Kinetics and selectivity of the copper-catalysed oxidative coupling of 4-(2′,6′-dimethylphenoxy)-2,6-dimethylphenol

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Abstract

The kinetics of the copper/*N*-methylimidazole catalysed oxidative coupling reaction with the C–O coupled dimer of 2,6-dimethylphenol (DMP or monomer), viz. 4-(2′,6′-dimethylphenoxy)-2,6-dimethylphenol (dimer), as the substrate have been studied. The reaction was found to obey Michaelis–Menten kinetics. The dimer is more easily oxidised than the monomer, but the formation of a copper–substrate complex is more difficult. The reaction rates are higher than in the case of the monomer, and the amounts of diphenoquinone (DPQ) formed are much lower. With the dimer as the substrate, the order of the reaction in copper is 2, confirming that the formation of a dinuclear copper complex is an important step in the reaction mechanism. The amount of DPQ formed is proportional to the initial amount of the dimer. A slight, but clear preference for the dimer over the monomer as the substrate has been observed from experiments with mixtures of monomer and dimer. The amount of DPQ formed decreases exponentially with an increase in the fraction of dimer in the mixture, which can be ascribed mainly to a statistical effect. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

The oxidative coupling of phenols, as shown in Fig. 1 for 2,6-dimethylphenol (DMP or monomer), was found to be catalysed by copper–amine complexes by A.S. Hay in 1959 [1]. The two main products of this reaction are an intensely coloured diphenoquinone (DPQ [2]), which arises from C–C coupling of two phenol moieties and is formed in less than 5% yield under good conditions, and a C–O coupled product that can react further to yield, ultimately, the linear polymer poly(1,4-phenylene ether) (PPE) in high yield and of high molar mass. PPE has very good mechanical properties and chemical stability, even at elevated temperatures and is therefore an important engineering plastic [2,3]. The other product, DPQ, degrades the polymer upon further processing at high temperatures, and therefore has to be removed and/or its formation has to be minimised.

Because of the excellent properties of PPE and the undesired effects of the DPQ side-prod-

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[1] Retired.
[2] Systematic name: 4-(3,5-dimethyl-4-oxo-2,5-cyclohexadienylidene)-2,6-dimethyl-2,5-cyclohexadienone.
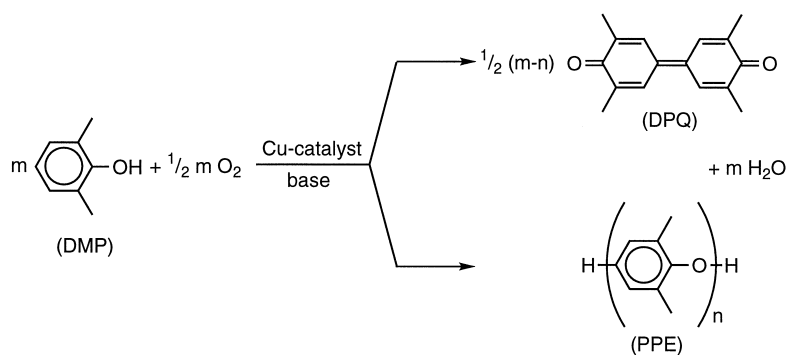
Fig. 1. Overall reaction scheme for the oxidative coupling of DMP to PPE and DPQ.

uct, this reaction has been the focus of extensive scientific research with respect to its reaction mechanism [4]. Early proposals involve mononuclear copper–phenoxo complexes as intermediates generating phenoxyl radicals as the active species [2,5,6]. Recent proposals are more inclined towards a mechanism featuring dinuclear copper–phenoxo species, which produce phenoxonium cations as active species [7–14].

