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Spirodienones Part 8[1]. The Direct Preparation of Spirodioxole - and Spirobenzoxazole - cyclohexadienones by the Oxidation of 4 - Aryloxyanilines.

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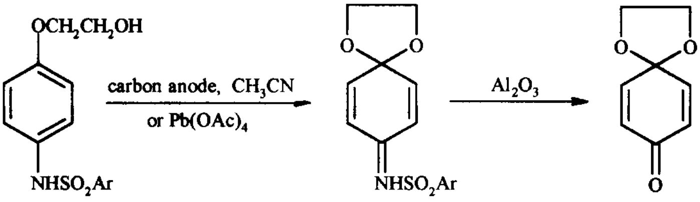
Abstract: Oxidation of 4(2 - hydroxyphenoxy)anilines **1b** to **1d** with active manganese dioxide leads directly to quinone mono - ketals **2b** to **2d** in reasonable yield. Similar reaction of 4 (2 - sulfonamidophenoxy)anilines **9a**, **9b** provides an efficient synthesis of spirobenzoxazolecyclohexadienones **10a** and **10b** but treatment with manganese dioxide of alcohol **3** and oxime **6** gives respectively azobenzene **4** and terphenyl **7** rather than spirodienones

The oxidation of phenols or of primary aromatic amines has historically constituted the major route to quinones[2]. Over the past two decades there has been considerable interest in an extension of this chemistry, in which the oxidation of phenols or their ethers is carried out in the presence of alcohols, resulting in the formation of synthetically useful quinone mono - or bis - ketals[3].

More recently some attention has been paid to the possibility of preparing analogous ketals of *para* - quinoneimines by the oxidation on *N* - substituted anilines. In the first examples of this class of compound, a comprehensive range of sulfonamides derived from 4 - alkoxyanilines yielded *N* - sulfonyl derivatives of quinoneimine ketals when oxidised electrochemically or with lead tetraacetate[4]: (it has recently been shown that iodosylbenzene is also an effective oxidant for this reaction[5]). In subsequent studies quinoneimine ketals have been prepared in which the imine nitrogen has carried an acyl[6], *tert* - butoxycarbonyl[7], aryl[1], or alkyl[8] substituent.

It has also been established[4] that sulfonimide ketals can be selectively hydrolysed by alumina to the corresponding *p* - benzoquinone monoketals (exemplified in Scheme 1), thus providing access to the latter compounds.

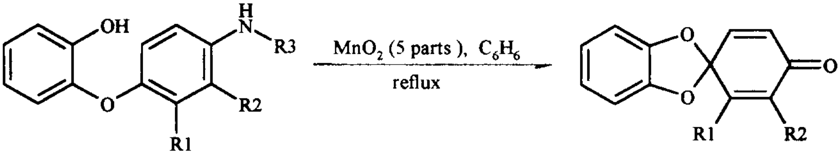
In an attempt[4] to apply this route to the synthesis of the benzodioxolespirodienone **2b**, (Table 1), the sulfonamidodiphenyl ether **1a** was subjected to chemical and anodic oxidation, but no intermediate sulfonimide was obtained. However, it has now been found that treatment of the *aniline* **1b** with active manganese dioxide in refluxing benzene results in the direct formation of dienone **2b**.



Scheme 1.

The conversion of **1b** to **2b** probably involves the intramolecular coupling of a diradical intermediate to form a quinoneimine, which then undergoes hydrolysis to the dienone. Since in both of these steps polymerisation of the intermediates is a major competing reaction, the yield of **2b** obtained (c. 40%) is reasonable, and is comparable with that obtained from oxidation of 2, 4$'$ - dihydroxydiphenyl ether.

Table 1. Reaction of 4 - (hydroxyphenoxy)anilines with active manganese dioxide.



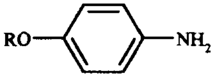
1a - f

2a - f

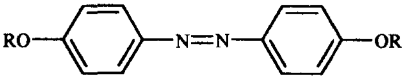
Starting Material	Product	% Yield
1a R1 = R2 =H, R3 = $SO_2C_6H_4$ - 4 - CH_3		
1b R1 = R2 = R3 = H	**2b**	40
1c R1 = F, R2 = R3 = H	**2c**	31
1d R1 = CF_3, R2 = R3 = H	**2d**	35
1e R1 = R2 = F, R3 = H		
1f R1 = R3 = H, R2 = CF_3		

Manganese dioxide from two commercial sources gave very similar results; both, by Karl - Fischer determination, contained about 25% water, sufficient for the hydrolysis of intermediate quinoneimine. Unfortunately, benzene was the only solvent found to afford greater than 10% conversion of **1b** to **2b**, although volumes of solvent could be reduced by use of Soxhlet procedures.

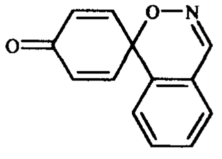
In view of competing polymerisation, it is not surprising that the formation of dienone is also sensitive to substituents in the anilines undergoing oxidation, with compounds **2c** and **2d** being obtained in 30% - 35% yield from **1c** and **1d** respectively, but with complex mixtures resulting from the oxidation of the anilines **1e** and **1f** which have an electron - withdrawing group *ortho* to the aniline.



