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CATALYTIC OXIDATION OF PHENOLS

ANALYSIS OF MINOR PRODUCTS FROM THE OXIDATIVE COUPLING REACTION OF 2,6-DIMETHYLPHENOL

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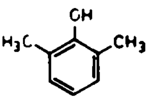
Abstract—The products formed in the early stages of the Cu^{I}-amine catalysed oxidation of 2,6-dimethylphenol have been isolated and identified. Apart from major quantities of 1,4-polyphenylene ether oligomers and a small amount of 2,6-dimethylbenzoquinone a number of C—C coupled minor products are formed and some of their reactions were studied. Special chromatographic techniques were developed for the detection and isolation of the compounds. Identification by spectroscopic methods and some typical chemical reactions are described.

INTRODUCTION

THE discovery of the catalytic oxidation of 2,6-disubstituted phenols as a new polymerization reaction leading to 1,4-polyphenylene ethers[1] has stimulated research on phenol oxidation systems. Two main types of reactions have been reported: dehydrogenation to C—O or C—C coupled products, or oxygenation of the phenolic nucleus or nuclear substituents. Examples of oxidants are transition metal compounds with or without hydrogen peroxide,[2] metal oxides, e.g. MnO_2,[3] PbO_2[4] and Ag_2O[5] and metal/amine/O_2 systems.[1] Bis(salicylidene)ethylenediimino cobalt (salcomine), proved an effective catalyst for the oxidation of phenols to *p*-benzoquinones.[6]



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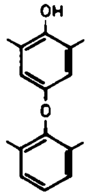

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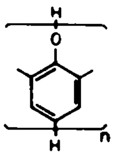

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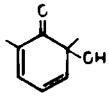

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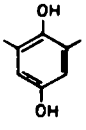

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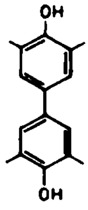

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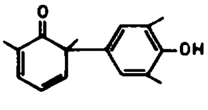

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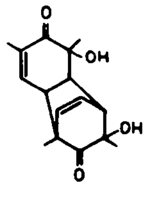

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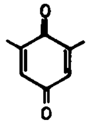

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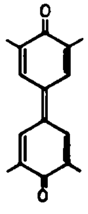

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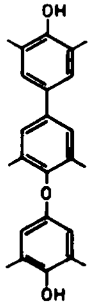

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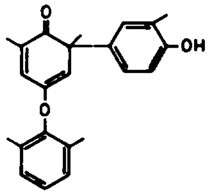

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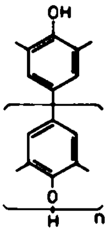

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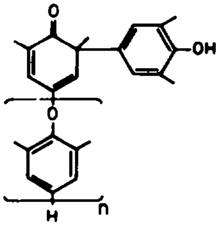

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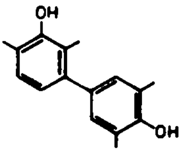

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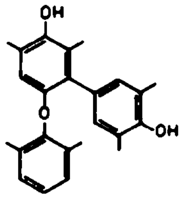

XVI

During oxidation of 2,6-dimethylphenol with the CuBr/diethylamine/O_2 system ($MgSO_4$ added as a drying agent) C—O coupling occurred mainly yielding polyether (III). The mechanism of this reaction has been described in terms of a phenoxy radical coupling yielding quinone ketals as intermediates, which decompose or rearrange to polyether oligomers (III).[3,7,8]

We now report the isolation and identification of several minor reaction products and some of their chemical transformations.

Isolation of the oxidation products

The products were isolated after 20% of the theoretical amount of oxygen had been consumed; the catalyst system used was CuBr/diethylamine, the drying agent $MgSO_4$, the solvent toluene and the reaction temperature 25°. These conditions were the most suitable for maximum byproduct formation, because some of the products were only built into the polymer during the later stages of the reaction. The reaction could be followed qualitatively by a two dimensional TLC (Fig. 1). A quantitative product analysis was accomplished in some cases by GLC of the trimethylsilyl derivatives[8] of the compounds (Fig. 2), coupled with TLC[9,10] for identification purposes (Fig. 3). The unreacted 2,6-dimethylphenol was removed by distillation, and the oxidation products were separated and isolated by crystallization, followed by column-chromatography. Details are given in the Experimental.