The most commonly used substrate in this reaction is 2,6-dimethylphenol, because it is readily converted into linear poly(1,4-phenylene ether) (PPE) due to the blocked *ortho*-positions [2], while only a relatively small amount of the unwanted diphenoquinone side-product is formed, contrary to phenols with larger *ortho*-substituents, such as 2,6-di-*tert*-butylphenol, where the diphenoquinone is formed exclusively [1,5]. Furthermore, mild reaction conditions can be employed as the methyl groups enhance the oxidisability of the phenol, in contrast to sterically comparable phenols, like 2,6-dichlorophenol, where relatively high reaction temperatures are needed to form only small amounts of polymeric material [2]. As a result, DMP is the only phenol commercially used on a large scale in this polymerisation reaction [3], and, although many different phenols have been tried as substrates in this reaction [3,15], mechanistic studies have so far been focused on DMP.

The use of other phenols may, however, very well give more insight into the mechanism of this reaction. If phenols with different acidities

and/or oxidation potentials are used, certain reaction steps may be favoured or disfavoured, compared to DMP. Such changes may influence the overall kinetic behaviour of the reaction, thereby rendering information on which reaction steps play a role in the mechanism.

An outstanding candidate for kinetic analysis is the C–O coupled dimer of DMP, 4-(2′,6′-dimethylphenoxy)-2,6-dimethylphenol, which has the advantage over other possible substrates that it will not affect the actual reaction mechanism which is operating with DMP as the substrate, since it is a normal intermediate in this reaction. The *para*-phenoxy substituent of the dimer phenol is a weak inductive electron acceptor, but a powerful resonance electron donor [16]. The latter effect outweighs the first one, so there is a net increase in electron density in the phenol aromatic ring. Compared to DMP, the dimer is expected to be somewhat less acidic. For comparison: the pK_a values of phenol and *para*-methoxyphenol are 10.00 and 10.21, respectively [16]. Also, the dimer will be more easily oxidised than the monomer, as it has a lower oxidation potential [17]. Especially this latter characteristic of the dimer phenol is expected to provide more insight into the mechanism of the oxidative coupling reaction, as the rates of reaction steps involving oxidation of the substrate will be accelerated compared to the monomer.

In the case of the monomer a fractional order in the copper catalyst was observed [13], which was found to be linked to the position of the

equilibrium between mono- and dinuclear copper species [14]. The rate-determining step is believed to be the oxidation of a bridging phenolate [10,12]. By using the dimer phenol as the starting substrate, this oxidation step may no longer be rate-limiting. Furthermore, by using mixtures of the monomer and dimer, it can be investigated whether or not a preference for either of the substrates occurs, which may afford more insight into the later stages of the reaction, when oligomeric phenols are present in higher concentrations.

So far, only limited studies have been performed with respect to the kinetics of the dimer [18–20]. However, some of these experiments were done with dimers having substituents other than methyl [18], and, consequently with kinetics different from the DMP dimer case. In other reports only small amounts (just over stoichiometric) of the dimer were used [19,20], which might have hidden several kinetic features. Therefore, experiments with the dimer as the substrate have been performed under normal catalytic conditions, the results of which are described in this paper.

2. Experimental

2.1. General

Solvents and chemicals were obtained from standard vendors as either reagent (ethanol (99%), diethyl ether, dimethylformamide, pyridine (99 + %), *n*-hexane, *n*-heptane, 2,6-dimethylphenol, 4-bromo-2,6-dimethylphenol, *N*-methylimidazole (99%), sodium methoxide (95%), sodium ethoxide (96%), methyl iodide (99%, stabilised), hydroiodic acid (57%)) or analytical grade (toluene, methanol, $Cu(NO_3)_2 \cdot 3H_2O$, K_2CO_3), and were used as received unless noted otherwise. Diethyl ether was distilled before use. Dimethylformamide (DMF) was distilled from molecular sieves (4 Å) under reduced dinitrogen pressure prior to use. Alternatively, analytical grade DMF was used from a

freshly opened bottle without further treatment. Water was demineralised prior to use. 2,6-dimethylphenol (DMP) was purified by repeated crystallisation from *n*-hexane. Sodium methoxide (95%) was found to have an active base content of 97%. The amounts of sodium methoxide used were corrected for this content. Copper(I) bromide was synthesised via a literature procedure [21].

