

## Effect of substituents and benzyne generating bases on the orientation to and reactivity of haloarynes

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### Abstract

The reaction of 1,4-dichlorobenzene with  $\text{NaNH}_2$  in liquid ammonia gave 4-chlorobenzynes which were trapped by the ammonia solvent to give a 63:37 mixture of 4-chloro and 3-chloroaniline, respectively, which is in contrast to an earlier report that 4-chlorobenzynes undergo regioselective amination at carbon-1. Furthermore, 4-halo fluorobenzenes ( $\text{X}=\text{Cl}$ , Br, and I) reacted with LDA to eliminate the less basic halogen atom, *i.e.* the better leaving group, to give 4-fluorobenzynes, which reacted with LDA to give a 70:30 mixture of 4-fluoro- and -*N,N*-diisopropyl-3-fluoroaniline, respectively. Attempts to trap 4-fluorobenzynes in the LDA-mediated reactions with furan gave mainly the aforementioned anilines plus a small amount of 6-fluorooxabenzonorbornadiene. However, 4-halo fluorobenzenes ( $\text{X} = \text{I}$ , Br, Cl, F) when treated with *tert*-BuLi in furan at  $-70^\circ\text{C}$  eliminated fluoride ion to give the corresponding 4-halobenzynes, which were trapped by furan to the 6-halo derivatives of oxabenzonorbornadiene in high yields. In the case of 3-halo fluorobenzenes, 3-haloarynes are generated in the normal way by the loss of the better leaving halogen atom and were also trapped with furan to give corresponding 5-halo oxabenzonorbornadienes. An explanation in terms of the relative base strengths of LDA and *t*-BuLi and influence of solvent on the aryne generation is presented.

**Keywords:** Benzyne, nucleophilic, addition, *tert*-butyllithium, lithium diisopropylamide

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### Introduction

In Roberts' seminal paper<sup>1</sup> on substituent effects in benzyne chemistry, *o*-haloarenes possessing electron-attracting groups ( $-\text{I}$ ) were shown to react with  $\text{NaNH}_2$  in liquid ammonia to generate 3-substituted arynes that undergo nucleophilic amination regioselectively at the 1-position to give *meta* substituted anilines. This conversion of an *ortho* substituted reactant to a *meta* substituted product, which is unique to benzyne chemistry, is known as *cine* substitution. Such substitutions have been used extensively in synthesis and as confirmation of the intermediacy of an aryne intermediate. The genesis of the regioselective addition to C-1 is probably due to the greater stabilization of the developing negative charge at the adjacent carbon (C-2) by the electron-

attracting 3-substituent in the amination transition state as compared to that of the developing negative charge at the remote site (C-1) from the  $-I$  group.

With 4-substituted benzyne the situation is complicated because the inductive effect of substituents is less strong and other electronic effects may be operable. For example, Roberts observed that 3- and 4-substituted anilines were obtained in a ratio of about 1:1 from the amination of 4-methoxy- and 4-trifluoromethylbenzyne, whereas the amination of 4-fluorobenzyne gave a 4:1 ratio of *para* to *meta* anilines.<sup>1</sup> Shortly thereafter, Wotiz reported that ammonia added exclusively to the 1-position of 4-chlorobenzyne yielding an isomer-free 4-chloroaniline.<sup>2</sup> This surprising result, which is listed as one of the most widely cited reviews on benzyne chemistry,<sup>3</sup> if correct, would be the first example of a regioselective addition to a 4-aryne.

However, a little-known study by Sanguini<sup>4</sup> in 1960 showed that amination of 1,4-dichlorobenzene under similar conditions used by Wotiz gave a mixture of 4- and 3-chloroanilines in a ratio of 4:1, respectively. In fact, subsequent studies by other workers, have further demonstrated that 4-chlorobenzyne undergoes nucleophilic addition to give mixtures of *para* and *meta* products. The nucleophiles reported include (*p:m* ratios of chloroanilines are shown in parenthesis): methanol under neutral conditions (83:17),<sup>5</sup> methanol catalyzed with methoxide ion (72:28),<sup>5</sup> ethanol (81:19),<sup>6</sup> methylamine (63:37),<sup>7</sup> and LDA (72:28).<sup>8</sup> These results clearly show that 4-chlorobenzyne does not undergo regioselective nucleophilic addition.

Recently, 4-chlorofluorobenzene was reported to react with *tert*-BuLi to give 4-chlorobenzyne to which benzonitrile added regioselectively to C-1 to give 2,8-dichloro-6-phenylphenanthridine.<sup>9</sup> We were intrigued not only with the reported regioselective addition to 4-chlorobenzyne, but also that fluoride ion was eliminated preferentially over chloride ion. This is opposite to what is observed when strong amide bases such as sodium amide or LDA are used to generate benzyne. Although *tert*-BuLi has been used to generate benzyne from fluoroarenes, to our knowledge, no study has been carried out on the orientation and reactivity of 4-haloarynes generated from *p*-fluorohaloarenes with *tert*-BuLi.