Identification of the oxidation products

a. *Spectroscopy.* The products isolated after 20% oxygen consumption were: major amounts of III oligomers, minor amounts (0·05–1·0 mole per cent totally based on

FIG. 1 Two-dimensional TLC of primary oxidation products from 2,6-dimethylphenol

starting material 2,6-dimethylphenol) of C—C coupled products (VI, VII, X and XII) and oxygenated products (V, IX and VIII, a Diels–Alder dimer from IV). The presence of higher oligomers (XIII and XIV) was indicated by TLC and GLC–TLC-coupling but the compounds were not isolated. In accordance with previous observations[2, 11] all the products were accounted for by coupling of 2,6-dimethylphenoxy radicals, in which the odd electron is delocalized over the aromatic ring or by reaction of these radicals with oxygen.

Known compounds (III,[1] V,[6] VI,[1] VIII,[12, *] IX,[6] X[1] and XI†) were readily identified by comparison with authentic samples and/or literature data. After elemental analyses

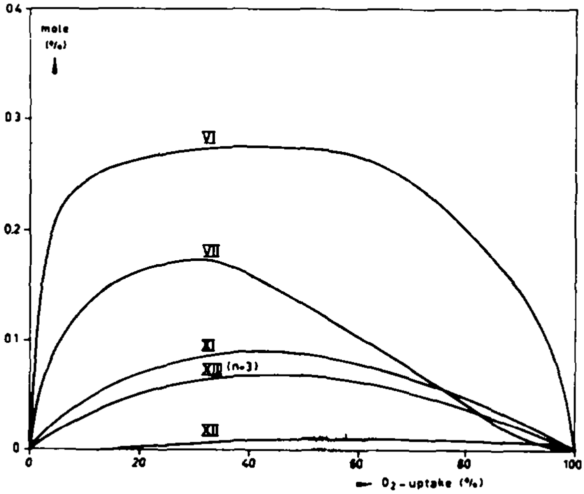

FIG. 2 Quantitative GLC analysis of C—C coupled products from oxidation of 2,6-dimethylphenol

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[*] The mode of Diels–Alder addition has been assumed on the basis of mechanistic considerations.[13]

† A sample of this compound, synthesized separately, was kindly provided by the General Electric Company, Schenectady (N.Y.) U.S.A.

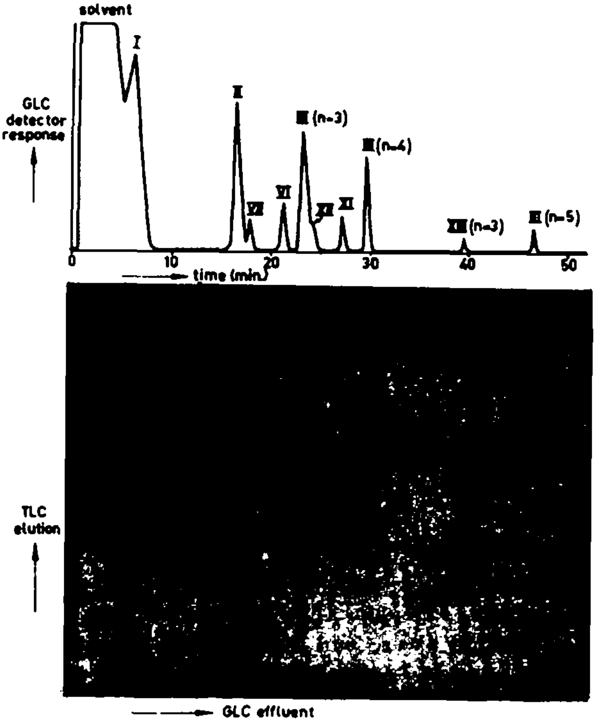
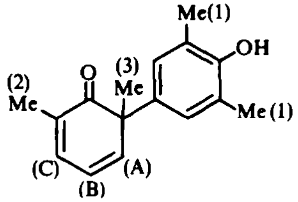


