

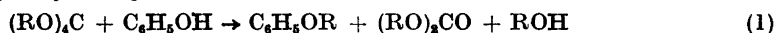
The Reaction between Phenols and Orthoesters. A New Synthesis of Aryl Alkyl Ethers

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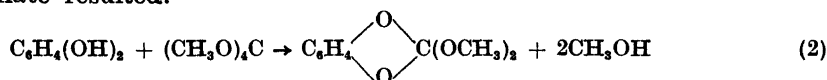
It has been shown that alkyl orthocarbonates and phenols react under very mild conditions with the formation of aryl alkyl ethers. The reaction between phenols and ethyl orthoacetate and ethyl orthoformate was also studied in some detail. Only by the former reaction were aryl alkyl ethers formed as the ultimate products.

In an attempt to prepare some carbon analogues of the phenoxyalkoxysilanes from alkyl orthocarbonates and phenol it was found that the reaction produced phenyl alkyl ethers, dialkyl carbonates, and alcohols instead of the expected phenyl alkyl orthocarbonates.



This reaction seems, with certain exceptions, to be a general one for phenols. The yield of ethers from phenol is good (80—90 %), but methyl groups in the *ortho* position to the hydroxyl group diminish the yield appreciably. In the case of 2,6-di-*tert.*-butyl-*p*-cresol no reaction took place. This is certainly caused by the shielding of the hydroxyl group by the butyl groups.

Among the dihydric phenols investigated resorcinol reacted regularly yielding the mono- and diethers while no ethers were formed in the reaction between pyrocatechol and methyl orthocarbonate. Instead *o*-phenylene dimethyl orthocarbonate resulted.

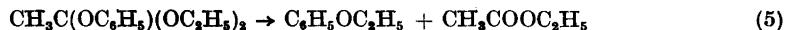


The mode of reaction between phenols and some other types of orthoesters was also examined in some detail. Phenol and ethyl orthoacetate reacted with the formation of phenyl diethyl orthoacetate



and a small amount of diphenyl ethyl orthoacetate. Depending on the conditions used for the synthesis smaller or larger amounts of decomposition products were also formed.

Phenyl diethyl orthoacetate was previously prepared by McElvain and Kundiger¹ from ketene diethyl acetal and phenol. They reported that it decomposed on distillation at atmospheric pressure yielding phenetole and phenyl acetate*. The phenetole and the ethyl acetate probably originate from the reaction**.



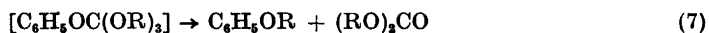
The particular reactions by which the ethyl alcohol, phenol and phenyl acetate are formed are obscure as yet. The reaction between *p*-nitrophenol and ethyl orthoacetate furnished directly *p*-nitrophenetole in fair yield. This result is in accordance with the observation made by McElvain and Kundiger¹ that aryl alkyl ethers were formed in high yields from ketene diethyl acetate and phenols with negative substituents, while no aryl diethyl orthoacetates could be isolated.

Phenol reacted with ethyl orthoformate in much the same way as with ethyl orthoacetate; the main product being phenyl diethyl orthoformate. Contrary to the decomposition of phenyl diethyl orthoacetate the phenyl diethyl orthoformate yielded no phenetole on distillation at atmospheric pressure. Only ethyl formate, ethyl alcohol, and a black brittle resin were isolated.

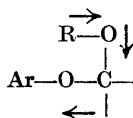
The course of the reaction between phenols and ethyl orthoacetate throws some light on the related reaction between phenols and alkyl orthocarbonates. It must be assumed that a labile phenyl alkyl orthocarbonate is formed,



which decomposes according to eqn. 7***



The instability of a structure containing one aryloxy group and three alkoxy groups bonded to a carbon atom must be due mainly to the presence of the aryloxy group since alkyl orthocarbonates are quite stable compounds at moderate temperatures. The resonance in the aryloxy group is likely to originate an electron displacement in the manner denoted by the arrows in the following formula,



* No mention is made in the cited paper of the simultaneous formation of ethyl alcohol, phenol, and ethyl acetate. (See the experimental part).