The actual synthesis of all organic substrates and starting compounds was performed under a dry dinitrogen atmosphere in all cases, but the subsequent purification of the products was commonly done in air. All the glasswork used was treated with an alkaline ethanol solution (except volummetric glasswork) and consecutive rinsing with dilute hydrochloric acid to remove traces of loose metal ions. Dioxygen-uptake experiments (vide infra) were performed using an in-house designed apparatus, which was described in detail in earlier publications [13,22–24]. NMR spectra were recorded on a Jeol JNM FX-200 (200 MHz) FT-NMR spectrometer using $CDCl_3$ as the solvent and TMS as internal reference. UV/Vis/NIR spectroscopy for DPQ analysis was performed using a Perkin Elmer 330 double-beam spectrophotometer, or a Camspec M302 single-beam spectrophotometer.

2.2. Synthesis of 4-(2′,6′-dimethylphenoxy)-2,6-dimethylphenol (dimer)

The C–O coupled dimer of DMP, 4-(2′,6′-dimethylphenoxy)-2,6-dimethylphenol, was synthesised by the Ullmann coupling of DMP with 4-bromo-2,6-dimethylanisole [25–28], followed by subsequent removal of the methyl ether group by treatment with hydroiodic acid [19] as schematically shown in Fig. 2. ^{1}H-NMR data of all organic compounds are listed in Table 1.

2.2.1. Synthesis of 4-bromo-2,6-dimethylanisole (BrDMA)

The starting anisole was prepared by adding 71.17 g of sodium ethoxide (1.046 mol) to a
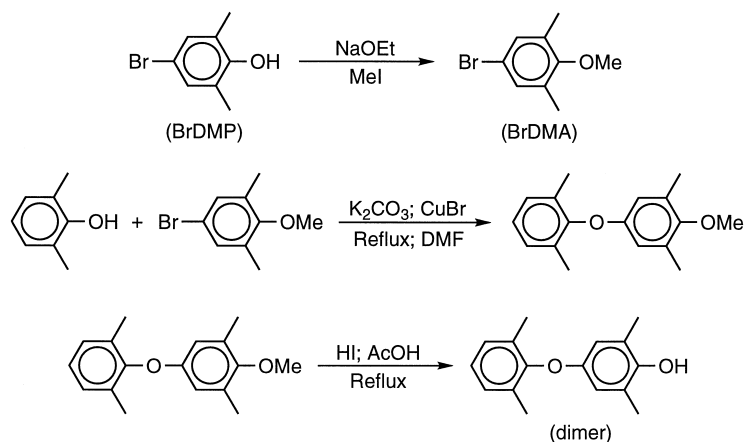
Fig. 2. Schematic representation of the synthesis of the C–O coupled dimer of DMP: 4-(2′,6′-dimethylphenoxy)-2,6-dimethylphenol (dimer).

solution of BrDMP (200.30 g, 0.996 mol) in 700 ml absolute ethanol. To the resulting solution, which was placed in an ice bath, 66 ml (1.06 mol) of methyl iodide was added dropwise over a period of 2 h. The resulting solution was stirred overnight under dinitrogen at room temperature, after which the main part of the ethanol was removed under reduced pressure with a rotary evaporator. The remaining slurry was dissolved in water and extracted with diethyl ether (2 × 300 ml). The combined diethyl ether solutions were washed with aqueous potassium hydroxide (2 × 400 ml), to remove any residual phenol, and with water till neutral (4 × 500 ml). The ether solution was dried on $MgSO_4$, filtrated, and evaporated to dryness with a rotary evaporator. The last traces of diethyl ether were removed in vacuo, yielding 162.19 g of a light brown oil. The product was further purified by vacuum distillation. The product was obtained between 67 and 72°C (at 0.05 mm Hg) as a clear, slightly yellow oil,