## Results and Discussion

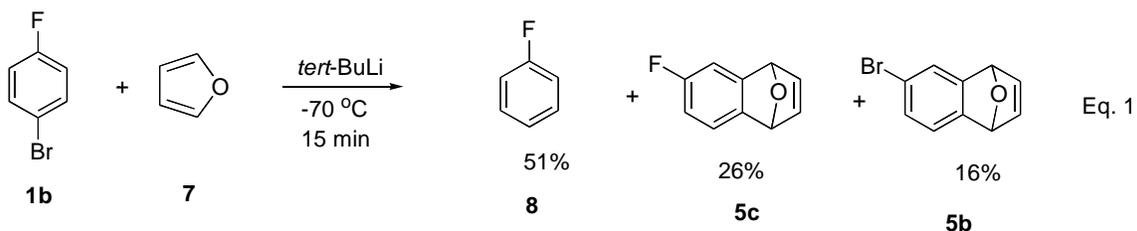
Before starting a detailed investigation on substituent effects in 4-arynes, we first repeated the reaction of 1,4-dichlorobenzene with  $\text{NaNH}_2$  in liquid ammonia. Using a more accurate analytical method, *i.e.* GC/MS on the crude reaction mixture, we determined the product distribution of 4-chloroaniline and 3-chloroaniline to be 83:17, respectively which is very similar to that obtained by Sanguini who used a less accurate UV analytical method.

To obtain more information on the chemistry of 4-haloarynes, we treated a series of 1,4-dihalobenzenes (**1a—g**) with LDA and THF, and the results are listed in Table 1. The data can be better discussed by dividing the dihaloarenes into two groups: those possessing the same halogen atom and those possessing two different halogen atoms. In the former case, 1,4-difluoro-

(**1c**), 1,4-dichloro- (**1e**), 1,4-dibromo- (**1f**), and 1,4-diiodobenzene (**1g**) reacted with LDA to form the corresponding 4-fluoro- (**2a**), 4-chloro- (**2b**), 4-bromo- (**2c**) and 4-iodobenzynes (**2d**). These arynes then underwent addition of LDA to give mixtures of 4-halo-(**4a-d**) and 3-halo-3-*N,N*-diisopropylanilines (**3a-d**). The magnitude of the 3:4 product distribution decreased as the halogen was varied along the series F (72:28), Cl (64:36), Br (59:41), and I (52:48). This trend parallels the decrease in the electronegativity of the halogen. The group of 1,4-dihaloarenes possessing two different halogens (**1a**, X = Cl and F, **1b**, X = Br and F, and **1d**, X = Br, Cl) generated 4-haloarynes by the loss of the less basic halide ion (*i.e.* the better leaving group). Thus both **1a** and **1b** formed 4-fluorobenzynes (**2a**) by the loss of Cl<sup>-</sup> and Br<sup>-</sup>, respectively, and bromide<sup>-</sup> was eliminated from **1d** to give 3-chlorobenzynes (**2b**). Similar 3:4 aniline product distributions were obtained for these arynes. This behavior is consistent with the observation that the temperatures at which arynes are generated increases along the series ArI (~ -60 °C) > ArBr (~ -45 °C) > ArCl (~ -30 °C) > ArF (~15 °C), which is in qualitative agreement with similar trends previously reported.<sup>10</sup> The **3a:4a** ratio increased from 72:28 to 82:18 when the reaction (entry 1) of **1a** was run in a two fold excess of isopropylamine, while the **3b:4b** ratio increased from 64:46 to 70:30 when these reactions were carried out in a similar two fold excess of diisopropylamine. This is consistent with the lower reactivity and hence higher selectivity of the free diisopropylamine as compared to its conjugate base, LDA.

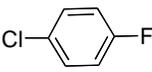
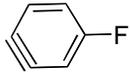
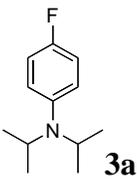
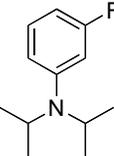
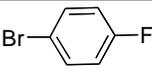
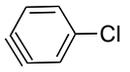
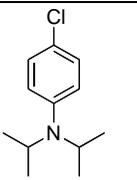
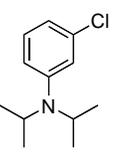
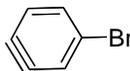
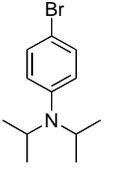
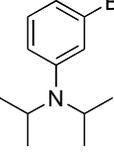
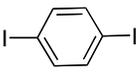
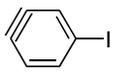
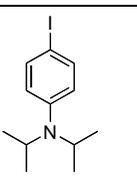
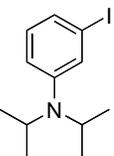
Interestingly, the reaction of 1-chloro-4-fluorobenzene (**1a**) with LDA also gave 4-chloro-*N,N*-diisopropylaniline (**3b**) in 22% yield, but none of the 3-chloroaniline product was found. This strongly argues that **3b** was not formed from the benzyne intermediate (**2b**), but was formed by a S<sub>N</sub>AR reaction involving direct displacement of fluoride by LDA. Such a substitution pathway is consistent with the higher leaving group reactivity of F<sup>-</sup> as compared to Cl<sup>-</sup> and would explain the observed product distributions.

