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PHENOXIDE AND NAPHTHOXIDE IONS AS NUCLEOPHILES FOR $S_{RN}1$ REACTIONS[1] : SYNTHESIS OF BIPHENYL AND PHENYLNAPHTHYL DERIVATIVES

René Beugelmans and Michèle Bois-Choussy*

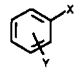
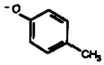
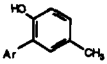
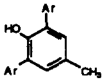
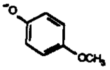
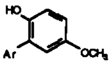
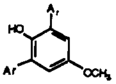
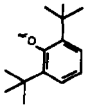
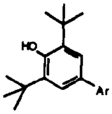
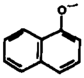
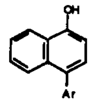
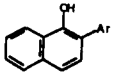
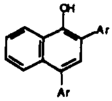
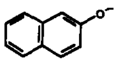
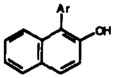
Institut de Chimie des Substances Naturelles, C.N.R.S.
91198 Gif-sur-Yvette, France.

Abstract : Biphenyl or phenylnaphthyl derivatives are obtained by photostimulated $S_{RN}1$ reactions between the anion of phenols or naphthols and variously substituted haloarenes.

Since more than a decade, the question is pending whether phenoxides can be used as nucleophiles on a reaction with halobenzene via $S_{RN}1$ mechanism. Reactions of halobenzene with the phenoxide ion $C_6H_5O^-$, stimulated either by solvated electrons from alkali metals[2] or electrolytically[3] or by light[4,5] gave negative results. A photostimulated reaction between iodobenzene and the sodium or potassium salts of p-methylphenol was reported to induce a slow disappearance of iodobenzene, while p-methylphenol was almost quantitatively recovered.[6] A very recent paper[7] reports that electrostimulated $S_{RN}1$ reactions between di-t-butylphenoxide and o-, m-, or p-chlorobenzonitrile gives hydroxy-biphenyls. This has led us to reinvestigate photostimulated $S_{RN}1$ reactions between various nucleophiles ArO^- and diversely substituted ArX as a possible new acess to biaryl derivatives. The results are tabulated (Table).

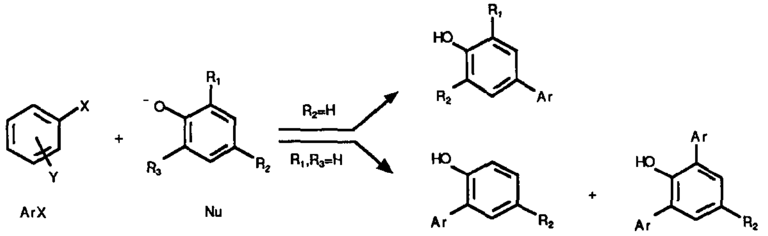
We first repeated the experiment between iodobenzene and p-methylphenol (Nu_1) which, as reported,[6] gave a complex reaction mixture from which we could nevertheless isolate the hydroxybiphenyl 1 (although in a very low yield) and identify 2. This same nucleophile Nu_1, when opposed to bromobenzonitrile Ar_2Br, which carries an electron-withdrawing group (E.W.G.), yielded an appreciable amount of the biphenyl 3. The p-methoxyphenoxide Nu_2, substituted by a stronger electron donating group (E.D.G.) than methyl, reacted under similar conditions much faster than Nu_1 towards Ar_1Br or Ar_2Br to give 5 + 6 (52%) or 7 (65%). The 2,6-di-t-butylphenoxide Nu_3 which was used for the electrostimulated $S_{RN}1$ reactions,[7] appeared also to be very efficient for photostimulated $S_{RN}1$ reactions, and gave 8 in almost quantitative yield when reacted with Ar_2Br.

