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Carbon - Oxygen Coupling Reactions with 2,2',3,3',5,5'-Hexaphenyl-(1,1'-biphenyl)-4,4'-dioxyl

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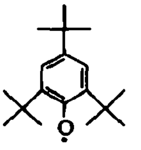
ABSTRACT: The synthesis of novel diether and diacetal compounds through carbon-oxygen coupling reactions of active methylene groups contained in benzylic and allylic compounds and in aliphatic ethers by reaction with 2,2',3,3',5,5'-hexaphenyl-(1,1'-biphenyl)-4,4-dioxyl, generated with potassium ferricyanide in an alkaline solution from the parent biphenol, is described.

The oxidation of hindered phenols to form relatively stable phenoxy radicals (e.g. **1** and **2**) in the presence of a variety of oxidizing agents, such as PbO_2, Ag_2O, MnO_2 and $K_3Fe(CN)_6$, has been intensively studied[1]. Potassium ferricyanide, in an alkaline solution, has been commonly used for the preparation of phenoxy radicals[2] from hindered phenols. These hindered phenols and their corresponding phenoxy radicals are important as stabilizers because they function as inhibititors of autooxidation reactions of organic compounds[3].



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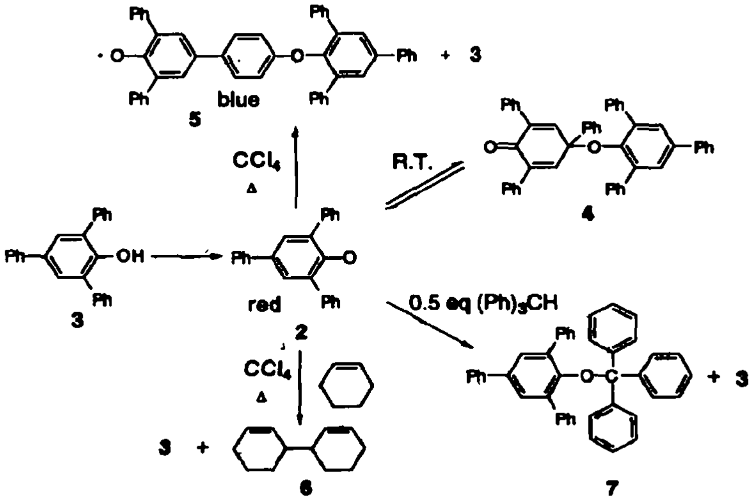
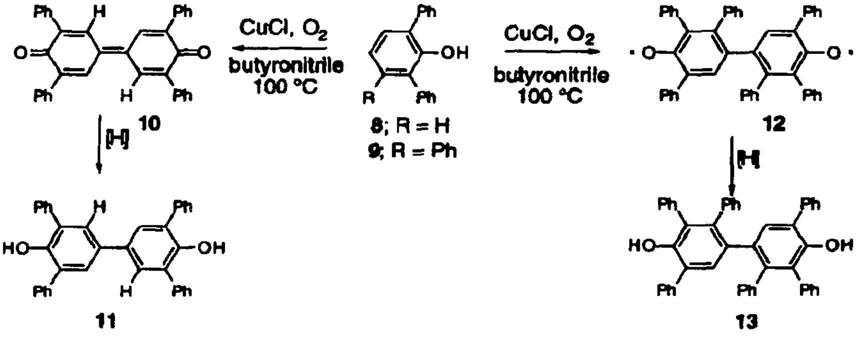
Dimroth and coworkers[4,5] have shown that the phenoxy radical **2** under an inert atmosphere at room temperature is in equilibrium with its corresponding quinol ether dimer **4**. In refluxing carbon tetrachloride the carbon-oxygen coupled dimer **5** was obtained. In the presence of an equivalent amount of cyclohexene in refluxing carbon tetrachloride the carbon-carbon coupled compound 3,3'-bicyclohexenyl **6** and phenol **3** were obtained. At room temperature when 2 equivalents of phenoxy radical **2** were reacted with 1 equivalent of triphenylmethane the carbon-oxygen coupled ether **7** was obtained in 80% yield along with phenol **3** (Scheme 1). The stability of phenoxy radical **2** and its reactivity towards a variety of activated methylene groups to give either the carbon-carbon coupled or carbon-oxygen coupled derivatives depending on the stoichiometry of the reactants have been studied.[5]