We attempted to trap the LDA-generated 4-haloarynes with furan in the anticipation of obtaining 6-halooxonorbornadienes. However, the yields of norbornadienes were severely compromised by the unavoidable amination side reaction. Encouraged by several reports on the use of *t*-BuLi to generate benzyne,<sup>10-14</sup> we treated the 4-chloro (**1a**)-, 4-bromo (**1b**)-, 4-fluoro (**1c**)- and 4-iodo (**1f**) derivatives of fluorobenzene with *tert*-BuLi in the presence of furan in THF. The reaction of **1b** was first carried using the same reaction conditions as the LDA mediated ones. However as shown in eq. 1,



when the mixture was initially stirred for 15 min at -70 °C before warming to room temperature, both 6-fluoro (**5c**) and 6-bromo (**5b**) derivatives of oxonorbornadiene as well as fluorobenzene (**8**) were obtained. A possible mechanism to account for these products is shown in Scheme 1.

**Table 1.** Reaction of 1,4-dihalobenzenes (**1a–f**) with LDA yielding 4-halo-*N,N*-diisopropylanilines (**3a–d**) and 3-halo-*N,N*-diisopropylanilines (**4a–d**) via 4-arynes (**2a–d**)

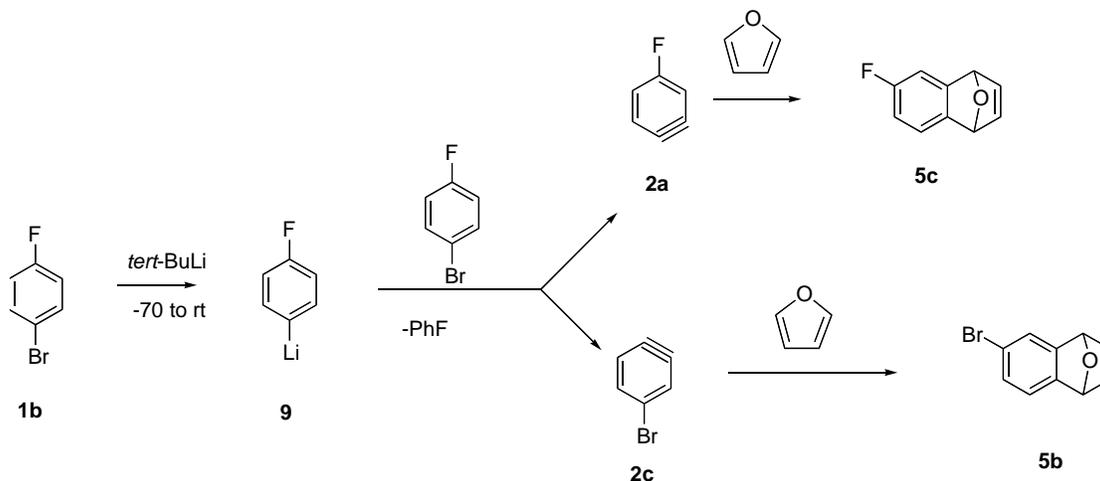
Entry	Dihaloarene <b>1a–f</b>	Benzyne <b>2a–d</b>	Products <b>3a–d</b>	<b>4a–d</b>	Total yield,%	<b>3:4</b> ratio
1	 <b>1a</b>	 <b>2a</b>	 <b>3a</b>	 <b>4a</b>	70	72:28 82:18 <sup>c</sup>
2	 <b>1b</b>	<b>2a</b>	<b>3a</b>	<b>4</b>	83	69:31
3	 <b>1c</b>	<b>2a</b>	<b>3a</b>	<b>4a</b>	68	70:30
4	 <b>1d</b>	 <b>2b</b>	 <b>3b</b>	 <b>4b</b>	86	63:37 70:30 <sup>b</sup>
5	 <b>1e</b>	<b>2b</b>	<b>3b</b>	<b>4b</b>	85	64:36
6	 <b>1f</b>	 <b>2c</b>	 <b>3c</b>	 <b>4c</b>	83	59:41
7	 <b>1g</b>	 <b>2d</b>	 <b>3d</b>	 <b>4d</b>	20	52:48

<sup>a</sup> Unless stated otherwise, the reactions were carried out in THF using 3 equiv of LDA per equiv of haloarene.

<sup>b</sup> Compound **3b** [shown in entry 4] was also obtained in 22% yield.

<sup>c</sup> Reaction was run using 6 equiv of diisopropylamine and 3 equiv of LDA per equiv of haloarene.

Thus **1b** undergoes lithium-bromine exchange to give the strong base (**9**) which could abstract a proton either *ortho* to F or Br from another **1b** to give ultimately 4-fluorobenzynes (**2a**) and 4-bromobenzynes (**2c**) with concomitant formation of fluorobenzene (**8b**). The arynes were then trapped by furan to give **5b** and **c**, respectively.