TABLE

Substrate $Ar_nX = YC_6H_4X$	phenoxide	Conditions a) Time	Products[13] yield b)		
					
Ar_1: Y = H; X = I	Nu_1	c) 1h	1 3%	2 traces	
Ar_2: Y = p.CN; X = Br	Nu_1	c) 2h	3 20%	4 traces	
					
Ar_1: Y = H; X = Br	Nu_2	c) 1h	5 40%	6 12%	
Ar_2: Y = p.CN; X = Br	Nu_2	c) 2h	7 65%		
					
Ar_2: Y = p.CN; X = Br	Nu_3	c) 1h	8 96%		
Ar_2: Y = p.CN; X = Br	Nu_3	d) 1h	0		
Ar_2: Y = p.CN; X = Br	Nu_3	c) e) 1h	8 45%	ArBr 39%	
Ar_3: Y = o.CN; X = Br	Nu_3	c) 1h	9 88%		
Ar_4: Y = o.CONH$_2$; X = Br	Nu_3	c) 1h	10 85%		
Ar_5: Y = o.COCH$_3$; X = Br	Nu_3	c) 1h	11 60%		
Ar_6: Y = o.OCH$_3$; X = Br	Nu_3	c) 1h	12 78%		
					
Ar_2: Y = p.CN; X = Br	Nu_4	c) 2h	13 40%	14 25%	15 8%
					
Ar_2: Y = p.CN; X = Br	Nu_5	c) 2h	16 85%		

a) General procedure : The phenoxide is generated from the phenol (3 mmol) by t-BuOK (3 mmol), in liquid ammonia (50 ml) at -33°C (dry ice condenser) in a Pyrex vessel and the substrate (1 mmol) is added under argon. After consuption of the substrate, NH_4Cl is added, NH_3 is evaporated and the extraction is carried out by CH_2Cl_2 after addition of water. b) Calculated on the substrate, pure isolated product. c) UV stimulation by a high pressure mercury UV source 550W. d) In the dark. e) +p-DNB-20 mmol%.

The substrate may carry as well an electro-attracting group (CN, $CONH_2$, COMe); as an electron-donating one (OMe) ortho to the leaving group[8,9] to give the corresponding biphenyl derivatives 9 - 12.



Scheme 1

The 1- or 2-naphthol derived nucleophiles also react with p-bromobenzonitrile under $S_{RN}1$ conditions. Whereas 1-naphthol gave a mixture of 2- and 4-phenylnaphthyl derivatives 13 and 14 together with the 2,4-diphenylnaphthyl derivative 15, 2-naphtol as expected gave the single product 16.

We have taken the highest yield reaction between Ar_2Br and Nu_3 for mechanistic investigation; no reaction takes place in the dark and a partial but significant inhibition of the photostimulated reaction is obtained by p-dinitrobenzene (p-DNB). These facts are compatible with an $S_{RN}1$ mechanism[4,10] depicted on Scheme 2 since : i) photostimulation is required to produce $ArX^{\cdot-}$ (step 1), ii) p-DNB is easily reduced to a stable $p\text{-}DNB^{\cdot-}$ by $ArX^{\cdot-}$ or $ArNu^{\cdot-}$ thus interrupting the chain propagation (steps 2, 3, 4).

$$\begin{array}{llcll}
\text{Initiation} & ArX & \xrightarrow[h\nu]{e^-} & ArX^{\cdot-} & (1) \\
\text{Propagation} & ArX^{\cdot-} & \longrightarrow & Ar^{\cdot} + X^- & (2) \\
 & Ar^{\cdot} + Nu^- & \longrightarrow & ArNu^{\cdot-} & (3) \\
 & ArNu^{\cdot-} + ArX & \longrightarrow & ArNu + ArX^{\cdot-} & (4)
\end{array}$$

Scheme 2

The synthetic scope of the photostimulated $S_{RN}1$[11] is thus considerably extended by the above reported reactions which provide a straightforward access to a variety of biphenyl or phenylnaphthyl derivatives starting from haloarenes and various phenols[12] or naphthols.

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