

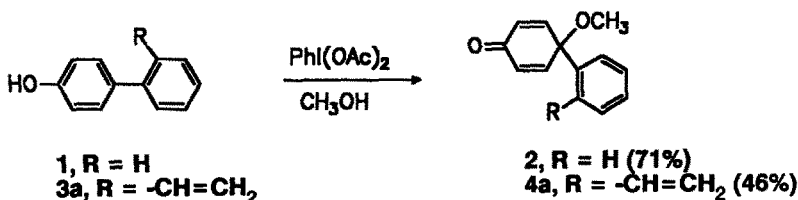
## SPIRO-ANNULATED 2,5-CYCLOHEXADIENONES VIA OXIDATION OF 2'-ALKENYL-*p*-PHENYL PHENOLS WITH IODOBENZENE DIACETATE

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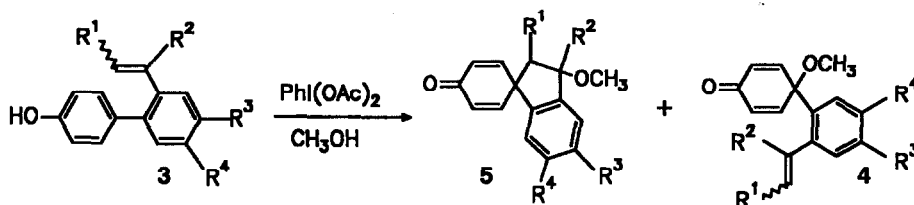
**Summary:** The oxidation of 2'-alkenyl-substituted *p*-phenyl phenols via iodobenzene diacetate gives spiro-annulated-2,5-cyclohexadienones.

Recently, the hypervalent iodine reagents, iodobenzene diacetate and its trifluoroacetate analog, have attracted interest as oxidants for phenolic compounds. Oxidation of *p*-substituted phenols in methanol produces the corresponding 4-methoxy-4-substituted 2,5-cyclohexadienones.<sup>1,2</sup> These oxidants have also been used to promote phenolic coupling reactions;<sup>3,4</sup> however, the yields for these reactions were only modest, ca. 30%. We have been interested in the anodic cyclization reactions of 2'-alkenyl-substituted *p*-phenyl phenols to spiro-annulated 2,5-cyclohexadienones.<sup>5</sup> To gain insight into the mechanism of these reactions and to explore other methods for effecting the above conversion, the iodobenzene diacetate oxidation of 2'-alkenyl-substituted *p*-phenyl phenols has been studied. We report herein the dramatic effect of structure on these iodobenzene diacetate-promoted oxidative cyclizations.

Early attempts to oxidize *p*-phenyl phenol **1** to the respective quinol ether with chemical oxidizing agents, DDQ and ferric chloride, were not successful. However, reaction of **1** with iodobenzene diacetate (1.1 equivalents) in methanol at room temperature gave **2** (71%). Having established conditions for oxidation of *p*-phenyl phenol, **3a** was reacted under similar conditions. However, only the *p*-quinol derivative **4a** was obtained from this reaction with no evidence for a product arising from cyclization of the olefinic side-chain to the oxidized phenolic ring.



Although the simple vinyl system **3a** did not afford the desired oxidative cyclization, this reaction is markedly dependent upon the substitution on the olefin and the aromatic ring (Table). Thus, the methyl-substituted system, **3b**, and the cyclopentenyl system **3c** afforded **5b** and **5c** in yields of 67% and 50%, respectively (entries 1 and 2). Although simple 2'-vinyl substituents ordinarily do not react to give spirodienones in good yield, a methoxy group *para* to the olefin linkage aids the oxidative cyclization reaction (entry 3). In contrast, a methoxy group *meta* to the olefinic center (entry 4) totally suppresses the cyclization reaction. However, a 2'-propenyl group counters the effect of a *m*-methoxy group (entry 5). Interestingly, having methoxy groups both *para* and *meta* to the olefinic center again results in good yield of the spirodienone (entry 6).

**Table. Iodobenzene Diacetate-Promoted Oxidative Cyclizations of 2'-Alkenyl-*p*-Phenyl Phenols<sup>a</sup>**

Entry	Compd	R <sup>4</sup>	R <sup>3</sup>	R <sup>2</sup>	R <sup>1</sup>	Yield 5 (%)	Yield 4 (%)
1	b	H	H	CH <sub>3</sub>	H	67	-
2	c	H	H	-(CH <sub>2</sub> ) <sub>3</sub> -	H	50	-
3	d	CH <sub>3</sub> O	H	H	H	56	34
4	e	H	CH <sub>3</sub> O	H	H	-	63
5	f	H	CH <sub>3</sub> O	CH <sub>3</sub>	H	48	-
6	g	CH <sub>3</sub> O	CH <sub>3</sub> O	CH <sub>3</sub>	H	76	-
7	h	-O-CH <sub>2</sub> -O-	H	H	H	34	9
8	i	-O-CH <sub>2</sub> -O-	CH <sub>3</sub>	CH <sub>3</sub>	H	79	-
9	j	-O-CH <sub>2</sub> -O-	H	H	CH <sub>3</sub>	75 <sup>b</sup>	-

a) For reactions showing a low material balance, the remaining material was a complex mixture of polar compounds.

b) A 6:1 mixture of *trans-cis* isomers was obtained.

The effect of methyl substitution on the yields of spirodienone could result from either an increased electron density on the double bond or stabilization of a benzylic intermediate involved in the reaction. Since the cyclization proceeds in comparable yield for **3i** and **3j** (entries 8 and 9) in which the methyl group is at the benzylic and terminal position, respectively, the reaction is best viewed as one involving symmetrical participation of the double bond in the cyclization process.

The chemistry serves as a simple and convenient procedure for preparation of spiro-annulated 2,5-cyclohexadienones and offers an alternative to anodic cyclization reactions.<sup>5</sup> Although the entire scope and limitations of the chemistry have not been established, the yield of the reaction is affected by ring and olefin substitution.

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- All structural assignments were consistent with IR, <sup>1</sup>H NMR, and exact mass or combustion analysis data. The mps for the products were: **2** 88-90 °C; **5b** 110-111 °C; **5c** 107-109 °C; **4d** 77-78 °C; **4e** 78-79 °C; **5f** 73-74 °C; **5g** 118-120 °C; **5h** 140-141 °C; **5i** 152-153 °C; *trans*-**5j** 176-177 °C; *cis*-**5j** 149-150 °C. Detailed procedures for preparation of the phenols **3a-j** will be furnished upon request.