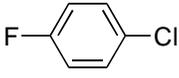
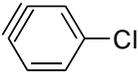
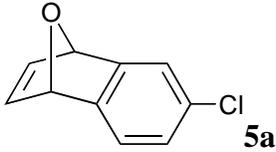
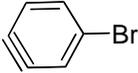
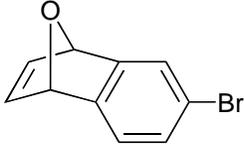
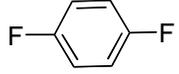
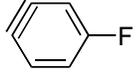
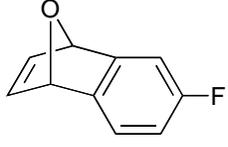
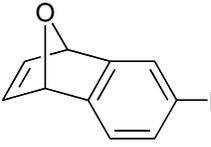
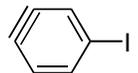
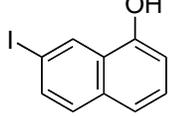
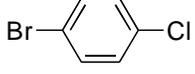
### Scheme 1

We subsequently found that excellent yields could be obtained by adding *tert*-BuLi to the 4-halofluorobenzene at  $-78\text{ }^{\circ}\text{C}$  and maintaining that temperature for 1h before allowing the reaction mixture to warm to room temperature. This allows the complete lithiation (deprotonation) of the 2-carbon which then is able to generate 4-halobenzynes with the absence of lithium-halogen exchange. These arynes were trapped by furan to give 6-chloro- (**5a**), 6-bromo- (**5b**), and 6-fluoro-oxabenzonorbornadienes (**5c**) respectively in 85-98% yields as shown in Table 2. GC/MS analysis of the successful *tert*-BuLi crude reaction mixtures consisted of essentially one peak, which was easily identified as the product. No *tert*-butylated products were observed. The vastly increased yields of oxabenzonorbornadienes in the *tert*-BuLi mediated reactions as compared to the LDA-mediated reactions most likely reflects the larger steric bulk of *tert*-BuLi as compared to LDA.

4-Iodobenzynes (**2d**) also reacted with furan to give 6-iodo oxabenzonorbornadiene (**5d**) in 55% yield and the regioselective ring opened product 7-iodo-1-naphthol (**6a**) in 12% yield. However, as shown in entry 5 of Table 2, *tert*-BuLi failed to generate a benzyne intermediate from 4-bromo-1-chlorobenzene (**1d**) but rather gave a complex mixture of non-aryne products. *p*-Dichlorobenzene, *p*-dibromobenzene, and *p*-chloriodobenzene (which are not shown in Table 2) behaved similarly.

The excellent yields (92%) 6-fluoro-oxabenzonorbornadiene (**5c**) compares favorably with the 94% yield reported from the reaction of *n*-BuLi and 1-bromo-2,4-difluorobenzene<sup>13</sup> while the yield of the 6-bromo derivative **5b** (98%) is significantly higher than the 45% yield by a multi-step, polymer based synthesis.<sup>15</sup> 6-Iodo-oxabenzonorbornadiene (**5d**) is a new compound that could serve as an important coupling reagent.

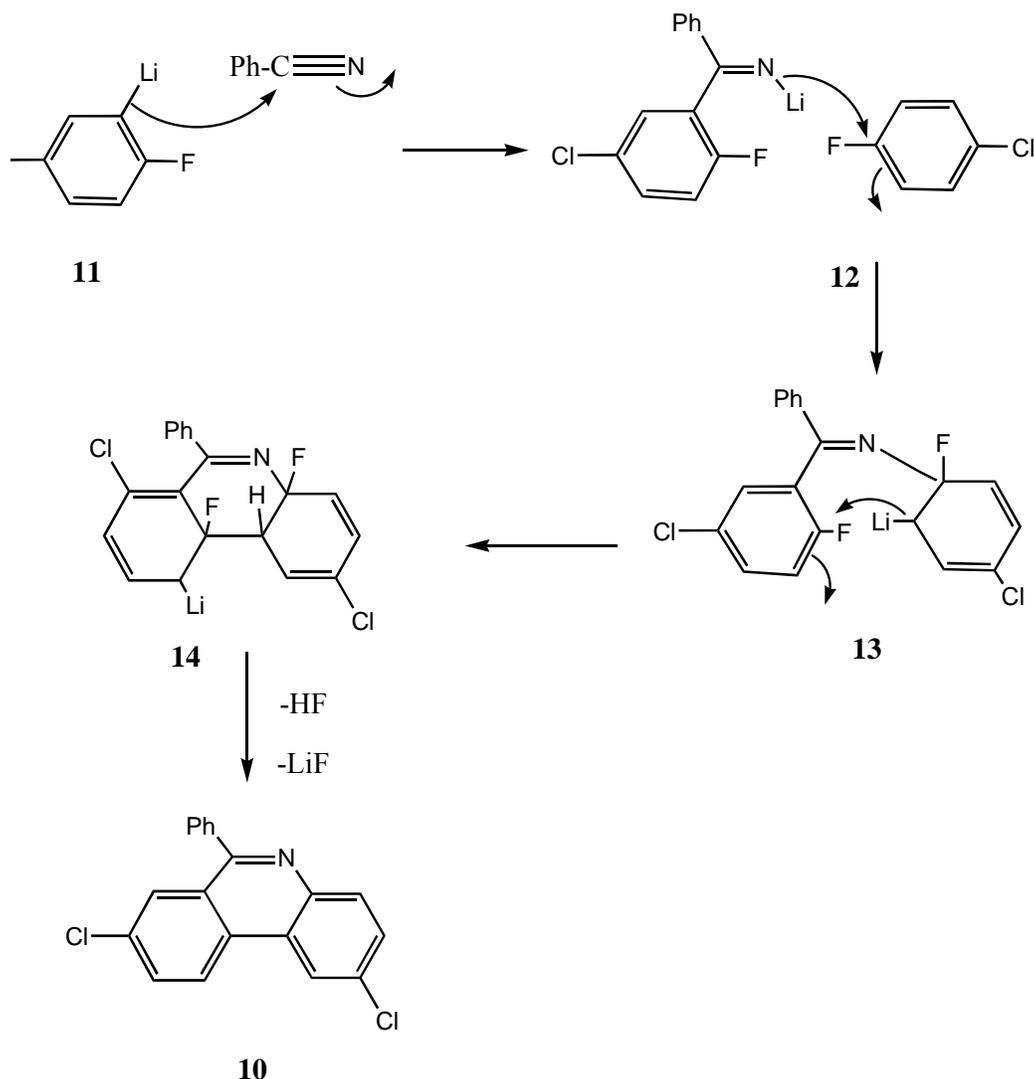
**Table 2.** Preparation of 6-halooxabenzonorbornadienes (**5a–d**) by *tert*-BuLi-mediated aryne reactions of 1,4-dihalobenzenes (**1a–c, f**)