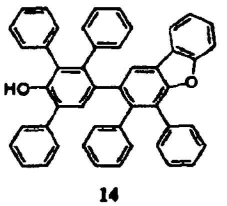


Scheme 1

We have previously synthesized 2,2',3,3',5,5'-hexaphenyl-(1,1'-biphenyl)-4,4'-diol[6,7] (**13**; HPBP) by the oxidative coupling of 2,3,6-triphenylphenol **9**. Oxidative coupling of 2,6-diphenylphenol **8** yields the very insoluble diphenoquinone **10** which preciptates from the reaction mixture as the reaction proceeds.[8] However, oxidative coupling of **9** under the same conditions yields a highly colored solution which remains homogeneous. Addition of a reducing agent such as hydrazine yields **13**. Reoxidation of **13** with either Ag$_2$O or K$_3$Fe(CN)$_6$ in an inert solvent gives an intensely permanganate colored solution. The product, presumably the bisphenoxy radical **12**, is very soluble and can only be recovered by evaporation of the solvent. The steric hindrance provided by the phenyl groups in the 3,3'-positions forces the biphenol **13** into a non-coplanar geometry and increases its oxidation potential. The oxidation potential[9] of the dianionic species of **13** is -228 mV which is 112 mV more negative than the dianionic species of **11**, suggesting that biphenol **13** is more difficult to oxidize than **11**.



Biphenoxy radical **12** is extremely stable in air both in solution and in solid form. When heated in a solution of o-dichlorobenzene at 120 °C under an inert atmosphere **12** slowly decomposes within 24 hours to yield the dibenzofuran derivatives **14** and **15**. It has been shown by Kim[10] that reacting the pregenerated radical **12** with diphenylmethane **16** in refluxing benzene gives the monofunctional carbon - oxygen coupled compound **17**. The reaction of **10** with **16** requires higher temperatures (140 °C/chlorobenzene) and the products are the diol **11** and 1,1,2,2-tetraphenylethane as previously demonstrated for the reaction with 3,3',5,5'-tetra-t-butyldiphenoquinone at 260°C.[11]



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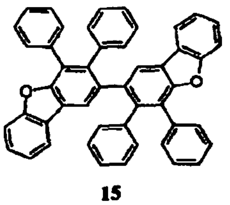

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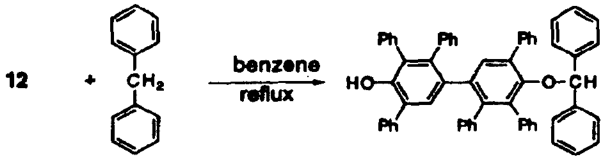
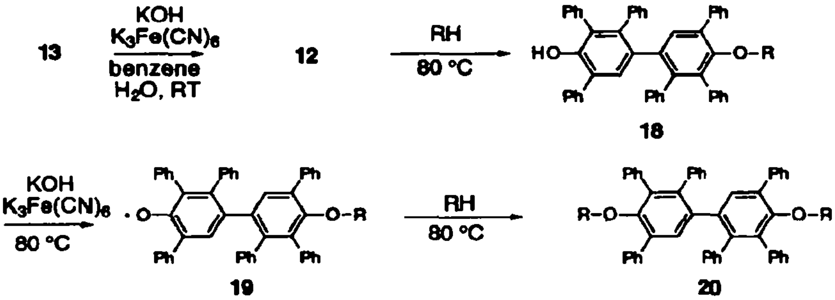


