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REGIOCHEMISTRY OF NUCLEOPHILIC DISPLACEMENTS IN CHLOROQUINONES

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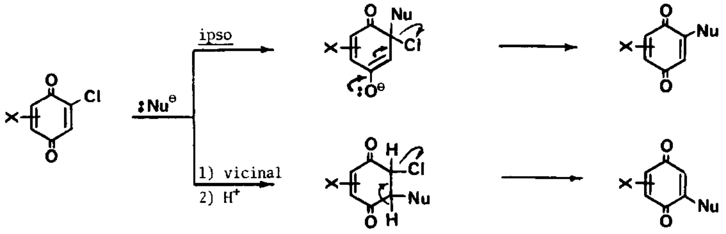
Summary. Nucleophilic displacement of halide from 2-halo 1,4-quinones occurs at the *ipso* carbon or at the carbon vicinal to it depending on the nature of the nucleophile and the solvent.

Nucleophilic displacement of halide from 2-halo 1,4-quinones is a preparatively important process in quinone chemistry because it is both versatile and often highly regioselective.[1] Attack of the nucleophile could reasonably occur either at the *ipso* carbon or at the carbon vicinal to it, leading respectively to a 2- or 3-substituted product (Scheme).

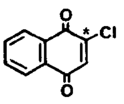


Scheme

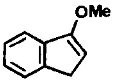
The regiochemistry of such a process has invariably been established by reference to a substituent X elsewhere in the molecule[2], since in the absence of such a substituent the alternative points of attack would normally be indistinguishable. But regiochemistry so deduced cannot safely be generalised since X itself may electronically or sterically influence the process, as is the case for addition of nucleophiles to non-halogenated quinones[3]. The present study has determined for the first time the intrinsic orientational influence of a 2-halo quinonoid substituent in the absence of such complications.

For this purpose 2-[^{13}C]-2-chloro-1,4-naphthoquinone (1) was selected as substrate. The choice of a naphthoquinone rather than a benzoquinone precluded competitive reaction on the non-halogenated side of the nucleus, while carbon labelling obviated the possibility of significant isotope effects or of exchange processes inherent in a deuterated substrate.

Addition of dichlorocarbene (derived from [^{13}C]-enriched chloroform under phase-transfer conditions) to the methoxy indene (2) proceeded with concomitant ring opening to give the naphthalene (3) (30% based on an equimolar proportion of labelled chloroform; virtually quantitative when chloroform was used in conventional excess)[4]. Oxidative demethylation with ceric ammonium sulfate then afforded (1) (63%). Only one signal δ 146.4 (C2) in its ^{13}C n.m.r. spectrum showed enhancement relative to unlabelled material. In addition the resonance corresponding to C3 (δ 135.9, natural abundance) was observed as a doublet J_{CC} 50 Hz).



1



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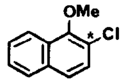
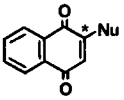
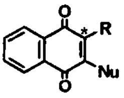


3 [* = ^{13}C]

Normalized results for reaction of (1) with selected nucleophiles from the first row of the Periodic Table are summarized in the Table. Reactions were carried out in the dark in air. Products (absolute yields 67 to 92%) were analyzed by ^{13}C n.m.r., ratios being determined by comparison of spectra of labelled and unlabelled material. Limited proportions of 2,3-disubstituted naphthoquinones produced by oxidation following vicinal attack were also observed.

Table: Reaction of Nucleophiles with the [^{13}C]-Quinone (1)

Nucleophile (Nu$^{\ominus}$ or NuH)	Solvent	Yield (%)		
		 ipso	 vicinal	
			R=H	R=Cl
F$^{\ominus}$	MeCN	100	0	0
MeO$^{\ominus}$	MeOH[ø]	93	7	0
aziridine	MeCN	25	70	5
pyrrolidine	MeCN	24	71	5
$CH_2 = C(OMe)_2$	MeCN	0	100[†]	0
pyrrolidine	C_6H_6	8	80	12
pyrrolidine	MeOH	84	10	6

[ø] action of MeO$^{\ominus}$ in MeCN led to decomposition. [†] product estimated as 9a-[^{13}C]-1,3-dimethoxyanthraquinone.

The data provide two important conclusions: (a) The hard nucleophiles F$^{\ominus}$ and MeO$^{\ominus}$ attack predominantly ipso whilst the soft 1,1-dimethoxyethene[5] shows exclusive vicinal addition. Amines are borderline in hard/soft terms and this is reflected in a lack of regiospecificity. (b) The preferred position of attack by amines is strikingly solvent dependent, vicinal attack being favoured in C_6H_6 and MeCN while in MeOH ipso substitution predominated.[6]

Experiments are in progress to examine the regiochemical preference of nucleophilic attack in a variety of solvents on 2(3)-halo quinones possessing other substituents known to exert directive influence in their own right.

Satisfactory analytical data have been obtained on all compounds mentioned in this work. We are grateful to the Australian Research Grants Committee for financial support and acknowledge an Australian Postgraduate Research Award (to PJC).

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