Run no.	Substrate	Benzyne	Products	Yield, %
1	 <b>1a</b>	 <b>2b</b>	 <b>5a</b>	85
2	 <b>1b</b>	 <b>2c</b>	 <b>5b</b>	98
3	 <b>1c</b>	 <b>2a</b>	 <b>5c</b>	92
4			 <b>5d</b>	55
	 <b>1h</b>	 <b>2d</b>	 <b>6a</b>	12
			 <b>6b</b>	16
5	 <b>1i</b>		<b>a</b>	

a: complex mixture in which no halooxonorbornadienes were detected.

A summary of the important features of the LDA and *tert*-BuLi results reported to here are: 1) without exception LDA adds to both positions of the isomeric 4-haloarynes, 2) deprotonation by *tert*-BuLi occurs at the carbon adjacent to the fluorine atom, and 3) LDA displaces the

fluorine atom in 4-chloro-1-fluorobenzene most likely by a  $S_NAr$  mechanism. Now in the reported reaction of *tert*-BuLi with 4-chloro-1-fluoroaniline with benzonitrile, it was assumed that the product (**10**) was formed by regioselective addition to 4-chlorobenzynes, although no formal mechanism was shown. Actually, our results indicate it is quite possible that 4-chlorobenzynes was not formed in that reaction but rather was the result of a non-arynic pathway shown in Scheme 2.

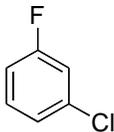
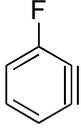
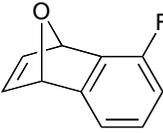
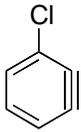
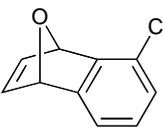
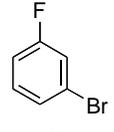
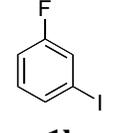


**Scheme 2.** Possible mechanism for the formation of compound **10**.

As shown 2-lithiated 4-chloro-1-fluorobenzene derivative **11** adds to benzonitrile to give adduct **12** in which the resulting nitrogen anion adds in *ipso* fashion to the fluoro atom in 4-fluoro-1-chlorobenzene affording carbanion **13**. This is followed by intramolecular cyclization to the tricyclic carbanion **14** which loses HF and LiF to give **10**. In support of a non-benzynes reaction, we repeated the phenanthrene synthesis in the presence of furan and failed to detect 5-chlorooxonorbornadiene.

The reactions of a series of *m*-fluorohalobenzenes (**1j–l**) with *tert*-BuLi were carried out in the presence of furan in order to determine which 3-haloaryne would be formed. The results are shown in Table 3. As can be seen, the reaction of 1-bromo-3-fluorobenzene (**1k**) and 3-iodo-1-fluorobenzene (**1l**) with *tert*-BuLi in THF (entries 2 and 3, respectively) yielded the same aryne, namely, 3-fluorobenzynes (**2e**) which subsequently reacted with furan to yield 5-fluoroxobenzonorbornadiene (**5e**) in 67% and 92% yields, respectively. The reaction of 3-chloro-1-fluorobenzene (**1j**) in THF (entry 1) also proceeded predominantly *via* 3-fluorobenzynes (**2e**) predominantly to yield **5e** (73% yield). In addition, a small amount of 5-chloroxobenzonorbornadiene (**5f**) was obtained *via* 3-chlorobenzynes (**2f**). On the other hand, when the reaction of **1j** was run in ether the 5-chloro derivative **5f** was obtained in 72% yield and the 5-fluoro derivative **5e** was obtained in only 11% yield. However, in the presence of 12-crown-4 the ether reaction of **1j** gave results similar to those found in THF, with the 5-fluoro derivative **5e** being formed in 62% yield and the 5-chloro compound **5f** in only 12% yield.

