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Synthesis Of Fluorinated Biaryl Derivatives *via* $S_{RN}1$ Reactions[1]

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Summary. *Fluorinated biaryl derivatives Y-C_6H_4-ArOH (Y = F, CF_3, OCF_3) are obtained by coupling Y-C_6H_4-Br(p) with anions derived from ArOH via a photostimulated $S_{RN}1$ reaction*

J.F. Bunnett et al. have shown that halofluorobenzenes F-C_6H_4-X treated under $S_{RN}1$ conditions by nucleophiles Nu- (CH_2=C(O-)R;[2a] -SR;[2b] -PO(OEt)$_2$)[2c] give substitution products F-Ar-Nu where fluorine is retained. The CF_3 group was reported to be compatible[3] but no mention of the effect of OCF_3 group on the $S_{RN}1$ mechanism was found in the literature. Recently electrochemically[4a,d] or photochemically[4b-8] stimulated $S_{RN}1$ reactions between Ar_1X and Ar_2O- were found to give biphenyl[4-6], phenyl-naphthyl[7,8] or binaphthyl[7,8] derivatives.

We report now the first examples of $S_{RN}1$ reactions between phenolates **A-D** and naphtholate **E** and **various fluorinated aromatic substrates** Y-C_6H_4Br (**1**, Y = F; **2**, Y = CF_3; **3**, Y = OCF_3) leading to fluorinated biaryl derivatives Y-C_6H_4-ArOH Results are summarized on Table.

Reacting *p*-Bromo-fluorobenzene **1** with the anion from 2,4-di-*tert*-butylphenol **A** or from 2,6-di-*tert*-butylphenol **B** gives the biphenyl derivatives **4a** or **5a** expected from the radical attack of FC_6H_4 on the only nucleophilic carbon site available. The anion from **C** is unexpectedly less reactive than that from **D** which carries the OCF_3 group, but both give biphenyl derivatives **6a** or **7a**, respectively.

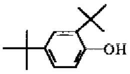
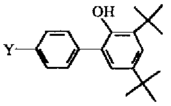
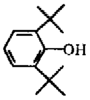
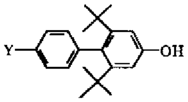
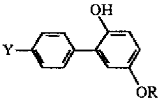
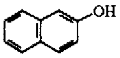
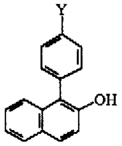
p-Bromo α,α,α-trifluorotoluene **2** yields biphenyl derivatives **4b** or **6b** when treated with the anions from **A** or **C**, while the outcome of the reaction is more complex when the anions from B and D are involved (Scheme 1).

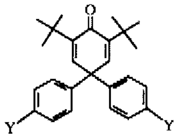
- **5b** is obviously derived from the initial biphenyl derivative which behaves as a nucleophile, and undergoes a second $S_{RN}1$ attack by CF_3-C_6H_4· on para position; such double substitution is unprecedented with phenolates.

- **5'b** is also derived from the initial $S_{RN}1$ product, which undergoes an ionic attack of CF_3 under base conditions of the medium. Similar defluorination reaction is known to occur when CF_3 is activated by an electron releasing group in the para position[9] as found on the precursor of **5'b** [P]. This compound (m.p. 155°C) is identical to that obtained in the laboratory in 96% yield from the photostimulated $S_{RN}1$ reaction between **B** and *p*-Br-C_6H-4-CN (Scheme 1).

The anion from **D** gives rise to the biphenyl **7b** together with the terphenyl **7'b** which is formed by a second $S_{RN}1$ reaction of the radical CF_3-C_6H_4 on the other nucleophilic site available on **7b** as previously observed.[6]

$S_{RN}1$ Reactions between substrates **1**, **2**, **3** and Anions from **A**-**E**.

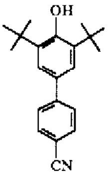
Nucléophiles	Substrates	Products (yield %)
 **A**		
	1 Y= F	**4a** (48)
	2 Y= CF_3	**4b** (27)
	3 Y= OCF_3	**4c** (63)
 **B**		
	1 Y= F	**5a** (30)
	2 Y= CF_3	**5b***, **5'b***
	3 Y= OCF_3	**5c***
		
C R= CH_3	**1** Y= F	**6a** (15)
	2 Y= CF_3	**6b** (20)
	3 Y= OCF_3	**6c** + **6'c*** (45)
D R= CF_3	**1** Y= F	**7a** (47)
	2 Y= CF_3	**7b** (29) ; **7'b*** (37)
	3 Y= OCF_3	**7c** (47)
 **E**		
	1 Y= F	**8a** (31)
	2 Y= CF_3	**8b** (55)
	3 Y= OCF_3	**8c** (40)