** In an attempt to prepare ketene acetals by thermal decomposition of orthoesters at 250–300°, Staudinger and Rathsam² observed the following reaction



for ethyl orthoformate, ethyl orthoacetate and ethyl orthopropionate.

*** In 1911 Einhorn and Rothlauf³ showed that certain aryl alkyl ethers could be prepared from the corresponding aryl alkyl carbonates (ArOCOOR) by heating them to 200–300° for long periods.

thereby causing the decomposition according to eqn. 7. The proximity of the R-group and the oxygen atom of the aryloxy group is probably also of significance for the decomposition. The existence of phenyl diethyl orthoacetate and the corresponding orthoformate shows that the stability increases when a methyl group or a hydrogen atom is substituted for an ethoxy group in the hypothetical phenyl triethyl orthocarbonate. This fact can be ascribed to the increased electron density at the central carbon atom, whereby the electron withdrawal from the R-group is opposed. Again, the presence of a *p*-nitro group on the benzene ring enhances the pull exercised by the aryloxy group on the electrons, thus making the *p*-nitrophenyl alkyl orthoester (*e. g.* orthoacetate) more susceptible to decomposition.

Orthoesters and especially alkyl orthocarbonates might be valuable in certain instances as alkylating agents for phenols because of the mild conditions under which the reaction proceeds. The orthocarbonates may be prepared conveniently from thiocarbonylperchloride (Cl_3CSCl) and sodium alkoxides⁴.

It is interesting to note the difference in their reaction with phenols of alkyl orthocarbonates and the corresponding organosilicon compounds, the tetraalkoxysilanes. In the latter case quite stable aryloxyalkoxysilanes are formed; no thermal decomposition of these compounds has been observed⁵. A contributive reason for this circumstance is, undoubtedly, the non-existence of compounds with silicon-oxygen double bonds⁶.

EXPERIMENTAL

Phenol and methyl orthocarbonate. A mixture of methyl orthocarbonate (27.2 g, 0.2 mole) and phenol (18.8 g, 0.2 mole) was slowly heated at atmospheric pressure. An azeotrope (10.2 g) mixture of methyl alcohol and dimethyl carbonate was distilled over between 62–64°, $n_D^{20} = 1.348$. Further distillation yielded dimethyl carbonate (9.7 g) b.p. 90–91°, $n_D^{20} = 1.369$, and a mixture (5.6 g) of the latter compound and methyl orthocarbonate b.p. 91–113°, $n_D^{20} = 1.377$. The residue, after removal of some phenol by alkali, was distilled under vacuum yielding *anisole* (18.8 g, 87 %) b.p. 46° (12 mm). (Found: OCH_3 , 28.4. Calc. for $\text{C}_7\text{H}_8\text{O}$: OCH_3 , 28.7).

Phenol and ethyl orthocarbonate. Ethyl orthocarbonate (38.5 g, 0.2 mole) and phenol (18.8 g, 0.2 mole) yielded on treatment as above a mixture (10.0 g) of ethyl alcohol and a small amount of diethyl carbonate, b.p. 78–79°, $n_D^{20} = 1.368$, and diethyl carbonate (20.1 g) b.p. 125–126°, $n_D^{20} = 1.384$. From the residue, after removal of some phenol, was obtained *phenetole* (20.7 g, 85 %) b.p. 55° (10 mm) $n_D^{20} = 1.507$. (Found: OC_2H_5 , 36.7. Calc. for $\text{C}_9\text{H}_{10}\text{O}$: OC_2H_5 , 36.9).

Alkylation of various phenols using methyl orthocarbonate. The general procedure for the alkylation of phenols using methyl orthocarbonate was the following. The phenol and methyl orthocarbonate were mixed in the molar ratio 1:1.2 for monohydric phenols and 1:2.5 for dihydric phenols. Gentle heating of the mixture was continued as long as any methyl alcohol was being distilled after which the dimethyl carbonate and residual methyl orthocarbonate were distilled rapidly. The residue was taken up in ether and this solution extracted with dilute sodium hydroxide to remove any phenol. After drying the solution and distilling the ether, the residue was fractionated under vacuum.