Table 1
^{1}H-NMR data (ppm) of the phenol and anisole compounds described in the experimental part. Spectra were recorded in $CDCl_3$ at 200 MHz. Values of the peak integrals and multiplicity are given in brackets[a]
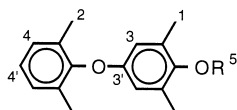
compound	δ_1	δ_2	$\delta_3 (+\delta_{3'})$	$\delta_4 (+\delta_{4'})$	δ_5
DMP	2.23 (6,s)		6.96 (2,d)		4.60 (1,s)
			6.75 (1,dd)		
BrDMP	2.20 (6,s)		7.09 (2,s)		4.57 (1,s)
BrDMA	2.24 (6,s)		7.13 (2,s)		3.68 (3,s)
dimer anisole	2.21 (6,s)	2.13 (6,s)	6.38 (2,s)	7.07 (3,m)	3.67 (3,s)
dimer DMP	2.17 (6,s)	2.12 (6,s)	6.37 (2,s)	7.07 (3,m)	4.23 (1,s)
PPE	2.17 (−,s)	2.09 (6,s)[b]		6.47 (2,s)[b]	

[a] s = singlet, d = doublet, dd = double doublet, m = multiplet.
[b] Values apply to the chemical shifts of the protons of the internal phenoxy groups, not of the phenoxy tail group.

pure according to ^{1}H-NMR. Yield: 156.55 g (73% with respect to BrDMP). F.w. = 215.09 g/mol.

2.2.2. Synthesis of 4-(2′,6′-dimethylphenoxy)-2,6-dimethylanisole

The Ullmann coupling of BrDMA with DMP to synthesise the methyl ether of the dimer of DMP was performed as follows: a mixture of DMP (31.02 g; 0.254 mol), K_2CO_3 (70.36 g, 0.509 mol) and Cu(I)Br (5.79 g, 0.040 mol) was dissolved in 500 ml of DMF (distilled [3]). To this solution was added BrDMA (61.49 g, 0.286 mol) and 40 ml of pyridine. This mixture was refluxed for a week at 165°C under a dry dinitrogen atmosphere. After cooling down, the blue reaction mixture was carefully acidified with 15% HCl to a pH of about 2. A red, metallic precipitate (possibly Cu^0) was formed, which could be removed by filtration over Celite®. This procedure is not essential, however, as the precipitate will be gradually removed during the washing steps in the rest of the purification procedure. The resulting mixture was extracted with diethyl ether (2×500 ml). The combined ether solutions were washed with 10% HCl (2×400 ml), water (500 ml), aqueous KOH (2×500 ml) and finally with water till neutral pH (3×500 ml). The ether solution was dried on $MgSO_4$, filtrated, and evaporated to dryness with a rotary evaporator. Any residual diethyl ether was removed in vacuo, yielding 62.49 g of a dark brown, viscous oil. 2,6-Dimethylanisole, a known side-product of this reaction [27], and the remaining BrDMA were removed by vacuum distillation (0.05 mm Hg), which was continued to about 90°C. The product was obtained by in vacuo bulb to bulb distillation of the residue (0.05 mm Hg), whereby a clear, slightly yellowish, highly viscous oil was obtained. This

oil crystallised overnight, leaving a small amount of a liquid, consisting mainly of BrDMA, which was removed. The dimer anisole was further purified by crystallisation (usually twice) from *n*-hexane. Yield: 27.63 g (42% with respect to DMP) of colourless plates. F.w. = 257.35 g/mol, m.p. = 58°C.

N.B.: The supernatant of the crystallisation is very rich in dimer anisole. It is therefore recommended to purify this dimer anisole after evaporation of the solvent, e.g., combined with a next batch, by distillation and crystallisation as described above.

2.2.3. Synthesis of 4-(2′,6′-dimethylphenoxy)-2,6-dimethylphenol

Removal of the methyl ether group of the anisole was performed by adding 21.43 g (83.3 mmol) of the dimer anisole to a mixture of 106 ml acetic acid and 106 ml 57% hydroiodic acid [19]. The reaction mixture was refluxed overnight under dinitrogen at 110°C. After cooling down, the mixture was poured into icewater (700 ml), and filtrated. The residue was washed several times on the filter with water, and was finally dissolved in 350 ml diethyl ether (distilled). The ether layer was washed with an aqueous sodium thiosulfate solution (2×300 ml), to remove traces of iodine, and with water till neutral (4×300 ml). The ether solution was dried on $MgSO_4$, filtrated, and evaporated to dryness using a rotary evaporator. The final traces of diethyl ether were removed in vacuo, yielding 20.96 g of an off-white substance. The final purification of the dimer phenol was done by recrystallisation (usually twice) from *n*-heptane. Yield: 17.78 g (88% with respect to the dimer anisole) of colourless needles. F.w. = 242.32 g/mol, m.p. = 107°C.

