Tetrahedron Letters No. 22, pp 2271 - 2274, 1972. **Pergamon Press. Printed in Great Britain.**

ANODIC COUPLING OF SIMPLE ARYL ETHERS. ELECTROCHEMICAL SYNTHESIS OF METHOXYBIPHENYL CATION RADICALS.

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(Received in UK 14 April 1972; accepted for publication 27 April 1972)

The oxidation of simple phenols (1) and aryl ethers (2) is generally accompanied by the formation of isomeric mixtures of biaryls and further oxidation products. Success has not been encountered during attempts to couple unsubstituted compounds such as phenol or anisole in high yields. We now report an excellent synthesis of methoxy biphenyls and related compounds from anodic oxidation of the corresponding aryl ethers in trifluoroacetic acid (TFA) or TFA-dichloromethane.

In general, the coupled products of phenols and aryl ethers are more easily oxidized than their precursors, a fact which contributes heavily to the complexity of phenol oxidation. We have previously reported the anodic coupling of 2,5-dimethoxytoluene in acetonitrile (3) and a preliminary survey of a number of methoxy-methylbenzenes in acetonitrile showed that coupling products could be obtained but due to extensive side reactions it was concluded that the method did not show much promise as a synthetic reaction (4). We have now found a way to circumvent the undesirable side reactions and thus obtain the coupled products in high yield. The extra-ordinary stability of organic cation radicals in TFA (5) or TFA-dichloromethane (6) allows the reaction to stop at the cation radical stage of the coupled product according to the equation:

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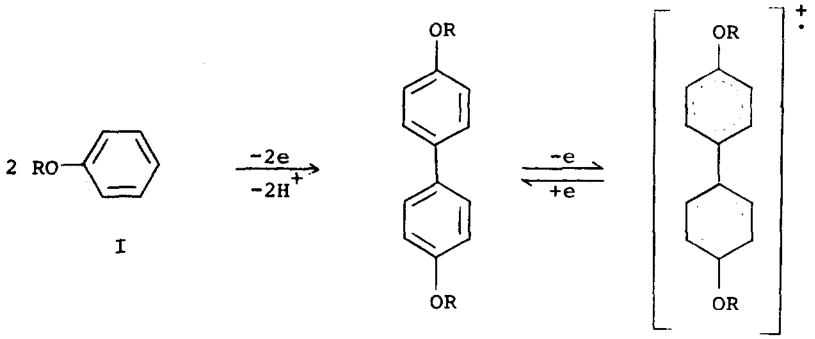

I

II

III

The mode of the reaction is clearly illustrated by the cyclic voltammetry of the anisoles in TFA-dichloromethane (1,2). The voltammogram for anisole (Figure 1a) shows an oxidation peak at +1.54 V* and the reduction peak for III appears at +0.92 V on the cathodic scan. Nearly identical behavior is shown for o-bromoanisole with the oxidation of the substrate taking place at +1.76 V and the reduction of the dimeric cation radical at + 1.23 V (Figure 1b). The third example, 2-methylanisole shows the corresponding peaks at +1.33 V and +0.75 V (Figure 1c). Quantitative yields of solutions of the cation radicals (III) were obtained by voltammetric oxidation at low concentrations (1 mM), however, exhaustive electrolyses on the preparative scale were accompanied by solution redox reactions and some byproduct formation. Nearly quantitative yields were obtained by carrying out the oxidation of 2 mmol of the substrates in TFA-dichloromethane (50 ml) to 50% conversion. Preparative electrolyses were carried out in a two compartment cell at a platinum gauze electrode. After

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*All voltages refer to oxidation or reduction at a platinum electrode versus the saturated aqueous calomel electrode.

oxidation, the polarity of the electrodes was reversed and electrolysis continued in order to reduce the cation radicals (III) to the biphenyls (II). The pure products were isolated by evaporating the solvent under reduced pressure, dissolving in a minimum amount of chloroform and separating by preparative thin layer chromatography. The identity of the products was established by mass, nmr, and ir spectra and comparision to the authentic compounds when available. We have been successful in preparing dimers of the following simple ethers; anisole, diphenyl ether, o-methylanisole, o-bromoanisole, and 2,6-dimethylanisole.

In contrast to our previous anodic work (3,4), we observe only para coupling in TFA or TFA-dichloromethane. In fact, when the para position is blocked, as in p-methoxytoluene, the reaction becomes complex and the cation radical of the biphenyl cannot be detected. Further work is in progress to extent the scope of the coupling reaction and to gain a better understanding of the effect of TFA on anodic reactions in general. The latter cannot be due only to acidity since it has recently been reported that pure TFA is not sufficiently strong to protonate water (7).

Acknowledgement. A. R. and V. D. P. wish to acknowledge the Swedish Natural Science Research Council for a grant convering travel expenses between Lund and Copenhagen.

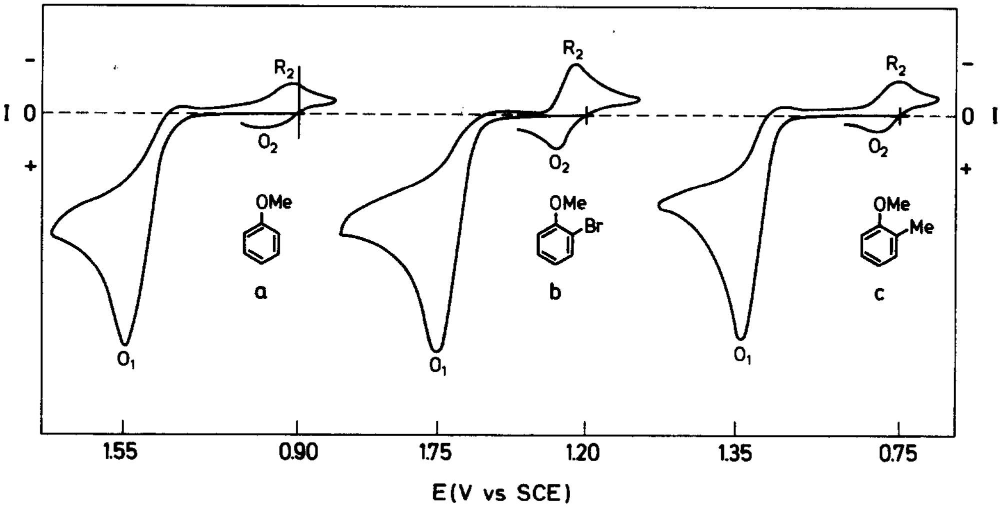

Figure. Cyclic voltammetry of the anodic coupling of anisoles; a. anisole, b. *o*-bromoanisole, c. *o*-methylanisole, in dichloromethane-TFA (2-1). Voltage sweep rate = 150 mV/sec.

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