

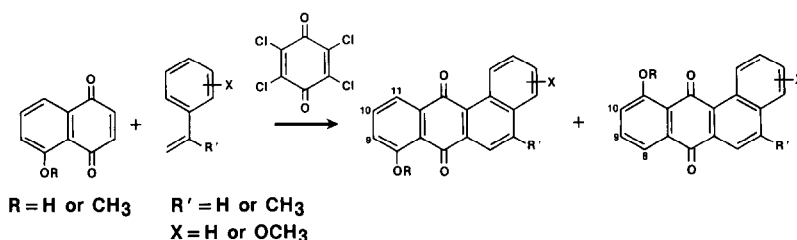
SUBSTITUTED STYRENE CYCLOADDITION TO JUGLONE AND DERIVATIVES-
REGIOCHEMICAL CONTROL

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Summary - No regiochemical directing effects could be attributed to methoxy styrene ring substituents in the cycloaddition of substituted styrene to juglone and its methyl ether. Control of quinone electron distributions, however, led to higher regioselectivity.

In a previous letter¹ we described the regioselectivity of the reactions of juglone, its methyl ether, and its acetate with styrene. In the absence of styrene substitution it seemed that electronic differences in the naphthoquinones could reasonably explain the results obtained. Reports by Boeckman et al^{2,3} have described the cycloadditions of a variety of non-styrene dienes to certain dienophiles and the authors have noted a strong relationship between regioselectivity and highly polarized dienes. To test this hypothesis on styrenes we have analyzed the products of the same reaction of methoxy ring-substituted and α -methyl-substituted styrenes with juglone and its methyl ether. In each case a toluene solution of 1 mmole of quinone, 3 mmoles of substituted styrene, and 2 mmole of chloranil was heated in a 105-110°C oil bath for 9 days. Due to the desire to evaluate regiochemical contributions of the reactants only, no catalysis was employed⁴, and due to the sluggish diene reactivity of the styrene, only 15 - 25% overall yields were obtained over a "convenient" reaction period of 9 days⁵.



The product mixtures were analyzed by two methods that were in excellent agreement. The first consisted of a gas chromatographic assay using the nematic phase of the liquid crystal BPhBT⁶ as stationary phase. This method has been shown to effect separations by size and shape

TABLE 1 - Substituted Benz[a]anthracene-7,12-diones Derived From Substituted Styrenes and Juglone

Benz[a]anthracene-7,12-dione	mp. (°C)	NMR (H-1 resonance, δ , in CDCl_3)
3,8-DiOCH ₃ -	206-7	9.56 (d, 9.7 Hz)
3,11-DiOCH ₃ -	186-7	9.35 (d, 9.7 Hz)
5-CH ₃ -8-OCH ₃ -	215-216	9.68 (m)
5-CH ₃ -11-OCH ₃ -	221-222	9.46 (m)
4,8-DiOCH ₃ -	226-227	9.18 (d, 9.7 Hz)
4,11-DiOCH ₃ -	217-218.5	8.91 (d, 9.7 Hz)
2,8-DiOCH ₃ -	199-201	9.20 (d, 2 Hz)
2,11-DiOCH ₃ -	191-193	9.02 (d, 2 Hz)

for molecules possessing similar volatilities and, in particular, is most effective in separating planar materials of different length-to-breadth ratios⁷. In this instance the quasi-planar dimethoxybenz[a]anthracene-7,12-diones exhibit characteristic differences in this ratio that lead not only to separation but to an ordered assignment of products⁸. This assignment was corroborated by the proton magnetic resonance spectra of the product diones isolated by column chromatography. The product diones are easily quantified by integration of either the intramolecularly-bonded hydroxyl proton in the 8- or 11-position or the distinctive C-1 protons whose resonance positions are strongly influenced by the paramagnetic deshielding of the C-12 carbonyl oxygen. This effect is strongly dependent upon oxygen substitution in the 11-position and is essentially independent of 2-,3-, or 4-substituents¹⁰.

All hydroxymethoxybenz[a]anthracene-7,12-diones produced in these reactions were quantitatively methylated by $\text{CH}_3\text{I}/\text{Ag}_2\text{O}$ in chloroform. This treatment facilitated gas chromatographic analysis and led to the isolation and characterization of the compounds in Table 1¹¹.