N.B.: It was found to be essential that during the purification procedure, especially at the washing stage, no basic reagents are used, e.g., for neutralising the acidic solutions. If this is done, the iodine present will immediately oxidise the phenolate anions formed, resulting in a

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[3] Instead of DMF distilled from molsieves (4 Å), analytical grade DMF from a freshly opened bottle may also be used, albeit at a small cost in yield.

disproportionation (redistribution) of the dimer phenol to a mixture of monomer and di-, tri- and higher oligomers of DMP.

2.3. Determination of the pK_a values of DMP and the dimer

The pK_a values of the monomer and the dimer phenol were determined by dissolving 5 mmol of the required phenol in 50 ml methanol, adding 25 ml of an aqueous 0.1 M NaOH solution (prepared from a Titrisol® package obtained from Merck), 10 ml of water and adding methanol up to 100 ml. Hence, the resulting solution is 0.05 M in the phenol and 0.025 M in base, so the ratio of phenol to phenolate is 1 to 1. The pH of such a solution is the same as the pK_a value of the phenol [29,30]. The pK_a values obtained at 20°C in this manner are 11.96 and 12.16 for the monomer and dimer phenol, respectively (the literature value for the pK_a value of DMP in water at 25°C is 10.6 [3,31]). So, as expected, the dimer phenol is indeed somewhat less acidic than the monomer. It should be stressed that the pK_a values obtained here are not suitable for comparison with literature values. They are only valid under the current conditions.

2.4. Catalyst and substrate solutions

For the dioxygen-uptake experiments with the dimer phenol, the same way of preparing and using the solutions as in the case of DMP [13] could not be used, as basic solutions of the dimer phenol proved much less stable under air than those of the monomer. Prolonged standing of a basic solution of the dimer under air, resulted in dramatically lower initial reaction rates (see Table 2). No such effect has been observed in the case of the monomer. The rates listed in this table were obtained from measurements with the dimer which were performed in the same way as with the monomer, at an N/Cu ratio of 30 and a base/Cu ratio of 1. On the

Table 2
Observed initial reaction rates and DPQ formation versus the age of the basic dimer phenol solution. Values for monomer DMP have been added for comparison

Age of the basic dimer phenol solution (h)	$R_0 (10^{-5}$ mol/l·s)	%DPQ
0.25	> 70.58[a]	0.37
0.5	63.17	0.41
1.5	57.01	0.39
4.5	42.47	0.40
6.5	40.96	0.39
monomer DMP	34.61	3.85

[a]At the time this particular measurement was performed, reaction rates faster than this value could not be determined.

other hand, no significant effect of the age of the solution on the amount of DPQ formed during the reaction was observed. To overcome the stability problem, the base was added to the dimer phenol solution just prior to the actual measurement. Therefore, the phenol and base solutions were prepared separately, as described below. Care was taken to ensure that for all measurements the same solvent composition was used as in the case of the monomer DMP [13]. The dioxygen-uptake experiments were performed as described in Section 2.5.

A typical catalyst solution was prepared by mixing, in a 10 ml volumetric flask, 4 ml of a 0.03125 M $Cu(NO_3)_2 \cdot 3H_2O$ solution in methanol, the appropriate amount of a 1.25 M Nmiz solution in toluene, and filling it up to 10 ml with toluene, which resulted in a 0.0125 M $Cu(Nmiz)_x(NO_3)_2$ solution in toluene/methanol (3/2 v/v). The substrate solution consisted of a 0.30 M solution of the dimer phenol in toluene containing 1 vol.% of methanol. As the base a 0.050 M solution of NaOMe in methanol was used. For the set of measurements where the amount of copper catalyst was varied, the 0.050 M base solution was diluted to the concentration required to maintain a base to copper ratio of 1 to 1, with a solvent mixture of methanol/toluene (63/37 v/v) in order to have the same solvent compositions as in the measurements with monomer DMP [13].

