Tetrahedron Letters,Vol.26,No.40,pp 4831-4834,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

ANODIC OXIDATION STUDIES OF OXYGENATED BIPHENYLS. CONVENIENT SYNTHETIC ROUTES TO CERTAIN FUNCTIONALIZED BIPHENYLS[1]

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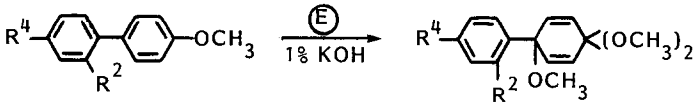
Summary. *The anodic oxidation of oxygenated biphenyls produces phenyl-substituted p-quinol ether ketals in good-to-excellent yield. These compounds are useful substrates for preparation of more highly functionalized biphenyls.*

Syntheses of biphenyl systems have been of continuing interest in organic chemistry since these compounds are often convenient building blocks for natural products,[2a] and certain biphenyls[3] and their higher analogs[3,4] (p-terphenyls) behave as liquid crystals. The classical Ullmann[2a-c] and Gomberg[2a] reactions for preparation of biphenyls are extremely useful for the syntheses of selected systems. However, the reaction conditions and purification problems complicate the preparation of many biaryls of synthetic interest. Recent work[2a,5] has focused on improved methods for the synthesis of biphenyls, and we report herein a strategy for the functionalization of biphenyls readily available via conventional methods.

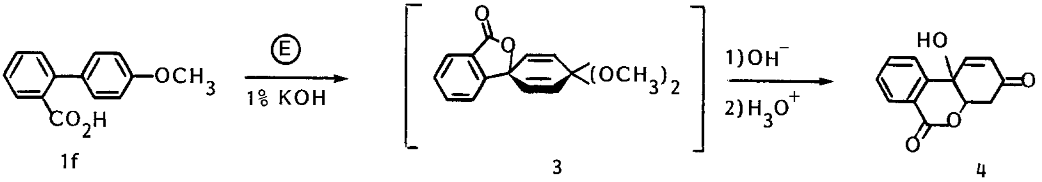
While anodic coupling reactions of aromatic rings to form phenolic coupling products and biphenyls have been extensively studied,[6] there are few reports[7] of the products from anodic oxidation of biphenyls themselves. The anodic oxidation chemistry of 4,4'-dimethoxybiphenyl, **1a**, was studied first since it is an aryl analog of 1,4-dimethoxy aromatic systems, compounds which undergo high-yield electrochemical oxidation to quinone bisketals.[8] Single-cell, constant current (2 amp) anodic oxidation[9] of **1a** (9 g) as a slurry in 1% methanolic potassium hydroxide (750 mL) using a platinum gauze anode was followed by UV spectroscopy or TLC and was judged to be complete after 8 hours of electrolysis (14% current efficiency). Conventional workup afforded an oil which was separated from minor impurities by short path distillation and assigned as **2a** (86%) on the basis of analytical and spectroscopic data. Similar electrochemical oxidations of the biphenyl derivatives **1b-e** gave the results recorded below. Even 2'-methyl-4-methoxybiphenyl, **1c**, in which the methyl group should further remove the aryl rings from coplanarity, afforded a good yield of product. It was important that the alcohol and aldehyde



1a, R^2 = H, R^4 = OCH_3	2a (86%)
b, R^2 = R^4 = H	b (74%)
c, R^2 = CH_3, R^4 = H	c (71%)
d, R^2 = $CH_2OSi(t\text{-}Bu)(CH_3)_2$, R^4 = H	d (96%)
e, R^2 = $CH(OCH_3)_2$, R^4 = H	e (83%)

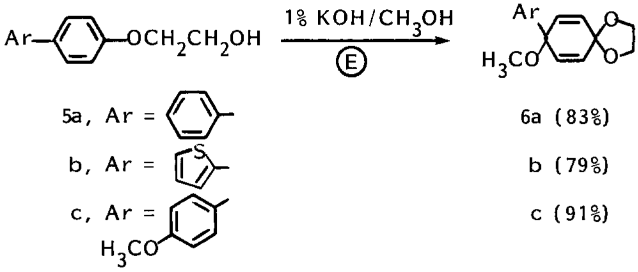
functionalities in **1d,e** be protected since anodic oxidation of the unprotected systems gave complicated reaction mixtures.

