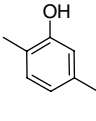
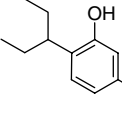
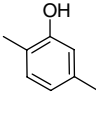
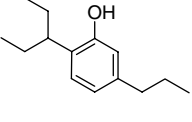
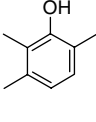
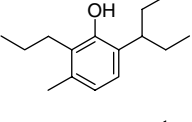

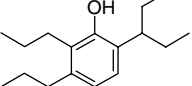
## 2. Results and discussion

The preparative route used is similar to that previously reported for hydrocarbons although there are some significant differences in reactivity and this is reflected in the range of products obtained. Phenols containing *ortho*-methyl groups, after initially having been converted to their lithium salts, are readily metallated in methylcyclohexane by the strongly basic reagent derived from *n*-butyllithium and the mixed alkoxide, lithium–potassium bis(2-dimethylaminoethanolate),<sup>6</sup> and subsequent reaction with ethylene gives rise to the products summarised in Table 1. In the presence of Mg(OCH<sub>2</sub>CH<sub>2</sub>OEt)<sub>2</sub>, the metallated products readily add one or two molecules of ethylene at the *ortho*-benzylic position to give the corresponding *o*-propyl or *o*-1-ethylpropyl derivatives (compounds **1–4**, **7**, **9** and **11**). Addition of two molecules of ethylene to the *ortho*-methyl groups occurs (compounds **1–4** and **9**) unless this group is flanked by another methyl group as well as by the OH group (Eqs. 1 and 2). In the latter cases, spectroscopic analysis of the products indicated that monoethylation at the hindered *ortho*-position occurs (compounds **9** and **11**) and this resembles the similar behaviour that was observed for the hydrocarbon series for the addition of ethylene to methyl groups flanked on both sides by other methyl groups.<sup>3</sup> Steric factors would seem to be the reason for this, the phenolates possibly existing as

**Keywords:** Bulky aromatic; Organolithium; Phenol; Superbase; Metallation; Carbometallation; Schiff base; Catalysis; Lipophilic.

\* Corresponding author. Tel.: +30 210 7273873; fax: +30 210 7273877; e-mail: [bsteale@cie.gr](mailto:bsteale@cie.gr)

**Table 1.** Major products from reactions of metallated phenols with ethylene

	Additive <sup>a</sup>	Major product	Yield (%) <sup>c</sup>
	Yes		<b>1</b> <sup>b</sup> 65
	Yes		<b>2</b> 70
	Yes		<b>3</b> <sup>b</sup> 72
	Yes		<b>4</b> 65
	Yes		<b>5</b> <sup>b</sup> 50
	No		<b>6</b> <sup>b</sup> 35 <sup>d</sup>
	Yes		<b>7</b> <sup>b</sup> 79
	No		<b>8</b> <sup>b</sup> 61
	Yes		<b>9</b> 48
	No		<b>10</b> 55
	Yes		<b>11</b> 62 <sup>e</sup>
	No		<b>12</b> 63 <sup>e</sup>

<sup>a</sup> Indicates whether or not Mg(OCH<sub>2</sub>CH<sub>2</sub>OEt)<sub>2</sub> is added to the reaction mixture.

<sup>b</sup> The following compounds have been previously reported (CAS RN in parentheses): **1** (80751-97-9),<sup>7</sup> **3** (96558-48-4),<sup>8</sup> **5** (621-27-2),<sup>9</sup> **6** (97218-43-4),<sup>10</sup> **7** (66142-79-8),<sup>11</sup> **8** (863418-21-7).<sup>12</sup>

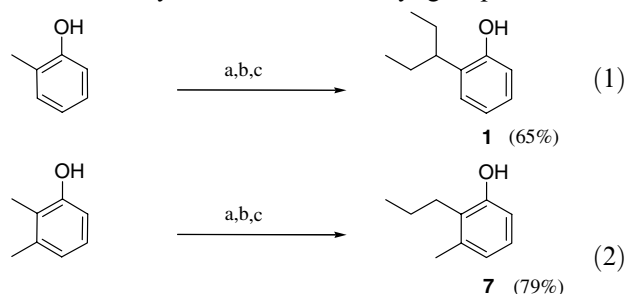
<sup>c</sup> Yield of isolated product unless noted otherwise.

