## PHENOLIC OXIDATION WITH (DIACETOXYIODO)BENZENE

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Abstract: (Diacetoxyiodo)benzene oxidises quinols and extended quinols to the corresponding quinones smoothly and in high yield. Excess of the reagent in methanol with monohydric phenols directly yields <u>p</u>-quinone ketals, also in good yields. 4-Alkyl and 4-alkoxyphenols give the corresponding 4-alkyl-4-methoxycyclohexadienones and 4-alkoxy-4-methoxycyclohexadienones.

Aryloxenium ions 1, have been implicated in biosynthetic processes either directly<sup>1,2</sup> or through derived quinone methides.<sup>3</sup> They have been proposed as intermediates in phenol oxidations by thallium(III)<sup>4</sup>, copper(II)<sup>5</sup> and periodic acid<sup>6</sup>; have been implicated in the release of 'metaphosphate' from quinol monophosphates<sup>7</sup>, and some ions 1 have been generated and characterised electrochemically<sup>8,9</sup> Certain highly delocalised aryloxenium ions have been isolated and characterised.<sup>10</sup>

An attractive route to 1 is shown in equation 1. The phenols are transformed first to intermediates 2 with a good leaving group bound to oxygen and then transformed either thermally or chemically to the oxenium ions.

 $\begin{array}{ccc} ArOH & & & \\ \hline & & & \\ 2 & & 1 \end{array}$  (1)

The leaving group 'X' has been NHTs<sup>11</sup>, pyridinium<sup>12</sup>, N<sub>2</sub><sup>+</sup> <sup>13</sup> and possibly Me<sub>2</sub><sup>+</sup> <sup>14</sup> In general yields of products have been low and conditions rather stringent. However, if 'X' could be chosen so that the reaction could be carried out under mild conditions, then the highly nucleophilic ions 1 would have been generated in a regiospecific 'non-oxidative' step and could be used for natural product synthesis, particularly <u>via</u> intramolecular coupling.<sup>15</sup> It has been pointed out,<sup>16</sup> and partly verified,<sup>12</sup> that aryloxenium ions should undergo C-C coupling rather than the C-O-C coupling experienced by the corresponding radicals. Self coupling of 1 should be minimal and instead controllable attack on neutral nucleophiles is to be expected. Loss of an appositely placed benzylic proton could lead to quinome methides, which could be utilised.

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As part of an extended survey of the potential of a variety of precursors 2, we first examined compounds  $ArOSR_{2}X^{-}$  (2 with X =  $SR_{2}$ ). These are species similar to those produced on oxidation of alcohols with DMSO<sup>17</sup> and related In general,  $ArOSMe_{p}X^{-}$  undergo Sommelet-Hauser type rearrangereagents.<sup>18</sup> ments to yield aryl methylthiomethyl ethers.<sup>19</sup> However, the presence of an ortho or para-hydroxyl group leads to quinones when the dimethyl sulphide. N-chlorosuccinimide (NCS) system is used.<sup>14</sup> We first confirmed the results of oxidation using 2 (X= $\dot{S}Me_{o}$ ) (Table 1, exp. 1,5) but in order to avoid Sommelet-Hauser rearrangements changed to a new system using Ph<sub>2</sub>S-NCS. This also successfully oxidises simple quinols to quinones (Table 1, exp. 2,6), after addition of triethylamine. No guinone results without base addition showing that 2  $(X={}^{s}Ph_2)$  are reasonably stable. However,  $Ph_2S$ -NCS reacted with 4-benzylphenol (Table 2, exp. 13) to give a complex mixture of chloro-substituted products, over a wide variety of conditions. To avoid this, we attempted to use the Martin sulphurane reagent<sup>20</sup>, which has once been observed to act as an oxidant.<sup>21</sup> In our hands guinones were not obtained from guinols with this reagent and we turned instead of iodonium leaving groups.

We first tried Koser's reagent, PhI(OH)OTs, which we hoped would react with phenols as shown in equation (2). We hoped that the tosyloxy anion generated would not be sufficiently nucleophilic to attack species generated from 2.

ArOH + PhI(OH)OTS  $\longrightarrow$  PhI(OAr)OTS  $\longrightarrow$  ArO<sup>†</sup>Ph  $\overline{O}TS \rightarrow \rightarrow$  (2) 2 (X=<sup>†</sup>Ph)

Indeed, the reagent readily oxidised simple quinols in excellent yields to the quinones (Table 1, exp. 3,7) but it failed to oxidise 4,4'-biphenol (Table 1, exp. 12) or 4-benzylphenol (Table 2, exp.14). We therefore turned to commercially available (diacetoxyiodo)benzene (phenyl iodosodiacetate) (DAIB), which with phenols could also yield 2 (X =  $\bar{1}$ Ph) with a poorly nucleophilic anion, Aco. This reagent has previously<sup>22</sup> been reported to give low yields of p-quinones from monohydric phenols and to substitute an acetoxy group into 4-substituted phenols.