The initial anodic addition product could not be isolated for the carboxylic acid derivative **1f**. Anodic oxidation of **1f** gave instead--after workup of the reaction mixture and acidification--the lactone **4**. The structural assignment for **4** rests on its combustion analysis, mass spectrum, and ^{13}C NMR and ^{1}H NMR spectra with associated decoupling and COSY experiments.



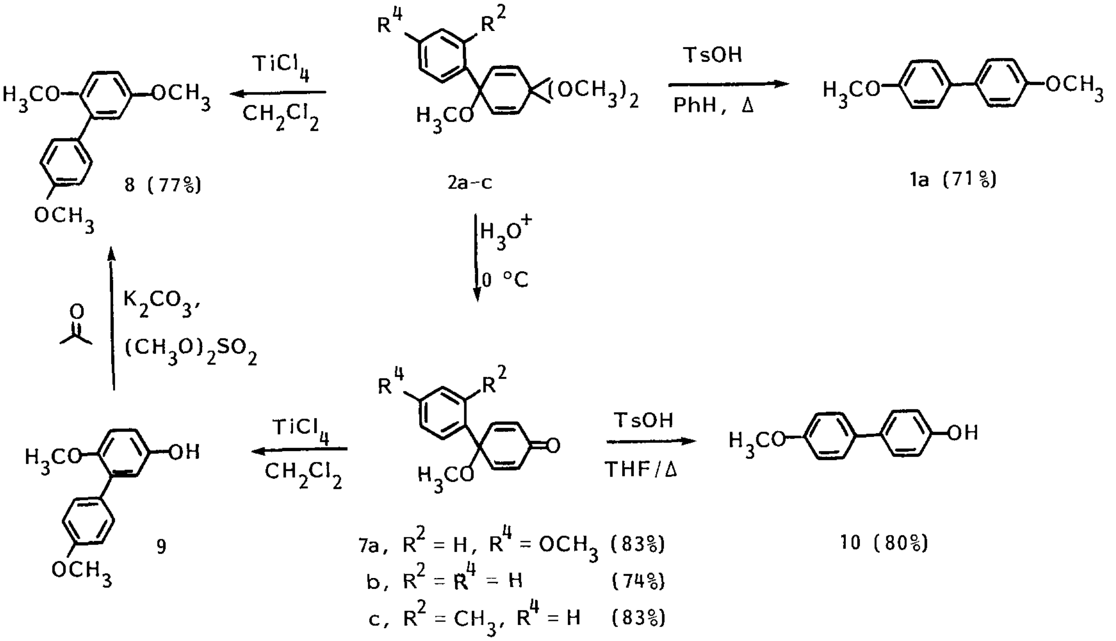
The ketal **3** is a logical precursor for the formation of **4**, and hydrolysis studies described later demonstrate that intramolecular Michael addition is a common process for certain *p*-quinols.

While the quinol ether ketals **2** can be handled in base-washed glassware and stored indefinitely at -20 °C, the dimethyl ketal linkage is quite acid labile, and methods to prepare the more stable ethylene glycol ketal were examined. Anodic oxidation of ethers **5a-c** again



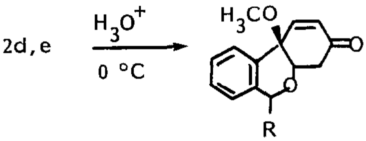
afforded the respective quinol ether ketals **6a-c** in excellent yield with increased efficiency (current efficiency$\sim$30%).[10] The anodic oxidation of **5c** is especially interesting since both rings of the biphenyl possess an ether substituent at the *p*-position, yet **6c** was formed with excellent selectivity.

A large part of the utility of the above anodic oxidations lies with the chemistry of the *p*-quinol ethers obtained from acid hydrolysis. Three reaction pathways have been observed for *p*-quinol ether ketals with acids, as illustrated by the reactions of **2a** (shown below). Aqueous hydrolysis of **2a-c** under mild conditions gave the quinol ethers **7a-c** in good yields. Thus, in two synthetic steps--anodic oxidation followed by hydrolysis--a readily available symmetrical biphenyl **1a** has been transformed into a *p*-quinol ether which can in principle be converted to a number of unsymmetrical biphenyls via standard chemical transformations. When **2a** was treated with titanium tetrachloride in methylene chloride at low temperature, aryl migration afforded **8** in 77% isolated yield. Finally, when **2a** was heated with a trace of anhydrous *p*-toluenesulfonic acid in benzene, **1a** was the major isolated product.[11]