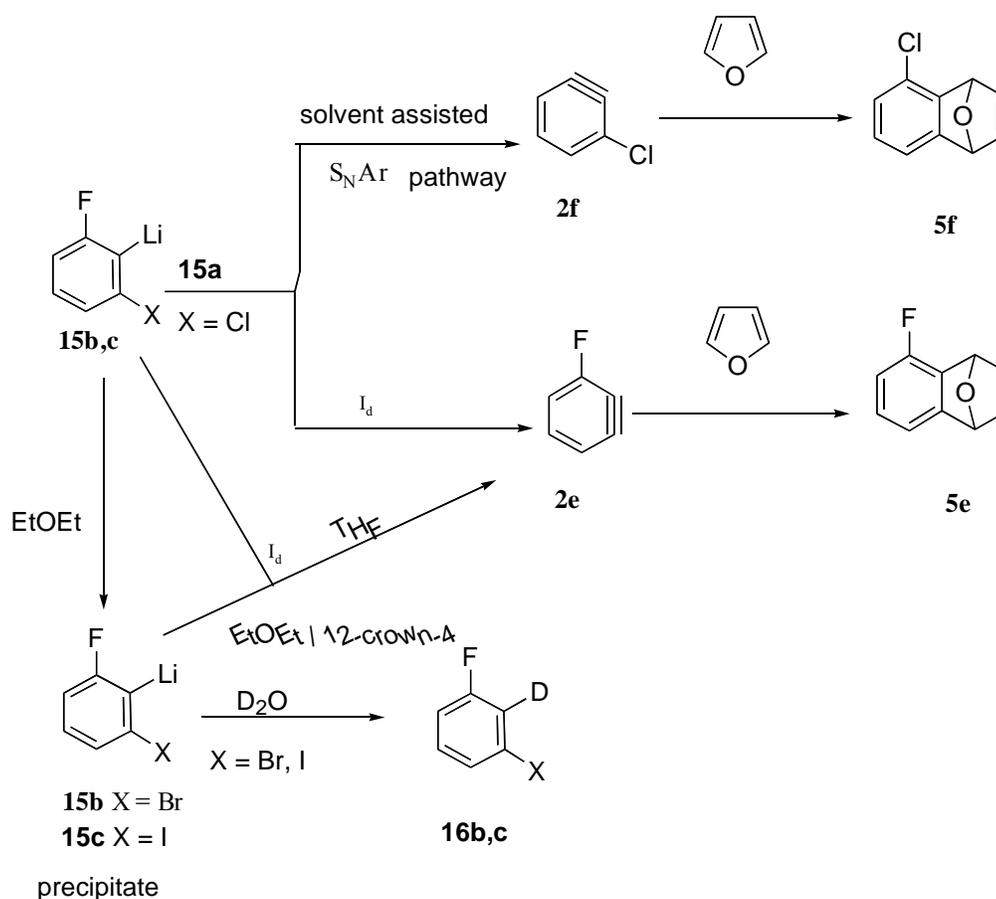
**Table 3.** Reaction of 1,3-dihaloarenes (**1j–l**) with *tert*-BuLi in presence of furan

Entry	Haloarene	Aryne	Product	Yield, %		
				THF	Et <sub>2</sub> O	Et <sub>2</sub> O/ 16-Crown-4
1	 <b>1j</b>	 <b>2e</b>	 <b>5e</b>	73	12	62
		 <b>2f</b>	 <b>5f</b>	11	73	12
2	 <b>1k</b>	<b>2e</b>	<b>5e</b>	67	0	72
3	 <b>1l</b>	<b>2e</b>	<b>5e</b>	92	0	54

Interestingly, the reaction of **1k** and **1l** with *tert*-BuLi in ether gave precipitates which were shown to be the 2-lithio salts 3-bromo- (**15b**) and 3-iodofluorobenzenes (**15c**). The identify of these salts was verified by treating the solids with D<sub>2</sub>O to give 3-bromo-2-deutero-1-

fluorobenzene (**16a**) and 2-deutero-1-fluoro-3-iodobenzene (**16b**), respectively. Furthermore, addition of 12-crown-4 to the reaction slurry containing the salts afforded a clear solution which after stirring for 2 h gave **5e** in 70% and 62% yields, respectively.

