



# The reaction of biphenyl radical anion and dianion with alkyl fluorides. From ET to S<sub>N</sub>2 reaction pathways and synthetic applications

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## ABSTRACT

The reaction of dilithium biphenyl (Li<sub>2</sub>C<sub>12</sub>H<sub>10</sub>) with alkyl fluorides has been studied from the point of view of the distribution of products. Two main reaction pathways, the nucleophilic substitution (S<sub>N</sub>2) and the electron transfer (ET), can compete to yield the same alkylation products in what is known as the S<sub>N</sub>2–ET dichotomy. S<sub>N</sub>2 seems to be the main mechanism operating with primary alkyl fluorides (*n*-RF). Alkylation proceeds in good yields, and the resulting alkylated dihydrobiphenyl anion (*n*-RC<sub>12</sub>H<sub>10</sub>Li) can be trapped with a second conventional electrophile (E<sup>+</sup>) affording synthetically interesting dearomatized biphenyl derivatives (*n*-RC<sub>12</sub>H<sub>10</sub>E). The reaction gives a higher amount of ET products as we move to secondary (*s*-RF) and to tertiary alkyl fluorides (*t*-RF), in which case the mechanism seems to be dominated by ET. In this case, alkylation by radical coupling is still feasible, giving access to the synthesis of *t*-RC<sub>12</sub>H<sub>10</sub>E, although in lower yields. A rational interpretation of this S<sub>N</sub>2–ET dichotomy is given on the basis of the full distribution of products observed when 5-hexenyl fluoride and 1,1-dimethyl-5-hexenyl fluoride were used as radical probes in their reaction with Li<sub>2</sub>C<sub>12</sub>H<sub>10</sub> and LiC<sub>12</sub>H<sub>10</sub>.

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## 1. Introduction

### 1.1. The radical anion and dianion of biphenyl

Radical anions and dianions of aromatic hydrocarbons of high reduction potential, such as naphthalene or biphenyl, should be considered among the strongest ET (electron transfer) reagents in solution.<sup>1</sup> They can be prepared, inter alia, by direct reaction of the aromatic hydrocarbon with an alkali metal. These anionic species have very high energy electrons, which are also highly delocalized in an extended π-cloud that spreads all over the molecule. This determines much of the reactivity displayed by these species, which is often dominated by ET to acceptors and reminiscent of the alkaline metal they originated from. Applications of these alkali metal-like solutions are well developed. Indeed, the use of naphthalene, biphenyl or alkylated derivatives (such as 4,4'-di-*tert*-butylbiphenyl) as an ET mediator in Li<sub>(s)</sub> reductions has been shown to be advantageous over the direct, non catalyzed Li<sub>(s)</sub> reduction,<sup>2</sup> and this has been rationalized by means of a quantitative consideration of the electron transfer kinetics involved.<sup>3</sup>

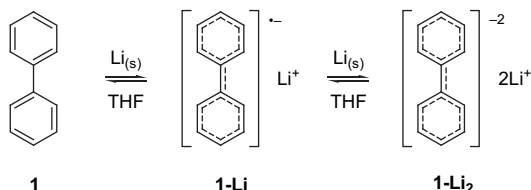
Lithium is the preferred alkali metal for these chemical reductions since the pair Li<sub>(s)</sub>/Li<sup>+</sup><sub>(H<sub>2</sub>O)</sub> is the most negative among alkali metals, with a standard potential E°<sub>(Li/Li<sup>+</sup>)</sub> = −3.04 V, in water relative