<sup>d</sup> **5** also produced (44% yield).

<sup>e</sup> Yields calculated from GC analysis of product mixtures obtained after vacuum distillation.

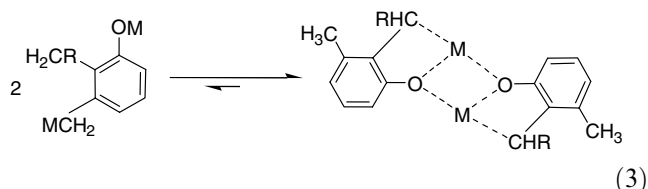
oligomeric rather than monomeric species or as mixed aryl-/alkoxide aggregates with the other components of the reaction mixture.

Addition to methyl groups in *meta* or *para* positions occurs only to a minor extent, if at all, when this reaction is carried out in the presence of Mg(OCH<sub>2</sub>CH<sub>2</sub>OEt)<sub>2</sub> (compounds **5**, **7**, **9** and **11**). GC/MS analysis of the products from prolonged reaction times at elevated temperatures indicated only the probable presence of some monoethylation of *meta*-methyl groups.



a) 1 eq. *n*-BuLi; b) 10 mol% *n*-BuLi / LiK(OCH<sub>2</sub>CH<sub>2</sub>NMe<sub>2</sub>)<sub>2</sub>, 2.5 mol% Mg(OCH<sub>2</sub>CH<sub>2</sub>OEt)<sub>2</sub>, 10 atm. C<sub>2</sub>H<sub>4</sub>, 80 °C, 24 h; c) H<sup>+</sup>/H<sub>2</sub>O

The metallation of benzylic protons in a position *para* to an electron donating group has been studied by others. For example, while the *para*-methyl group of *N,N*-4-trimethylaniline can be metallated using *n*-BuLi/KOBu-*t* in THF at -75 °C,<sup>13</sup> metallation with TME-DA-activated butyllithium in hexane at room temperature occurs exclusively at the ring position *ortho* to the amino group.<sup>14</sup> Our system, which not only contains a tertiary amino group but also uses an inert hydrocarbon solvent, more closely resembles the latter system and this is consistent with the lack of reaction that we observe at the *para*-position. This lack of reactivity has been ascribed to a strong interaction of the metallating reagent with the heteroatom, which directs its reactivity almost exclusively to the *ortho*-position.<sup>13,15</sup> The reduced reactivity at the *meta*-position is probably due to similar factors while electronic factors may also be responsible for the observed differentiation in reactivity between the *para* and *meta* positions. However, when there are no methyl groups *ortho* to the hydroxy group, as in the case of *m*-cresol, it proved possible to monoethylate to some extent to give compound **5**, albeit using somewhat more severe conditions. A reasonable explanation for this would be that, using the base system comprised of *n*-butyllithium, lithium-potassium bis(2-dimethylamino-ethanolate) and Mg(OCH<sub>2</sub>CH<sub>2</sub>OEt)<sub>2</sub>, a carbanion derived by metallation at the *meta*-benzylic position is rapidly protonated by *ortho*-benzylic protons to give a species which can give a favourable aggregate structure such as that speculated in Eq. 3,<sup>16</sup> and that only when these protons are not available can ethylation at this position occur to any significant extent.



Download English Version:

<https://daneshyari.com/en/article/5279782>

Download Persian Version:

<https://daneshyari.com/article/5279782>

[Daneshyari.com](https://daneshyari.com)