In this way there was obtained: From *o*-cresol (10.8 g, 0.1 mole) *o*-cresyl methyl ether (6.6 g, 54 %) b.p. 68° (18 mm). (Found: OCH_3 , 25.3. Calc. for $\text{C}_9\text{H}_{10}\text{O}$: OCH_3 , 25.4.). From *m*-cresol (10.8 g, 0.1 mole) *m*-cresyl methyl ether (7.0 g, 57 %) b.p. 71–72° (17 mm). (Found: OCH_3 , 25.5. Calc. for $\text{C}_9\text{H}_{10}\text{O}$: OCH_3 , 25.4). From 2,6-xyleneol (12.2 g, 0.1 mole)

2,6-xylyl methyl ether (3.0 g, 22 %) b.p. 72° (15 mm). (Found: OCH₃, 22.8. Calc. for C₈H₁₀O: OCH₃, 22.8). From resorcinol (11.0 g, 0.1 mole) *resorcinol monomethyl ether* (2.0 g, 16 %) b.p. 137° (18 mm). (Found: OCH₃, 25.0. Calc. for C₇H₈O₂: OCH₃, 25.0) and *resorcinol dimethyl ether* (9.1 g, 66 %) b.p. 103° (18 mm). (Found: OCH₃, 44.8. Calc. for C₈H₁₀O₂: OCH₃, 44.9). The last two ethers were separated by extracting the former with alkali. No reaction could be traced between methyl orthocarbonate and 2,6-di-*tert.*-butyl-*p*-cresol.

Pyrocatechol and methyl orthocarbonate. Pyrocatechol (11.0 g, 0.1 mole) and methyl orthocarbonate (34.0 g, 0.25 mole) were treated in the usual way. There was obtained methyl alcohol (6.4 g) b.p. 64–65°, $n_D^{20} = 1.334$ and methyl orthocarbonate (18.4 g) b.p. 111–113°, $n_D^{20} = 1.384$. Further fractionation under vacuum yielded *o*-phenylene dimethyl orthocarbonate* (16.5 g, 91 %) b.p. 115–116° (19 mm), $n_D^{20} = 1.4978$, $d_4^{20} = 1.1959$, $MR_D = 44.64$. (Found: OCH₃, 33.6, H 5.61, C 59.4. Calc. for C₈H₁₀O₄: OCH₃, 34.0, H 5.53, C 59.33). Guaiacyl methyl carbonate which has the same composition as *o*-phenylene dimethyl orthocarbonate might also be formed in the reaction above. The proof that *o*-phenylene dimethyl orthocarbonate was actually obtained was given by the hydrolysis of the reaction product in a mixture of dilute hydrochloric acid and methyl alcohol to yield pyrocatechol quantitatively. Furthermore the refractive index of guaiacyl methyl carbonate is reported as $n_D^{15.7} = 1.51736$.⁷

Phenol and ethyl orthoacetate. A mixture of phenol (18.8 g, 0.2 mole) and ethyl orthoacetate (32.4 g, 0.2 mole) was heated to 70–110° at 70 mm pressure. A liquid (7.8 g), distilled over between 26 and 49°. It was composed mainly of ethyl alcohol but also contained some ethyl acetate and ethyl orthoacetate. On continuation of the distillation at 15 mm there was obtained a fraction (8.9 g) boiling between 50 and 100° and comprising unchanged starting materials and decomposition products. The main fraction, phenyl diethyl orthoacetate (24.2 g, 58 %), distilled at 104–105° (15 mm), $n_D^{20} = 1.4801$, $d_4^{20} = 1.0099$, $MR_D = 59.16$. (According to McElvain and Kundiger¹ $n_D^{25} = 1.4783$). Found: Equiv. wt.** 35.0. Calc. for C₁₃H₁₈O₅: Equiv. wt. 35.04). A small amount of diphenyl ethyl orthoacetate* (3.5 g, 7%) was obtained at 135–136° (4 mm), $n_D^{20} = 1.5369$, $d_4^{20} = 1.0934$, $MR_D = 73.77$. (Found: OC₂H₅, 17.1, equiv.wt. * 21.9. Calc. for C₁₆H₁₈O₅: OC₂H₅, 17.4, equiv. wt. 21.5).