to SHE.<sup>4</sup> This allows in principle the highest reduction power in coordinating solvents.<sup>5</sup> Biphenyl (**1**, C<sub>12</sub>H<sub>10</sub>) has the highest first reduction potential E°<sub>1</sub> (giving rise to the radical anion), and the second higher E°<sub>2</sub> (which affords the dianion) among polycyclic arenes: E°<sub>1</sub> = −2.68 V, E°<sub>2</sub> = −3.18 V, in Me<sub>2</sub>NH versus Ag/AgCl.<sup>6</sup> It is important noticing that these values rival with those of lithium metal itself, both in water and in THF, for which similar values are reported.<sup>5</sup> In spite of the imprecision inherent to the comparison of electrochemical data obtained from different sources under different experimental conditions, it is evident that there is only a narrow window for a feasible double reduction of biphenyl in solution. Indeed, the information found in the literature regarding the existence of the biphenyl dianion is ambiguous in that respect. The biphenyl dianion, **1**-Li<sub>2</sub> (Li<sub>2</sub>C<sub>12</sub>H<sub>10</sub>) was suggested in early studies as a component of the Li<sub>(s)</sub>-biphenyl solutions of stoichiometry 2:1 in THF, and was used for reductive-cleavage applications akin to Li<sub>(s)</sub>.<sup>7</sup> Since **1**-Li<sub>2</sub> was not isolated or characterized in this work, the idea that some of the Li<sup>+</sup> in solution could come from side reactions prevailed. Further studies on Raman spectroscopy reported the view that the dianion of biphenyl was not a component of biphenyl-alkali metal solutions, in particular, in the case of sodium.<sup>8</sup> Later, descriptive work of the biphenyl dianion was reported, dealing with the <sup>1</sup>H NMR and <sup>13</sup>C NMR of **1**-Li<sub>2</sub> (Li<sub>2</sub>C<sub>12</sub>H<sub>10</sub>) at −80 °C in THF-*d*<sub>8</sub>.<sup>9</sup> In the solid phase there is better consensus. The UV and IR and Raman spectra of different alkali metal salts of biphenyl in sublimated layers and codeposits are described by different groups.<sup>10</sup> We have observed previously that, in the presence of an excess of Li<sub>(s)</sub>, naphthalene is

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doubly reduced in THF or better in THP to its dianion,<sup>11</sup> and this has been substantiated with the determination of the crystal structure of the naphthalene dianion,  $(\text{Li}^+\text{TMEDA})_2\text{C}_{10}\text{H}_8^{2-}$ , obtained by direct reduction of naphthalene with  $\text{Li(s)}$ .<sup>12</sup> Based on reduction potential criteria,<sup>1</sup> biphenyl (**1**) would be also expected to be reduced to the corresponding dianion (**1-Li<sub>2</sub>**) at least to some extent under similar conditions, according to Scheme 1.<sup>13</sup>



Scheme 1.

In this paper we report on the reactivity of biphenyl radical anion and dianion with different (primary, secondary, and tertiary) alkyl fluorides in order to establish the mechanistic and synthetic aspects of these reactions.

## 1.2. Alkyl fluorides as electron acceptors

The carbon–fluoride bond cannot be electrochemically reduced below the solvent cut-off limit.<sup>14</sup> Solvents or supporting electrolytes are invariably reduced at lower potentials than that required for an alkyl fluoride, therefore there are no reports of cathodic reductions of regular alkyl fluorides by electrochemical means. They can however be the electron acceptor counterpart in homogeneous reactions with arene radical anions as ET reagents. In this regard, the alkyl halide series including alkyl fluorides (RI, RBr, RCl, and RF) has been the subject of numerous studies in their reactions with arene radical anions.<sup>15</sup> A widely accepted mechanism of reaction for alkyl halides has been described in identical terms for *all* alkyl halides, including alkyl fluorides.<sup>16</sup> It involves ET from the arene radical anion and dissociation of the alkyl halide with generation of the alkyl radical. Thus, the reaction of alkyl halides (R–X) with sodium naphthalene affords similar crude products mainly consisting in mixtures of reduction (R–H) and coupling products (R–C<sub>10</sub>H<sub>9</sub>, R<sub>2</sub>C<sub>10</sub>H<sub>8</sub>), regardless the nature of X (F, Cl, Br or I). According to the authors, the lack of effect of halogen variation on the distribution of products mitigates the possibility of an S<sub>N</sub>2 reaction pathway.<sup>16</sup> This statement remained unchallenged until