5b* Y= CF_3 (16)

5c* Y= OCF_3 (10)

;



5'b* (38)

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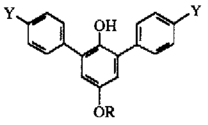
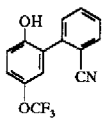


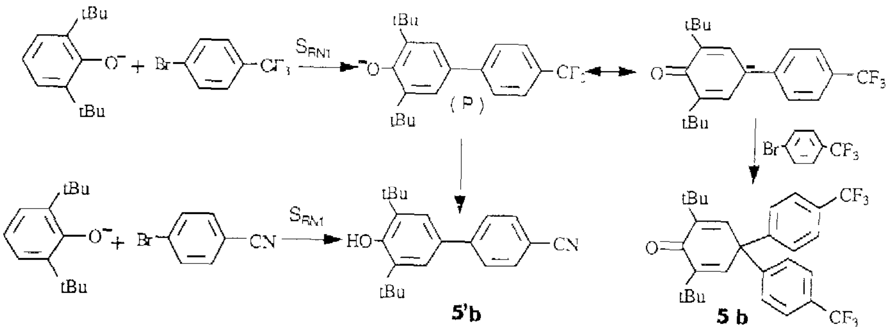
6'c* Y= OCF_3, R= CH_3

7'b* Y= R = CF_3

;



9 (86)

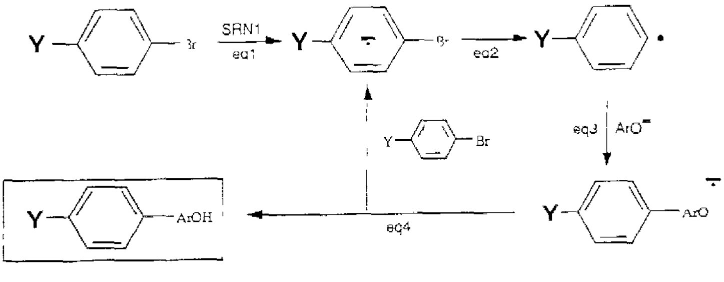


Scheme 1

p-Br-C_6H_4-OCF_3 **3** reacts efficiently with anions from **A** or **D** to give the biphenyl derivatives **4c** or **7c**, but a surprisingly sluggish reaction with **B** yields the disubstituted derivative **5c**, analogous to **5b**. The reaction with the anion **C** gives a mixture of biphenyl and terphenyl derivatives **6c** + **6'c**. There is to notice that **D** behaves excellently as a nuclophile as evidenced by the exploratory reaction with o-Br-C_6H_4-CN which gives **9** in 86% yield

The naphtholate anion from **E** reacts with Br-C_6H-4-Y to give variously fluorinated phenyl-1-naphthyl derivatives **8a**, **8b**, **8c**.

All the above substitution reactions proceed *via* the classical four-step $S_{RN}1$ mechanism depicted on Scheme 2 as evidenced by the reaction leading to **8b** taken as a model. The reaction did not start in the absence of photostimulation and was significantly slowered by addition of i) p-dinitrobenzene which is an electron trap for the radical anions, CF_3-C_6H_4-$Br^{-\bullet}$ (Eq. 1) or CF_3-C_6H_4-$Ar^{-\bullet}$, (Eq. 3), ii) galvinoxyl which scavenges the radical CF_3-$C_6H_4^{\bullet}$ (Eq. 2)



Y =F, CF3 OCF3 , ArO⁻ = anions from A-E (see table)

Scheme 2

The straighforward coupling between Br-C_6H_4-Y and ArO- provides thus an access to a new group of fluorinated biphenyl or phenyl-1-naphthyl derivatives[10], and extends the scope of the $S_{RN}1$ reaction.

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10. All reactions were carried out in liquid ammonia at -33°C (20 ml) in which ArOH (**A-E**) (4 mmol) and *t*-BuOK (4 mmol), and then the substrate (**1**, **2**, **3**; 1 mmol) were successively introduced. The solution was irradiated by UV light through Pyrex until consumption of the substrate (1 to 2 hours). Products were purified by preparative thin layer chromatography and the yields (calculated upon substrates $Y\text{-}C_6H_4Br$) are those of pure products. All products, except **5'b** are new and have spectroscopic data (MS, NMR) consistent with the structures.

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