A better yield of phenyl diethyl orthoacetate was obtained if the ethyl orthoacetate was used in excess. In a synthesis performed as above but with phenol and ethyl orthoacetate in the molar ratio 1:3 the yield of phenyl diethyl orthoacetate was 92 %.

When the initial stage of the reaction between phenol and ethyl orthoacetate was allowed to proceed at atmospheric pressure instead of at 70 mm, the yield of phenyl diethyl orthoacetate dropped to about 30 % as the higher bath temperature (140–160°) caused an increased decomposition of the latter compound.

Thermal decomposition of phenyl diethyl orthoacetate. The thermal decomposition of this compound was previously studied by McElvain and Kundiger¹ who reported the formation of phenetole and phenyl acetate. Here it was of principal interest to determine the amount of phenetole formed.

Phenyl diethyl orthoacetate (21.0 g, 0.1 mole) was heated to 170–180°. A mixture of ethyl alcohol and ethyl acetate (6.0 g), $n_D^{20} = 1.370$, containing about 80 % of the latter distilled between 72–78°. Further heating afforded a mixture (10.2 g) of phenetole, phenyl acetate and some phenol all boiling at about 170°. On redistillation under vacuum it distilled between 63–86° (13 mm), $n_D^{20} = 1.510$. Boiling this fraction with ethanolic sodium hydroxide produced pure phenetole (7.6 g, 62 %) b.p. 62° (15 mm), $n_D^{20} = 1.507$.

As phenyl diethyl orthoacetate under favourable conditions may be prepared in about 90 % yield from phenol and ethyl orthoacetate it appears that the overall yield of phenetole from phenol by this method is at best about 50 %.

* New compound.

** Titration with 0.1 N bromide-bromate solution.

p-Nitrophenol and ethyl orthoacetate. *p*-Nitrophenol (13.9 g, 0.1 mole) and ethyl orthoacetate (24.3 g, 0.15 mole) were heated together to 140–160°. A liquid (13.5 g) containing principally ethyl alcohol and ethyl acetate distilled at 77°. Further distillation under vacuum afforded, along with other products, *p*-nitrophenetole (11.2 g, 67 %) b.p. 112–115° (3 mm). After recrystallization from light petroleum m.p. 59–60°. (According to Jaeger * m.p. 60°. Found: OC_2H_5 27.0. Calc. for $\text{C}_8\text{H}_9\text{NO}_3$: OC_2H_5 26.96).

Phenol and ethyl orthoformate. A mixture of phenol (18.8 g, 0.2 mole) and ethyl orthoformate (29.6 g, 0.2 mole) was heated at 140–170° until 9.2 g of a liquid boiling at 78–79° had distilled. It was composed mainly of ethyl alcohol, but contained also some ethyl formate. By continued fractionation under vacuum there was obtained unchanged starting materials and phenyl diethyl orthoformate* (22.4 g, 57 %), b.p. 111° (11 mm), $n_D^{20} = 1.4799$, $d_4^{20} = 1.0185$, $MR_D = 54.72$. (Found: Equiv. wt. ** 32.7, H 8.28, C 67.4 Calc. for $\text{C}_{11}\text{H}_{16}\text{O}_3$: Equiv. wt. 32.71, H 8.22, C 67.32). A small amount of a black resin remained in the distillation flask.

Thermal decomposition of phenyl diethyl orthoformate. Phenyl diethyl orthoformate (18.5 g, 0.094 mole) was heated to about 200°. A mixture (6.9 g) of ethyl alcohol and ethyl formate distilled over between 53 and 73°. At the end of the heating period carbon dioxide and other gases were evolved. A black brittle resin (9.3 g) remained in the distillation flask. The losses amounted to 2.3 g.

If the heating were discontinued before all of the material in the distilling flask had resinified, fractions boiling between 40 and 80° at 10 mm could be isolated. They were composed mainly of ethyl orthoformate and phenol. No phenetole was found.

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* New compound.

** Titration with 0.1 N bromide-bromate solution.