FIG. 3 Analysis of primary oxidation products from 2,6-dimethylphenol by GLC coupled with TLC

and mol wt data, identification of the unknown substances (VII and XII) was accomplished by spectroscopic methods. The 2,4-cyclohexadienone system was apparent[14] from IR spectra (C=O and C=C stretching vibrations at 1660, 1600 cm^{-1} resp in VII and at 1655, 1603 cm^{-1} resp in XII) and UV data ($\lambda_{max} = 300$ nm, $\varepsilon_{max} = 4350$ in VII and $\lambda_{max} = 275$ nm, $\varepsilon_{max} = 2710$, $\lambda_{max} = 340$ nm, $\varepsilon_{max} = 2170$ in XII). The presence of the 2,6-dimethylphenol moiety was indicated by IR (aromatic ring at 1580, 1485 cm^{-1} and OH stretching vibration at 3615 cm^{-1} both in VII and XII). Detailed NMR analyses then gave a complete proof of the structure. The single resonance spectrum of VII supported the following assignments: the triplet (2·06 ppm, splitting 0·6 Hz) was assigned to Me groups on the aromatic ring[15] [Me(1)], the double doublet structure (1·82 ppm, splittings 1·3 Hz and about 0·5 Hz) to the Me at the double bond in the quinonoid ring [Me(2)] and the signal at 1·48 ppm to the Me group at the sp_3 C atom [Me(3)]. The OH resonance was found at about 5·4 ppm. The low field multiplets between 6·0 and 7·0 ppm are due to the protons of the aromatic and quinonoid rings.

A more detailed assignment of these signals could only be given by spin-decoupling. Upon irradiation of the Me(1) group the multiplet centered at 6·71 ppm collapsed to a sharp singlet and the Me(1) group became a singlet by irradiating at 6·71 ppm. So the 6·71 ppm multiplet represents the aromatic ring protons. No other couplings of the Me(1) protons could be detected.

Irradiation at the Me(2) group clears the other low field signals (6·0–6·4 and 6·8 ppm). The Me(2) group is part of an $ABCY_3$ spin system (approximated as $ABXY_3$): Y representing the Me(2) protons and A,B,C the quinonoid ring protons, A being adjacent to the 2,6-dimethyl-phenol group, C adjacent to the Me(2) group and B in between A and C.



Irradiation at the X part (6·78 ppm) and analysis of the remaining ABY_3 system gives approximately a doublet structure for the Y_3 part (splitting 0·5 Hz). Strong irradiation at 6·2 ppm (A + B part) yields an XY_3 system with J_{XY} $(=J_{CY}) = 1{\cdot}3$ Hz). Therefore the 6·78 ppm resonance can be assigned to the C proton. Decoupling from Y_3 gave an ABC system from which chemical shifts and coupling constants were calculated. The relative signs were derived from spin-tickling experiments on the ABC system. The parameters are: $\delta_A = 6{\cdot}26$ ppm, $\delta_B = 6{\cdot}14$ ppm, $\delta_C = 6{\cdot}78$ ppm, $J_{AB} = +9{\cdot}45$ Hz, $J_{AC} = +1{\cdot}9$ Hz, $J_{BC} = +5{\cdot}7$ Hz (J_{AB} taken as positive). The positive sign for J_{AC} is at variance with what is generally accepted for homo-allylic couplings.

Analysis of the Y_3 part of the $ABCY_3$ system decoupled from A + B or from C protons yielded the following coupling constants: $J_{CY} = 1{\cdot}3$ Hz, $J_{AY} = 0{\cdot}9$ Hz and $J_{BY} = 0{\cdot}3$ Hz. All these data are in agreement with those by Regel and von Philipsborn[16] in their general NMR analysis of 2,4-cyclo-hexadienones.

The analysis of the more simple NMR spectrum of XII was easily performed along similar lines. Noticeable is the high field position (doublet centered at 4·65 ppm) of the quinonoid ring proton adjacent to the 2,6-dimethylphenol substituent. Further relevant data are: OH 4·96 ppm (one proton), three ring-protons of the phenoxysubstituent 6·97 ppm (the corresponding protons in the dimer III ($n = 2$) are found in the same position,[17] two ring-protons of the 2,6-dimethylphenol substituent 6·61 ppm, and the other quinonoid ring-proton just visible as a multiplet on the high field edge of the 6·97 ppm signal.