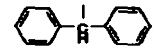
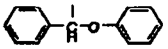
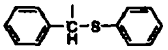
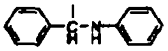
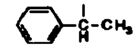
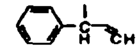
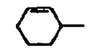
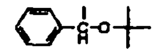
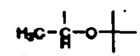
We now report an efficient synthesis of diether and diacetal derivatives **20** from the reaction of biphenoxy radical **12** with a series of activated methylene compounds in a two-phase oxidation at 80 °C for several hours in the absence of oxygen. Quantitative yields of the diether derivatives were obtained (see Table 1) except for N-phenylbenzylamine which gave a mixture of N-benzylideneaniline and benzaldehyde. Allylbenzene gave isomeric products coupled in both the 1 and 3 positions of the allyl group as determined by NMR analysis.

The large difference in reaction times for the formation of the various diether and diacetal compounds



can presumably be attributed to the rate at which the intermediate methylene radical is generated, as Dimroth and coworkers[5] have shown. The reaction times appear to follow the same trend as the bond dissociation energies (D°_{298}) of the methylene proton. For example, diphenylmethane (D°_{298} of 81.4 Kcal/mol)[12] reacts within 3 hours while ethylbenzene (D°_{298} of 85.4 Kcal/mol)[12] reacts within 9 hours.

Table 1: Carbon - Oxygen Coupled Compounds

R	Rxn Time (hours)	m.p. (°C)	% Isolated Yield	% Conversion[a]	Chemical Analysis %calc. [found]	
					C	H
	3	243-245	97	100	91.14 [90.77]	5.58 [5.33]
	5	242-243	80	90	88.24 [88.13]	5.40 [5.20]
	1.5	145-148	79	100	85.52 [85.95]	5.24 [5.48]
	42	---	--	NR	---	---
	9	245-248	97	100	90.32 [90.05]	5.92 [5.94]
	5[b]	---	85	96	---	---
	21	252-253	90	100	89.74 [89.57]	6.28 [6.39]
	2	240-243[c]	86	100	81.14 [80.87]	5.84 [5.60]
	20	213-217[c]	80	100	85.48 [85.44]	6.93 [7.19]

NR= No reaction

a. Based on HPLC analysis; b. Two isomeric diether products; c. Decomposition temperature

The stability of the biphenoxy radical **12** combined with its high oxidation potential leads to unique chemistry which we are currently exploring. Other hindered biphenols are being synthesized and studied. The cleavage of the diethers and diacetals in the presence of acid to regenerate the biphenol, along with the respectve alcohol or aldehyde, is currently under study.

General Procedure:

To a solution of biphenol **13** (0.503 g; 0.783 mmol) in 20 mL of benzene was added a solution of potassium ferricyanide (2.63 g; 8.00 mmol) and potassium hydroxide (0.455 g; 8.11 mmol) in 15 mL of distilled water. The organic layer immediately turned dark red in color and the mixture was stirred vigorously at room temperature for 2 hours at which point diphenylmethane (0.544 g; 3.23 mmol) was added and the reaction mixture was heated to reflux for 3 hours. The organic layer was washed several times with water (3 x 25 mL), extracted, dried over Na_2SO_4, filtered and the filtrate was evaporated to dryness. The crude product was recrystallized from a methanol-chloroform solution to yield 0.740 g (97%) of the diether compound (**20**; R = Ph_2CH-), mp 242-245 °C.

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9. The oxidation potentials of the hindered biphenols were determined using differential pulse voltametry done on a BAS 100A electrochemical analyser. The working electrode was a glassy carbon electrode disk (2mm diameter). The counter electrode was a platinum wire and the reference electrode was Ag/Ag^+ (0.1M $TBAPF_6$ / CH_3CN). Millimolar quantities of sample were used in an acetonitrile - water solution (9:1) with 0.01M tetra-n-butylammonium chloride as the supporting electrolyte and 0.01M tetra-n- butylammonium hydroxide as the base used to generate the anionic species.
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