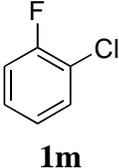
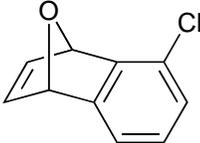
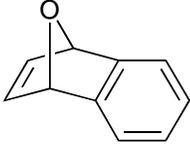
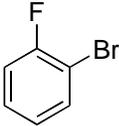
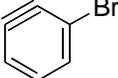
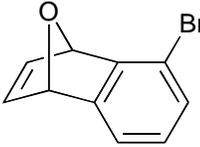
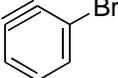
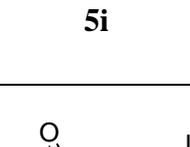
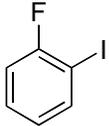
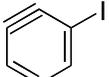
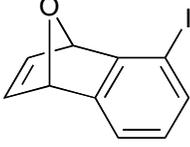
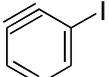
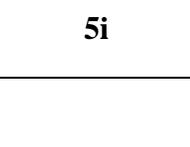
A possible explanation for the regiochemistry observed in the reactions of **1j—l** is shown in Scheme 3. The regiochemistry is dictated first and foremost by the acidities of the benzene hydrogen atoms. The most acidic hydrogen, which is the between the fluorine and the other halogen atom, is lost first in all cases; its loss would lead to the intermediates **15a-c**. Intermediate **15a** could decompose to give either 3-chlorobenzene (**2f**), or 3-fluorobenzene (**2e**), leading to 5-chloro **5f** or 5-fluoro **5e** products. In the case of **15a** the dissociative pathway predominates yielding **5e** via 3-fluorobenzene (**2e**). This pathway is favored due to the good leaving group abilities of the halide ions. In the case of **15a** (X = Cl) reactions in THF, a small amount of **5f** is also formed via 3-chlorobenzene (**2f**) by the  $S_NAr$  solvent assisted pathway. This pathway is actually favored when the reaction is run in ether. However, with the use of 12-crown-4, the negative charge on the 2-lithio site is increased which perhaps decreases the ability of ether to assist in the  $S_NAr$  pathway. Intermediates **15b** and **15c** proceed by the dissociative pathway most likely due to the better leaving abilities of Br and I vs Cl.



Scheme 3

Finally, the reaction with 2-halo-1-fluorobenzenes (**1m—o**) and furan with *tert*-BuLi was carried out, with the results shown in Table 4. As might be expected, the fluorine atom was eliminated in each case yielding the appropriate 3-haloaryne (**2e,j**). However, benzyne (**2i**) was formed in each reaction (by the loss of FX) which subsequently reacted with furan giving 9-oxonorbomadiene (**5i**). The formation of **2i** most likely is the result of initial lithium exchange of Cl, Br, or I, respectively by *tert*-BuLi followed by loss of LiF. Consequently these reactions give mixtures of oxonorbomadiene which diminishes the use of 1,2-dihaloarenes in the synthesis of 5-halo derivatives of oxonorbomadiene.

**Table 4.** Reaction of 1,2-dihaloarenes (1k-m) with furan and *tert*-BuLi

Entry	Haloarene	Aryne	Product	
1	 <b>1m</b>	 <b>2f</b>	 <b>5f</b>	47
			 <b>2i</b>	 <b>5i</b>
2	 <b>1n</b>	 <b>2j</b>	 <b>5j</b>	50
			 <b>2i</b>	 <b>5i</b>
3	 <b>1o</b>	 <b>2k</b>	 <b>5k</b>	30
			 <b>2i</b>	 <b>5i</b>

In conclusion we have shown that 4-haloarynes generated from the reaction of 1,4-dihaloarenes and LDA in THF give mixtures of *m*- and *p*-diisopropylamino products. In cases where the halogen atoms are different, the 4-aryne is formed by the loss of an HX containing the halogen with the better leaving group ability. On the other hand, 4-halo-1-fluorobenzenes lithiate exclusively at the carbon adjacent to the fluorine atom with *tert*-BuLi. These intermediates then eliminate fluoride ion to give 4-halobenzyne which are trapped by furan to give 5-halooxonorbornadienes in excellent yields. 1-Fluoro-2-halobenzenes behave similarly with *tert*-BuLi, with the exception that some oxynorbornadiene is formed by the reaction of furan with benzyne formed by an alternate loss of XF. 1-Fluoro-3-halobenzenes undergo lithiation at the carbon between the two halogen atoms. 3-bromo- and 3-iodofluorobenzene, the 2-lithio intermediates proceed to give 5-fluorooxonorbornadiene when the reactions are run in THF. However when these reactions are carried out in ether the lithiated intermediates precipitate from solution and do not undergo benzyne formation. However, with the addition of 12-crown-4, the precipitates dissolve and proceed to give 5-fluorooxonorbornadiene. On other hand, the reaction of 3-chlorofluorobenzene gives predominantly 5-fluorooxonorbornadiene and a minor amount of 5-chlorooxonorbornadiene when the reactions are run in THF or ether/12-crown-4, while the reaction conducted in ether gives mainly 5-chlorooxonorbornadienes and minor amounts of 5-fluorooxonorbornadiene.