2.5. Dioxygen-uptake measurements

In a typical quantitative, time-resolved dioxygen-uptake experiment, one compartment of a special 2-compartment reaction vessel was filled with 4 ml of the 0.0125 M copper(II)/Nmiz solution, and the other with 10 ml of the substrate solution. 1 ml of the NaOMe solution was added to the phenol solution just prior to flushing the system with dioxygen and starting the experiment. A time difference of 4–5 min was usual between adding the base to the phenol and actually starting the measurement. This short time was found to have no effect on the reaction rate observed, as was proved by performing the same experiment in a special 3-compartment reaction vessel where the three reactant solutions were mixed only at the very moment the measurement was started. The same initial rates were found with both procedures.

The resulting reaction mixture was generally 3.33 mM in copper and 0.20 M in dimer phenol, in a mixed solvent consisting of 18 vol.% of methanol in toluene. All reactions were performed at 25°C under pure dioxygen at atmospheric pressure. These are the conditions referred to as 'normal' or 'good' conditions, which furthermore imply an N/Cu ratio of at least 30 and a base/Cu ratio of 1. A wide gas burette of ∼ 100 ml was used to allow measurement of the high reaction rates observed with dimer phenol as the substrate. When an experiment was finished, the amount of DPQ formed during the reaction was determined by diluting the reaction mixture, and measuring the UV-ab-sorbance of DPQ at 421 nm. A detailed description of the dioxygen-uptake experiments and the processing of the experimental data is given in previous publications [13,23,24].

A noticeable difference between the dioxygen-uptake curves of measurements conducted with the monomer and those with the dimer was observed. In the case of the monomer the curve could be divided in two major parts, apart from a short initiation period: a linear part where most of the dioxygen uptake was observed, and a part where the dioxygen uptake subsided because of substrate shortage. With the dimer as the substrate, however, three such parts can be distinguished in the uptake curve, because the linear part is split in two parts, as shown schematically in Fig. 3 for low (a) and normal (vide supra) (b) copper concentrations. For normal copper concentration, the first linear part is rather short, and encompasses only about 1.5 min, after which a bend in the curve is observed and the second, longer, linear part starts. Remarkably, for low copper concentrations the slope of the first linear part is lower than that of the second linear part, resulting in a sigmoid uptake curve. Upon increasing the copper concentration, the slopes of both linear parts gradually increase. The slope of the first part increases more rapidly than that of the second part, so that at normal copper concentrations the slope of the first part is even higher than that of the second part (see also Section 3.2.).

It is known that during the oxidative coupling reaction, substantial amounts of monomer DMP can be formed from oligomers by a dispropor-
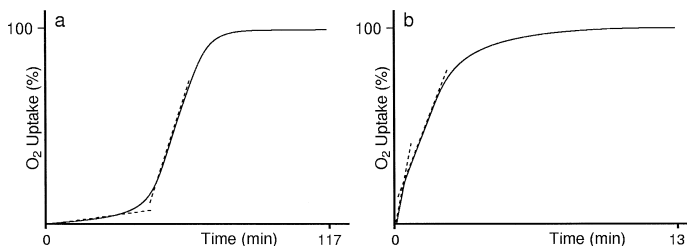

Fig. 3. Representations of the dioxygen-uptake curves obtained at low (0.33 mM) (a) and normal (3.33 mM) (b) copper concentrations with the dimer phenol as the substrate. The dotted lines emphasize the slopes of the different linear parts of the curves. Note the different time-scales.

tionation (redistribution) reaction [23,24,32–34], which is also the subject of a forthcoming publication [35]. Therefore, the break in the linear part of the curves is most probably caused by a build-up of monomer, which competes with the dimer phenol as the substrate after some time, resulting in a different kinetic behaviour (vide infra). So, for the calculation of the initial dioxygen-uptake rate, the slope of the first linear part of the uptake curve is used, to be sure that only the kinetics of the dimer phenol are taken into account. The small amount of DPQ which is formed during the reaction results from monomer DMP, as DPQ cannot be formed directly from the dimer phenol.