b. *Chemical evidence.* Acid catalysed acetylation of VII was accompanied by rearrangement, exclusively involving migration of the aryl group, to the acetylated biphenol derived from XV. This preferential migration of aryl groups over alkyl groups has been observed earlier.[18] The reaction is initiated by protonation of the carbonyl-oxygen and the subsequent 1–2 shift of the aryl group presumably occurs through a phenonium ion transition state, favouring aryl over alkyl migration. The same type of rearrangement was found to occur in an NMR tube when dissolving VII in $CDCl_3$ containing HCl. The resulting biphenol XV was easily characterized from the 100 mHz spectrum (2·16 ppm: one Me group; 2·27 ppm: three Me groups; 4·49 ppm: two OH groups; 6·70, 6·77, 6·94, 7·01: AB system, two *ortho* ring-protons; $J_{AB} = 7$ Hz; 6·89 ppm: two equivalent *meta* ring-protons). Similarly the biphenol XVI was formed from XII, as indicated by TLC. Another rearrangement reaction was observed with VII in solution upon adding catalytic amounts of oxidant. A series of linear oligomers of type III was rapidly formed, the dimer II being the primary product. This dimer is known to "redistribute" rapidly upon catalytic oxidation, yielding the same series of oligomers.[7,8] Since solutions of VII and the dimer II were found to be stable under nitrogen, the first step may be the oxidation of VII to the corresponding phenoxy radical, which, when the delocalized odd electron is in the *para* position, can undergo an internal rearrangement to dimer radical of II, which then undergoes redistribution to oligomers of type III. However, owing to the instability of the intermediates involved a detailed study of the mechanism of this rearrangement reaction is difficult.

Compound XII was shown by TLC to undergo the same type of oxidative rearrangement also yielding linear oligomers of type III.

EXPERIMENTAL

Thin-layer chromatography. Thin-layers: Silica gel GF_{254} (Merck), wet-spreading thickness 0·25 mm, dried 30 min at 110° and stored in equilibrium with humidity about 50% R.H. Chambers: Vapour saturated (lined with filter paper); after spotting the plates are pre-conditioned in the chambers for 10–20 min. Development, first dimension: Vapour saturation and elution with CH_2Cl_2; second dimension: Vapour saturation with CCl_4–MeOH (9:1), elution with CCl_4. Detection: Phosphomolybdic acid, 15 g/100 ml EtOH, followed by heating at 110° for 10 min.

Gas-liquid chromatography. Dual column apparatus with temp programming, flame ionization detection and septum cooling; temp injector 300°, detector 300°, oven linearly programmed from 70–300°, 10° per min; carrier gas N_2, 75 ml per min; columns $\frac{1}{8}$-inch stainless steel, length 2 m; stationary phase Chromosorb W (HMDS-treated, 60–80 mesh), coated with 10% silicone gum SE-30. The phenolic mixtures were silylated with the reagent bis-trimethylsilylacetamide[19] (Aldrich 12,891–0), which was used in excess of 100%. After addition of the reagent the sample was quickly concentrated to dryness in a vacuum evaporator; silylation was complete after heating at 30° for 30 min.

Partial oxidation of the 2,6-*dimethylphenol.* In a 100 l. reaction vessel with stirring equipment, 20 moles (2·44 kg) of I were dissolved in 40 l. of toluene. Et_2NH (4 moles, 292 g) and cuprous bromide (0·4 moles, 57·4 g) were added, together with 2·5 kg $MgSO_4$ as a drying agent. The mixture was vigorously stirred with O_2 at room temp, until 50 l. O_2 (about 20% of the theoretical amount) had been consumed (about 1 hr).

Isolation of the unknown minor products. The remainder of the O_2 in the reaction vessel was replaced by N_2 and the mixture extracted twice with 10 l. 0·5N HCl, to remove the catalyst and the drying agent. All subsequent steps were carried out in an atmosphere of N_2, each step being controlled by 2-dimensional TLC. The toluene layer was washed 5 times with 20 l. water, and concentrated at 50° to about 2 l. The concentrate was transferred to a 5 l. distilling flask and the bulk of the unreacted I distilled off *in vacuo* at 70°/1 mmHg. The residue was redissolved in 5 l. pet ether (b.p. 60–80°) and cooled in ice in order to precipitate most of VI. The ppt was filtered off and the soln concentrated until II started to crystallize. After completion the crystals of II were removed by filtration.

The remainder of the monomer and lower oligomers in the mixture were largely removed during a preliminary separation by column chromatography. A column was prepared, containing 1600 g silica gel (Merck, particle diameter 0·2–0·5 mm), slurried in a mixture of pet ether (b.p. 40–60°) and benzene, volume ratio 4:1. Adsorbent and eluent were previously deaerated with a stream of N_2. The oily phenolic mixture was poured slowly upon the bed of adsorbent and the column was drained until the mixture had been taken up completely by the silica gel. The column was eluted with 15 l. pet ether–benzene (4:1), the effluent contained monomer I, lower oligomers III ($n = 2$, 3, 4, etc) and a small fraction of the minor products were discarded. Elution was continued, using 5 l. MeOH, giving an effluent which was largely enriched in the required minor products—total weight after removal of the solvent 120 g.