## Experimental Section

**General Procedures.** All reagents and solvents, unless otherwise specified were treated according to standard methods.  $^1\text{H}$  NMR spectra were recorded in  $\text{CDCl}_3$  at rt. Chemical shifts are given in parts per million relative to that of TMS as an internal standard.

**General procedure for the LDA-mediated aryne reactions.** A 50 mL flask was dried overnight at 150 °C in an oven and then cooled to rt under Ar atmosphere. Diisopropylamine (1.92 mL, 1.39 g, 13.7 mmol) and 20 mL of dry THF was added via syringe into the flask. The contents in the flask was cooled in a dry-ice bath with stirring to -70 °C. At -70 °C, *n*-BuLi (1.6M) in hexanes (8.2 mL, 13.7 mmol) was added and the resulting solution was stirred for 10 min. Then the appropriate dihalobenzene **1** (4.5 mmol) was added *via* syringe and stirred for 30 min at -70 °C. The dry-ice acetone bath was removed and the reaction mixture was allowed to warm to rt, where it was stirred an additional 3 h. The reaction mixture was quenched with 5 mL of water, diluted with 75 mL of ethyl acetate, and washed with water (3 X 200 mL) then with brine (50 mL). After the solution was dried ( $\text{Na}_2\text{SO}_4$ ), it was filtered and the mother liquor was concentrated (rotatory evaporator). The resulting crude product was then subjected to GC/MS and  $^1\text{H}$  NMR analysis in order to access product distributions of 4-halo-(**3**) and 3-haloanilines (**4**).

**General procedure for the *tert*-BuLi-mediated aryne reactions**

**Using 1,4-dihaloarenes 1a—g and 1,2-dihaloarenes 1l—n.** To a dried round-bottom flask under argon was added 15 mL of dried THF and 15 mL of furan (which was freshly distilled from furan that had been dried over sodium), and the contents of the flask cooled to  $-70\text{ }^{\circ}\text{C}$ . The appropriate dihalobenzene (**1**, 13.8 mmol) was added followed by 24.3 mL of a 1.7M solution in hexane of *tert*-BuLi (41.3 mmol), and the resulting solution was stirred for 1 h at  $-70\text{ }^{\circ}\text{C}$  in an ethanol/dry ice bath. The ice-bath was removed, and the reaction mixture was allowed to warm to rt where it was stirred for 2-3 h. The reaction was then quenched with 5 mL of water, diluted with 75 mL of ethyl acetate, and washed with water (3 X 200 mL) followed by brine (50 mL). After the solution was dried ( $\text{Na}_2\text{SO}_4$ ), it was filtered and the mother liquor was concentrated (rotatory evaporator) to yield crude reaction mixture which GC/MS revealed to be the corresponding oxabenzonorbornadiene (**5**). The oxanorbornadienes were purified by flash chromatography using silica gel and ethyl acetate in hexane (1:5) as eluent.

**Using 1,3-dihaloarenes (1h—j) and 1,2-dichloro-4-fluorobenzene (1k).** The reactions of **1h—k** were carried in the same way as described above. However in the case of 1-bromo-3-fluorobenzene (**1i**) and 1-fluoro-3-iodobenzene (**1j**) a solid precipitate was formed during the reaction. In these cases, the slurry was treated with 1 eq of 14-crown-4 which resulted in the dissolution of the precipitate. The resulting solution was stirred for an 1 h and then work up in the usual way described above for the reaction of 1,4-dihaloarenes to give the 6-halo-9-oxabenzonorbornadiene (**5a-d**). Compound **5d** and **5k** were new compounds and their spectral properties and elemental analysis are shown below.

**6-Iodo-9-oxabenzonorbornadiene (5d).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  5.69 (s, 2 H), 7.02 (d,  $J = 7.4$  Hz, 1 H), 7.00-7.03 (m, 2 H), 7.34 (d,  $J = 7.4$  Hz, 1H), 7.60 (s, 1 H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  81.8, 82.0, 90.0, 121.9, 129.3, 133.7, 142.5, 143.0, 149.0, 151.8. Anal. Calcd for  $\text{C}_{10}\text{H}_7\text{IO}$ : C, 44.47; H, 2.61. Found: C, 44.20; H, 2.60.

**5-Iodo-9-oxabenzonorbornadiene (5k).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  6.55 (m, 1 H), 7.0-7.01 (m, 1H), 7.07 (d,  $J = 3.7$  Hz, 1 H), 7.42 (dd,  $J = 7.7$  Hz, 7.6 Hz, 1H), 7.55 (d,  $J = 1.5$  Hz, 1 H), 7.65 (dd,  $J = 7.7$  Hz, 1.5 Hz, 1 H), 7.99 (d,  $J = 7.6$  Hz, 1 H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  95.1, 110.4, 111.7, 128.7, 129.6, 129.9, 135.8, 141.4, 142.9, 154.1. Anal. Calcd for  $\text{C}_{10}\text{H}_7\text{IO}$ : C, 44.47; H, 2.61. Found: C, 44.55; H, 2.65.

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