We carried out our reactions by mixing DAIB and substituted phenol dissolved in methanol at room temperature, the results being presented in Tables 1 and 2.

Table 1 shows that the interaction of DAIB (one equivalent) with 1,4- and 1,2-hydroxybenzenes yields 1,4- and 1,2-quinones in good yields. (Table 1, exp. 4,8,9,10). Furthermore, 4,4'-dihydroxybiphenyl gives the extended quinone, dibenzoquinone (Table 1, exp. 11).

4-Alkylphenols give good isolated yields of the corresponding 4-alkyl-4methoxycyclohexadienones (Table 2, exp. 15,16,17) and 4-alkoxyphenols give the corresponding 4,4-dialkoxycyclohexadienones (quinone-ketals) in excellent yields (Table 2, exp. 18,19). Mixed quinone ketals<sup>3</sup> are thus made readily available (exp.19).

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TABLE 1									
<u>Expt</u> .	<u>Substrate</u>	Oxidation of 1,4- Oxidant	and 1,2-Dihydroxyl Product	<u>Yield (%)</u> a	<u>M.p(°C)</u>				
1	но	Me <sub>2</sub> S-NCS <sup>b</sup>	0=	77	115				
2		Ph <sub>2</sub> s-NCs <sup>b</sup>	89	84	**				
3	11	PhI (OH)OTs <sup>C</sup>	"	80	"				
4	"	PhI(OAc)2 <sup>d</sup>	"	94	Ħ				
5		Me2s-NCSb	0 = He	98	28-29 <sup>f</sup>				
6 7	F18 "	Ph <sub>2</sub> S-NC6 <sup>b</sup> PhI (OH)OTs <sup>C</sup>	"	98 84	14 17				
8	"	Phi(OAc) <sup>d</sup>	"	100	11				
9	8u'	PhI(OAc) <sup>d</sup> 2	Bu'	99	65 <sup>g</sup>				
10		PhI(OAc) <sup>d</sup>	8u'	91	114-115 <sup>h</sup>				
11	но Средон	PhI(OAc) <sup>d</sup> PhI(OH)OTs <sup>c</sup>	₀= <b></b> = <b>_</b> □ No reaction	70 (94 <sup>e</sup> )	165 <sup>i</sup>				
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a)Unless otherwise stated, all yields are of isolated, pure characterised product. b)Reaction at -40°C in MeCN-CH\_Cl\_.NEt\_ added. C)Reaction at r.t. in MeCN-CH\_Cl\_. d)Reaction at r.t. in MeCH\_e)H.p.I.c. yield. 26°C. g)Lit.65°C. h)Lit. m.p.112-114°C. Lit. 165°C decomp.

			TABLE 2		
		Oxidation	of monohydric phenols	<b>h</b>	•
Expt.	Substrate	Oxidant	Product	Yield (%)	<u>M.p. (<sup>°</sup>C)</u>
13		Ph2S-NCSC	Chlorinated phenols	-	-
14	"	PhI (OH)OTs <sup>d</sup>	Starting material	-	-
15		Phi(OAc) <sub>2</sub> e	Heo	65	011
16	Me	PhI(OAc) <sub>2</sub> e		72	42-44 <sup>f</sup>
17		PhI(OAc) <sup>e</sup> 2	Bu' Me0	94	58-59 <sup>g</sup>
18	Me0 - OH	PhI(OAc)2 <sup>e</sup>	MeQ =0	99	011
19	РКСН 20 ОН	PhI(OAc) <sub>2</sub> e	Рысн <sub>а</sub> 0 Неоходно развити	92	011
20	Не	PhI(OAc) <sub>2</sub> e,h		80	59-61
21	CH <sub>2</sub> Ph	PhI(OAc) <sub>2</sub> e,h	He0 He0	83	011

a) One equivalent of oxidant unless otherwise stated. b) Yield of isolated, characterised pure product. C) Reaction at -40°C in MeCN-CH\_Cl\_2, 1 equiv. NEt added. g) Reaction at r.t. in MeCN\_CH\_Cl\_2. Reaction in MeOH at r.t. i) Lit.m.p.43-44°C<sup>27</sup>. g) Lit.m.p.58-59°C. Two equivalents of PhI(OAc)<sub>2</sub> used. By using <u>two</u> equivalents of DAIB, <u>p</u>-quinone ketals are readily obtained directly from 4-unsubstituted monohydric phenols. (Table 2, exp. 20,21). Even when a highly stabilised <u>ortho</u>-quinone methide might be produced (exp. 21) only the <u>para-quinone</u> ketal results.

The method described is of obvious preparative value, particularly for natural product synthesis. Although the products are typical of two electron oxidations, the mechanisms remain open.

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