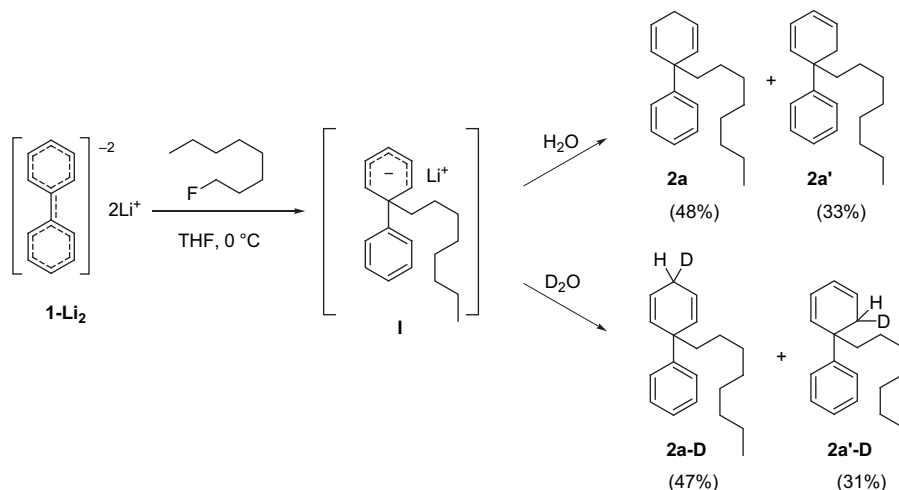
a first hint suggesting a special behavior of alkyl fluorides was anticipated by Ebersohn.<sup>17</sup> He observed the failure of the alkyl fluorides to conform in a reasonable way with the Marcus theory of ET, which adequately fitted the ET reaction between arene radical anions and the rest of alkyl halides (RI, RBr, and RCl). The thermodynamic/electrochemical data needed (e.g., the unavailable  $E^\circ$  of RX) were estimated from indirect thermodynamic measures, according to the method given by Hush.<sup>18</sup> After being overlooked for two decades, recent studies of competitive kinetics on lithium naphthalene ( $\text{LiC}_{10}\text{H}_8$ ) and dilithium naphthalene ( $\text{Li}_2\text{C}_{10}\text{H}_8$ ) confirmed an ET reactivity profile with alkyl chlorides (*n*-, *s*-, and *t*-octyl chlorides), while revealed an apparent mechanistic shift toward the S<sub>N</sub>2 when alkyl fluorides (*n*-, *s*-, and *t*-octyl fluorides) were employed as electron acceptors.<sup>19</sup> The reactivity was shown to decrease in the order primary > secondary > tertiary for reactions of octyl fluorides in both the naphthalene radical anion and dianion, just the opposite behavior that would be intuitively expected if ET was the main process.

## 2. Results and discussion

We want to report here the differences in chemical reactivity between the lithium salts of biphenyl radical anion ( $\text{LiC}_{12}\text{H}_{10}$ , **1-Li**) and its dianion ( $\text{Li}_2\text{C}_{12}\text{H}_{10}$ , **1-Li<sub>2</sub>**), specifically their differences when reacting with alkyl fluorides as an example of poor electron acceptors. The synthetic applications derived from this study are also evaluated.

### 2.1. Previous studies

Some aspects of the reactivity of these species (**1-Li**, **1-Li<sub>2</sub>**), postulated as coexisting in more or less extension in solutions containing biphenyl and an excess of an alkali metal, have already been reported, in part as a preliminary communication.<sup>20</sup> For instance, **1-Li<sub>2</sub>** reacts with terminal alkenes, affording dearomatized carbolithiation products, which can be further functionalized in subsequent steps.<sup>21</sup> Instead, **1-Li** is unreactive under the same reaction conditions. Analogous results were obtained for lithium naphthalene dianion and the corresponding radical anion.<sup>21</sup> The reaction is not an ET process, but rather a nucleophilic attack to the alkene resulting a carbolithiation. Lithium naphthalene radical anion and dianion were also studied in concern with their roles with the mechanism of the arene-catalyzed lithiation.<sup>11</sup> Also, the reaction of a large number of dianions of polycyclic aromatic hydrocarbons (PAHs) with alkyl fluorides provided a route to alkylated dihydro-PAHs, which was



**Scheme 2.** Alkylation of dilithium biphenyl ( $\text{Li}_2\text{C}_{12}\text{H}_{10}$ ) with *n*-fluorooctane. Yields were determined by quantitative GLC using pure isolated products for the calibration curve and dodecane as internal standard. 4-Deuterio-1-octyl-1,4-dihydrobiphenyl (**2a-D**, 47%, 53:47 dr, >98.5% deuterium incorporation) and 2-deuterio-1-octyl-1,2-dihydrobiphenyl (**2a'-D**, 31%, 62:38 dr, >99.8% deuterium incorporation) were obtained using D<sub>2</sub>O for deuterolysis (diastereomeric ratio by <sup>1</sup>H NMR and <sup>13</sup>C NMR, deuterium incorporation by MS and <sup>1</sup>H NMR, natural isotopic distribution corrected). Product characterization: Ref. 22.

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