A more refined column chromatographic purification was then carried out, using a column with adsorbent silica gel and CH_2Cl_2 as eluent. The mixture (120 g) was dissolved in a small portion of CH_2Cl_2 and chromatographed. The fractions, containing compounds XIII ($n = 1,2,3,4$) together with XIV ($n = 1,2,3,4$) and a small portion of VII, were collected and the solvent removed, total weight 37 g (to be used on the third column). Further elution gave an effluent, containing largely compound VII, which could be crystallized from n-hexane–benzene (1 : 1) to yield pure VII, 22 g. Final elution with MeOH gave compound VIII, after recrystallization from hot benzene, yield 5 g.

The third column was filled with 1000 g silica gel, slurried in a mixture of CCl_4 and MeOH 1 : 1. The column was washed with CCl_4/MeOH 99 : 1 until the effluent was constant and then loaded with the 37 g from the previous column. Elution was performed with the same 99 : 1 composition. Those fractions containing compound XII were collected (23 g) but were contaminated with the dimer II; this was removed using a final column with 320 g silica gel and CH_2Cl_2 eluent. The dimer II was present in the first fractions. Some of the following fractions were sufficiently rich in compound XII to allow crystallization (from n-hexane–toluene 1 : 1), yield 2 g.

Analytical data (except IR and NMR). Compound VII: pale yellow crystals, m.p. 126·5–127·5°; (Found: C, 79·07; H, 7·46, O, 13·33. $C_{16}H_{18}O_2$ requires: C, 79·31, H, 7·49; O, 13·21%; mol. wt (mass spectr.): 242, required: 242). Compound XII: pale yellow crystals, m.p. 176·0–177·5°; (Found: C, 79·68; H, 7·33; O, 13·16. $C_{24}H_{26}O_3$ requires: C, 79·53; H, 7·23; O, 13·24%; mol. wt (mass spectr): 362, required: 362).

Rearrangement products of VII *and* XII. Oxygen-catalysed rearrangement of VII, yielding the dimer II as a primary product, was carried out in an air-saturated benzene soln of VII—concentration 5 mg/ml. Samples were taken after standing at room temp for 0 hr, 1 hr and 2 hr resp., and immediately silylated prior to GLC analysis. The 0-hr sample contained pure silylated VII, the 1-hr sample showed the presence of 0·12% of II, the 2-hr sample 0·49% of II, together with 0·16% of I, due to redistribution of II. A blank experiment in an atmosphere of N_2 showed no reaction after at least 24 hr. The same rearrangement could be observed qualitatively with TLC (omitting the silylation step) and in an NMR tube filled with a $CDCl_3$ soln of VII, to which was added a small amount of 2,3-dichloro-5,6-dicyanoquinone as an oxidant. TLC and NMR experiments with XII showed the same type of oxidative rearrangement. The acid-catalysed rearrangement of VII and XII was performed in $CHCl_3$ soln with some HCl added; formation of XV on XVI resp. was shown by TLC. Desilylation with HCl vapour of the silylated derivates of VII and XII, as performed with the GLC–TLC-coupling technique (Fig. 3) also gave high yields of XV and XVI resp.

A quantitative rearrangement was obtained by dissolving 10 mg of VII in 2 ml Ac_2O, to which one drop of conc H_2SO_4 was added. Immediate rearrangement, together with acetylation, occurred, yielding 11 mg of the crystalline diacetate of XV. Hydrolysis of this compound with LAH in $CHCl_3$ yielded about 8 mg of crystalline XV. XV–diacetate: white crystals, m.p. 90·5–92·0; (Found: C, 72·82; H, 6·75; O, 19·61. $C_{20}H_{22}O_4$ requires: C, 73·60; H, 6·79; O, 19·61%). Compound XV: white crystals, m.p. 141·5–143·0°; (Found: C, 77·81; H, 7·46; O, 13·83. $C_{16}H_{18}O_2$ requires: C, 79·31; H, 7·49; O, 13·21%).

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