3 R = $CH_2C(CH_3)_2OH$



4 R = $CH_2C(CH_3)_2OH$



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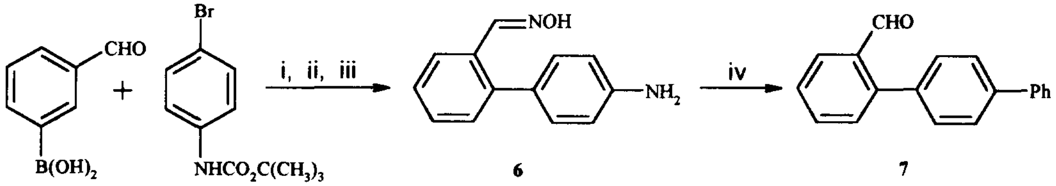
Support for the intermediacy of a diradical in the conversion of aniline to dienone is provided by an attempt to prepare a quinone mono - ketal by the oxidation of the aminophenoxypropanol **3**. The sole product of the reaction[9] was the azobenzene **4**, presumably formed by intermolecular coupling of amino radicals following the failure of the tertiary alcohol in the side chain to undergo one - electron oxidation.

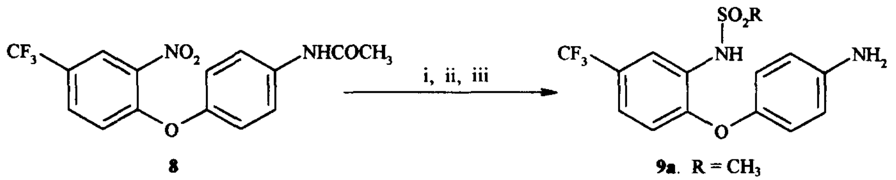
Since spirocyclic dienones have been synthesised by the oxidative cyclisation of phenolic oximes[10], the amino - oxime **6**, prepared as shown in Scheme 2, was subjected to manganese dioxide oxidation, with the aim of obtaining **5**.



i) $Pd(Ph_3P)_4$; ii) CF_3CO_2H; iii) H_2NOH; iv) MnO_2, C_6H_6.

Scheme 2.

From the reaction was isolated in low yield terphenylaldehyde **7** as the only product[11]. It has subsequently been reported[12] that active manganese dioxide is an efficient reagent for the conversion of oximes to aldehydes, and presumably it transformed **6** to the corresponding aminoaldehyde, but it is not clear why this aniline, in benzene solution, oxidised to the Gomberg - Hey product, rather than giving an azobenzene corresponding to **4**.



9a. R = CH_3
9b. R = C_6H_4 - 4 - CH_3

i) H_2 / Pd - C; ii) RSO_2Cl / pyridine; iii) 2M HCl.

Scheme 3.

The oxidation of anilines can, however, be extended to the formation of spirobenzoxazoledienones using a sulfonamide as a phenol equivalent in an intramolecular oxidative coupling[13]. The diphenylether **8**, readily available[1] from 4 - acetamidophenol and 4 - chloro - 3 - nitrobenzotrifluoride was converted (Scheme 3) to the sulfonamidophenoxyanilines **9a** and **9b**, which on treatment with manganese dioxide in refluxing benzene afforded the spirobenzoxazoles **10a** and **10b**, respectively, in 50% yield. The structures of these dienones was confirmed by their synthesis, in similar yield, by the oxidation of the synthetically less accessible sulfonamidophenols **11a** and **11b**. This provides easy access to stable examples of *p* - benzoquinone hemiaminal ethers, the chemistry of which is presently under investigation.

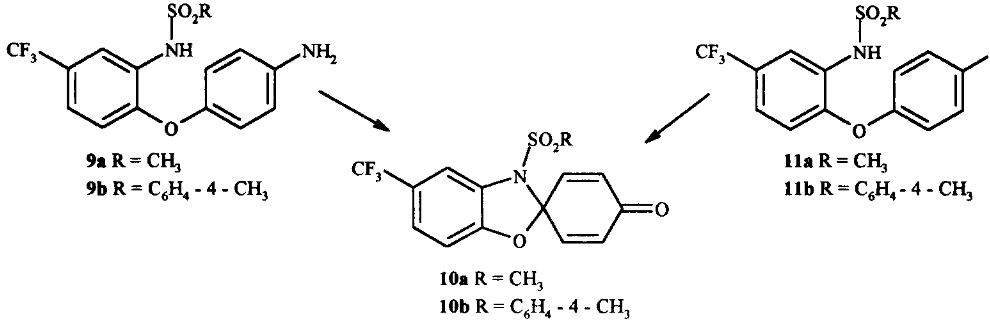


Figure 1.

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9. 4,4 - Bis (2 - hydroxy - 2 - methylpropyloxy)azobenzene (4). Yield 48%, mp 165°c. δ_H 1.25 (12H, s, $4CH_3$), 3.88 (4H, s, OCH_3), 7.03 (4H, d, ar), 7.9 (4H, d, ar). (Found: M^+ 358.1913. C, 66.5; H, 7.1; N, 7.7. $C_{20}H_{26}N_2O_4$ requires *M* 358.1892, C, 67.0; H, 7.3; N, 7.8%).
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11. *p* - Terphenylaldehyde (7). Yield 8%, mp 95°c. ν (KBr) 1684 cm-1 (C=O), δ_H 7.4 - 8.1 (13H, m, ar), 10.06 (1H, s, CHO). (Found: M^+ 258.1032. $C_{19}H_{14}O$ requires *M* 258.1044).
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