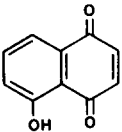
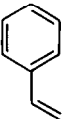
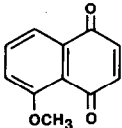
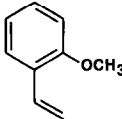
QUINONE	STYRENE					
		33:67	33:67	34:66	37:63	27:73
		77:23	78:22	77:23	76:24	80:20

TABLE 2 - RATIO OF "8." TO "11." SUBSTITUTED BENZ[A]ANTHRACENE-7,12-DIONES

The results of the analyses of the reaction of juglone and its methyl ether with a variety of styrenes is shown in Table 2. As can be seen, the proportions of 8- and 11-substituted products are essentially unaffected by ring substituted methoxy groups. The one case of α -substitution does appear to affect product distribution¹² slightly, but cannot compare to the effect of the quinone substituent. Other work in this lab¹³ has shown that methoxy styrene ring substitution also has little regiochemical directing effects on 6-methoxy-1,4-naphthoquinone. These results suggest that derivatization and catalysts that affect quinone electronics will strongly control regioselectivity. In accordance with this, the cycloaddition of m-methoxystyrene to juglone in the presence of boron triacetate gave a ratio of 11- to 8-substituted benz[a]anthracene-7,12-diones of 92:8. Other catalysts affecting quinone electronics have been employed in cycloadditions¹⁴ and may have even stronger directing effects.

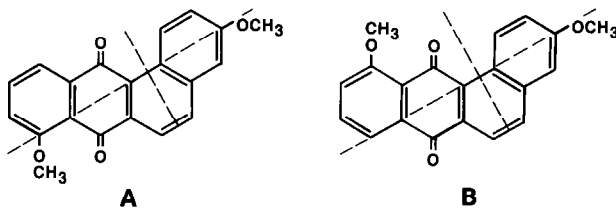
These results indicate that the electronic difference contributed by methoxy styrene ring-substitution has no regiochemical directing effects, in contrast to the strong regiochemical effects of the aliphatic dienes used by Boeckman^{2,3}. Although this may constitute an anomalous characteristic of the methoxyl group, it is not surprising that complications brought on by dienes, part of whose reactive centers lie within aromatic systems, may leave a valid comparison wanting. Therefore, the Boeckman results may be rationalized in systems using non-styrene type dienes whose mechanism fall within a well-defined scope. Here, however, it cannot be used as a forecasting tool.

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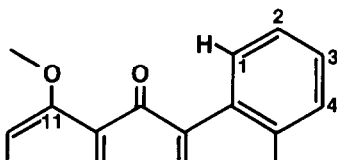
References and notes

1. W.B. Manning, Tetrahedron Lett., 1661 (1979).
2. R.K. Boeckman, Jr., T.M. Dolak, and K.O. Culos, J. Amer. Chem. Soc., **100**, 7098, (1978).
3. R.K. Boeckman, Jr., M.H. Delton, T.M. Dolak, T. Watanabe, and M.D. Glick, J. Org. Chem., **44**, 4396 (1979).
4. We have observed that catalysts such as trichloroacetic acid increase the rates of reactions in certain instances but have also found appreciable regiochemical effects using these catalysts.
5. During this period although little else occurred to consume the substituted quinones, the quantities of substituted styrenes were depleted considerably. It must be noted that we have not optimized reaction conditions but have arbitrarily chosen a fixed set of conditions to conduct the comparative studies.
6. G.M. Janini, G.M. Muschik, J.A. Schroer, and W.L. Zielinski, Jr., Anal. Chem., **48**, (1976).
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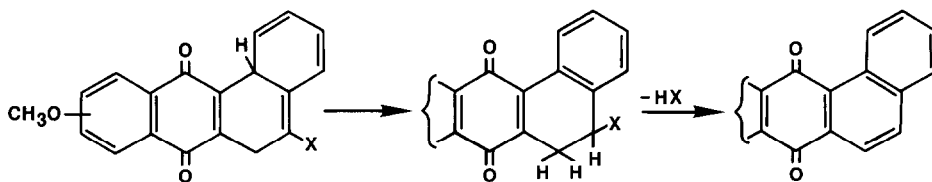
8. The liquid crystal stationary phase, in its nematic range, interacts with the solutes in a manner that retains the materials possessing the larger length-to-breadth ratio for a longer time. In the example shown below, the "length" of both A and B are the same. The "breadth" of B is greater than A, so the order of elution is B, then A.



9. The preparative separations were rather difficult but were conducted on Silicar CC-7 (Mallinkrodt) columns (500:1 ratio of adsorbent to material chromatographed) using gradients of either benzene in hexane or ethyl acetate in hexane.
10. The presence of the 11-methoxy group would be expected to affect the electron distribution of the C-12 carbonyl which deshields the C-1 proton.



11. All compounds yielded mass spectra and PMR spectra consistent with the expected structures.
12. Due to a rearrangement of the dihydro intermediates in these reactions [W.B. Manning and D.J. Wilbur. *J. Org. Chem.*, 45, 733 (1980)], other α -substituents, such as methoxy or halo, were not used. The rearranged intermediates in these cases have led to other products by elimination or aromatization, thereby complicating product analysis.



13. W.B. Manning and G.M. Muschik, *J. Chem. Eng. Data.* 25, 289 (1980).
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