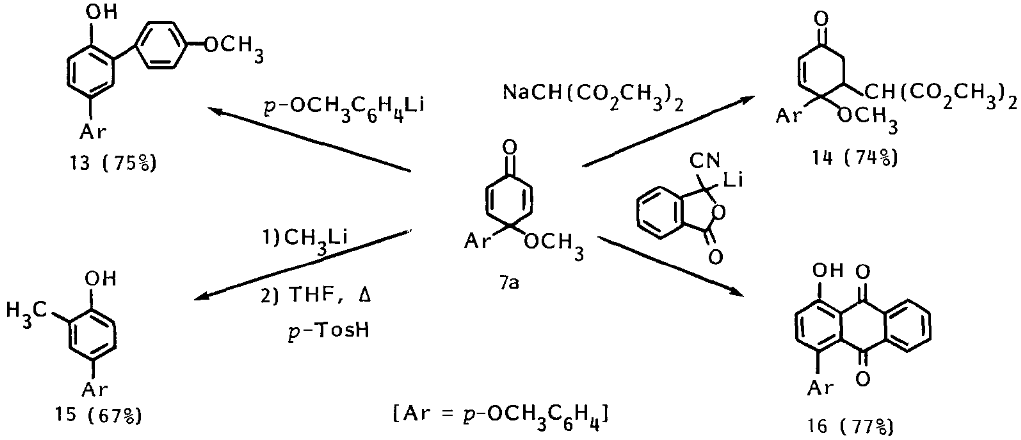
7a, $R^2 = H$, $R^4 = OCH_3$ (83%)
b, $R^2 = R^4 = H$ (74%)
c, $R^2 = CH_3$, $R^4 = H$ (83%)

As implied from the chemistry of **1f**, hydrolysis of systems (**2d,e**) having nucleophilic groups at the original 2'-position affords products of intramolecular Michael addition (**11,12**).



11, R = H (53%)
12, R = OH (70%)

While organometallic additions[8,12] to these p-quinol ethers have not been extensively studied, some representative 1,2-additions of organometallics and the 1,4-initiated reactions have been successfully performed with **7a** as illustrated below. Thus, these readily available p-quinol ethers are attractive candidates for the synthesis of functionalized biphenyls and their higher homologues.[13]



[Ar = p-$OCH_3C_6H_4$]

Acknowledgment. We wish to thank the National Science Foundation for financial support, Mr. Carl Engelman for the COSY and decoupling studies, and Mr. Tony Sercel for some preliminary experiments.

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9) The experimental set-up for these types of anodic oxidations has been described in detail: D. R. Henton, R. L. McCreery, and J. S. Swenton, *J. Org. Chem.* **1980**, *45*, 369.

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11) Reductions of this type are commonly observed when quinone monoketals are heated with acid.^{8} Apparently, methanol is oxidized to formaldehyde in what is formally a disproportionation reaction.

12) The complications of reduction accompanying organometallic additions to quinone monoketals^{7} and quinol acetates are well known and have been studied mechanistically in the latter series of compounds: F. Wessely, L. Holzer, H. Vilcsek, *Monatsh. Chem.* **1952**, *83*, 1255; *Ibid.* **1953**, *84*, 655; O. Polansky, E. Schenzel, F. Wessely, *Ibid.* **1955**, *87*, 24; B. Miller, E. R. Matjeka, J. G. Haggerty *J. Org. Chem.* **1984**, *49*, 3121 and references cited therein.

13) The compounds reported herein showed IR and ^{1}H NMR spectra in agreement with those for assigned structures and correct exact mass measurements. The quinol ether ketals were isolated by chromatography on Activity III neutral alumina and were used directly in the next step. Phenol **9** was not purified but was converted directly to **8** for identification. Compounds obtained as crystalline solids showed the following mp °C (all other compounds reported were obtained as colorless thick oils): **1a**, 174-175; **1b**, 77-79; **1f**, 142-143; **4**, 72-74; **5a**, 109-110; **5b**, 123-125; **5c**, 130-133; **7a**, 112-114; **7b**, 85-87; **7c**, 87-88; **8**, 57-60; **10**, 171-173; **11**, 79-81; **12**, 170-172; **13**, 114-116; **14**, 118-120; **15**, 103-105; **16**, 199-201.

(Received in USA 24 May 1985)