Metallation of Aryl Ethers by Lithium Arenes

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Summary Metallated aryl ethers are shown to be secondary products of their cleavage reaction with lithium metal or lithium arenes.

THE metallation of anisole in the *o*-position was accomplished using lithium metal in tetrahydrofuran (THF), *i.e.* under conditions normally used, for the generation of radical anions.[1]† Lithium arenes were also found to metallate anisole and related aryl ethers at the same sites that are attacked by conventional lithiating agents.[2] These findings could be of importance to the mechanism of carbon–heteroatom bond cleavage,[3] as well as to the understanding of "the strange behaviour of the anisoles" in e.s.r. studies.[4]

We followed the decay of paramagnetism by n.m.r.,[5] in THF solutions of lithium biphenyl, naphthalene, and phenanthrene, upon treatment with anisole. The decay appears to obey the first-order rate law (Figure),‡ although the conditions for pseudo-first-order kinetics were not met.

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† One week reaction time, room temperature, THF free of anti-oxidant. 12% yield of *o*-methoxybenzoic acid based on lithium consumed.

‡ Cyclohexane (10%) was used as external–internal standard. Signals were recorded with a Varian A60 NMR spectrometer. First-order rate constants were determined by least-squares.

Table 1

Arene	k_1 (min^{-1})	$-m_{m+1}$[a]
Biphenyl	$0{\cdot}243 \pm 0{\cdot}010$	0·705
»	$0{\cdot}248 \pm 0{\cdot}011$	
Naphthalene	$0{\cdot}074 \pm 0{\cdot}005$	0·618
»	$0{\cdot}086 \pm 0{\cdot}003$	
Phenanthrene	$0{\cdot}017 \pm 0{\cdot}005$	0·605
»	$0{\cdot}011 \pm 0{\cdot}007$	

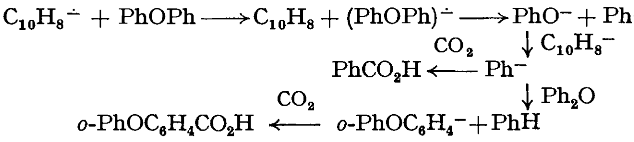
[a] m_{m+1} is the Hückel value of the coefficient of the molecular orbital resonance integral in the expression for the energy of the lowest unoccupied orbital of the arene: taken from A. Streitwieser, jun., 'Molecular Orbital Theory for Organic Chemists,' Wiley, New York, 1961, p. 178.

Table 1 summarizes the kinetic results obtained with initial concentrations of lithium arene and anisole of 0·50 and 0·90 M, respectively, at 40·5 ± 0·5 °C.

Apparently there is a strong dependence of k_1 on the type of arene. An obvious trend is that the k_1's vary antiparallel to the electron affinity of the parent hydrocarbon. This could be strong evidence for the involvement of electron transfer from the radical anion to the aryl ether, in the rate-limiting step, followed by the decomposition of an unstable[4] aryl ether radical anion.

Table 2 summarizes the results of metallation of various aryl ethers with 10 mmol of lithium naphthalene.

The experiment with $Li^+C_{10}H_8^{\dot{-}} : Ph_2O$ (2 : 1) was suggested by our hypothesis that the decomposition of unstable radical



$$\begin{tikzcd}
C_{10}H_8^{\dot{-}} + PhOPh \arrow[r] & C_{10}H_8 + (PhOPh)^{\dot{-}} \arrow[r] & PhO^- + Ph\cdot \arrow[d, "C_{10}H_8^-"] \\
& PhCO_2H & Ph^- \arrow[l, "CO_2"'] \arrow[d, "Ph_2O"] \\
o\text{-}PhOC_6H_4CO_2H & & o\text{-}PhOC_6H_4^- + PhH \arrow[ll, "CO_2"']
\end{tikzcd}$$

Scheme 1

anions should represent a two-electron process. In this case phenyl-lithium was the sole organometallic product, indicating that the observed products arise by the route shown in Scheme 1. On the basis of 2 : 1 stoicheiometry, the yields of lithiated products can be considered to be good.

Table 2

Aryl ether	$Li^+C_{10}H_8^{\dot{-}}$: ArOR	Reaction time (h)	Temp. (°C)	Acid from Carbonation	Yield[a] (%)
Anisole	1 : 2	24	16—23	o-MeO·C_6H_4·CO_2H	48
1,3-Dimethoxybenzene	1 : 2	24	16—23	2,6-$(MeO)_2$·C_6H_3·CO_2H	36
Diphenyl ether	1 : 2	24	16—23	o-PhO·C_6H_4·CO_2H	70
»	1 : 2	2	20—25	o-PhO·C_6H_4·CO_2H	62
»	1 : 2	0·1	0—12	$PhCO_2H$	75
»	2 : 1	2	0—20	$PhCO_2H$	85
»	2 : 1	2	0—7	$PhCO_2H$	86

[a] Yields are calculated on the basis of 2 : 1 stoicheiometry of the limiting reagent $Li^+C_{10}H_8^{\dot{-}}$. Products were > 90% pure, as shown by n.m.r. spectra.

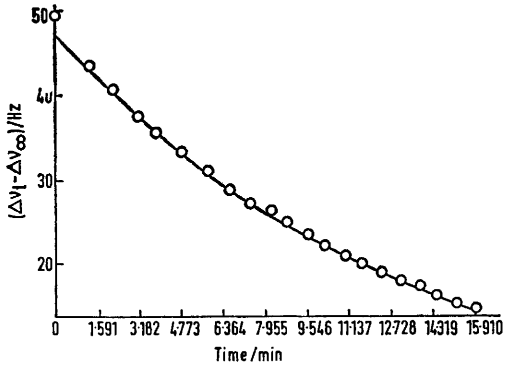
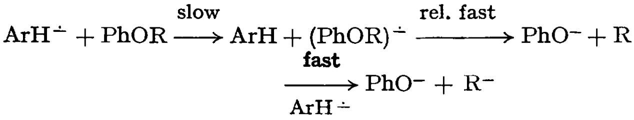


Figure. *Computer-plotted data for the decay of paramagnetism in lithium naphthalene–anisole. The solid line is the least-squares fit to the first-order rate function.*

Combining the kinetic and metallation results we visualize the reaction to occur as shown in Scheme 2. This reaction



$$\begin{tikzcd}
ArH^{\dot{-}} + PhOR \arrow[r, "slow"] & ArH + (PhOR)^{\dot{-}} \arrow[r, "rel.\ fast"] \arrow[dr, "fast", "ArH^{\dot{-}}"'] & PhO^- + R\cdot \\
& & PhO^- + R^-
\end{tikzcd}$$

Scheme 2

sequence differs from that suggested by Eargle,[6] according to which fragmentation occurs in the dianion of aryl ether.

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[6] D. H. Eargle, jun., *J. Org. Chem.*, 1963, **28**, 1703.