3. Results and discussion

3.1. General

Several experiments performed earlier with monomer DMP as the substrate were repeated analogously with the dimer phenol, such as the variation of the catalyst concentration and variation of the initial amount of the phenol [13,14]. The variation of the Nmiz-to-copper (*abbr.* N/Cu) ratio was also repeated, [4] which afforded the same results as with monomer phenol, viz. maximum activity and selectivity (towards PPE) were only observed at an N/Cu ratio of at least 30 [13].

All experiments described here have been performed at a base-to-copper (*abbr.* base/Cu) ratio of 1 to 1. Attempts have been made to do

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[4] When the measurements for this series of experiments were performed, the dependence of the initial reaction rate on the age of the basic dimer phenol solution (see Section 2.4 and Table 2) was not recognized as yet, and therefore these measurements were performed in the same way as those with the monomer phenol [13]. Consequently, the results for the initial rates of the measurements themselves cannot be very reliable. However, from the results of the entire set of measurements it was nevertheless clear that at least an N/Cu ratio of 30 had to be used in order to achieve maximum rate and minimal DPQ formation, just like with monomer phenol. Therefore is was not considered necessary to repeat these measurements in the 'right' way.

measurements at a higher base/Cu ratio, resulting in very high initial reaction rates, which could not be measured with the present equipment. For illustration: at a base/Cu ratio of 2 to 1 a reaction rate of more than $100 \cdot 10^{-5}$ mol/l s was observed, which is the maximum rate that can be determined with the current equipment.

3.2. The order in copper

As stated in the introduction, the dimer phenolate is more readily oxidised than the monomer phenolate, because of the electron-donating *para*-phenoxy group. This lower oxidation potential might have some implications for the rates of some of the reaction steps compared to the monomer, which in turn may result in a different order in copper when the reaction is started with the dimer phenol as the substrate. Therefore, a series of experiments was performed in which the copper concentration was varied at an N/Cu ratio of 37.5 and a base/Cu ratio of 1. The results for the initial reaction rates as a function of the copper concentration are shown in Fig. 4 as a double logarithmic plot.

At the lowest copper concentration used, the initial slope of the dioxygen-uptake curve is very small, as shown in Fig. 3a. Therefore, the initial dioxygen-uptake rate derived from this slope is not reliable, and the corresponding data-point in Fig. 4 ($\log([Cu]) \sim -3.48$) has not
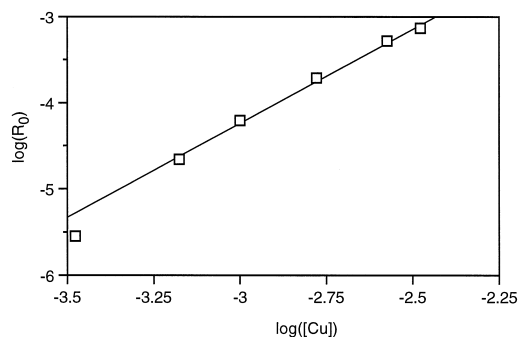

Fig. 4. Plot of $\log(R_0)$ vs. $\log([Cu])$ at N/Cu = 37.5, base/Cu = 1, $[dimer]_0 = 0.20$ M and $T = 298$ K. The drawn line represents the linear least-squares analysis of the data-points, excluding the one at the lowest copper concentration.

been taken into account for further kinetic analysis. Applying linear least-squares analysis to the remaining data-points resulted in the straight line shown in Fig. 4. The slope of this line equals the order in copper of the reaction, and is 2.2 ($\pm$ 0.2). The rate constant, obtained from the intercept with the y-axis, is 219 's^{-1}'. The order in copper is higher than the order of 1.42 observed with monomer DMP as the starting substrate under the same conditions [13]. Since an order of about 2 is observed with the dimer phenol, it appears that under these conditions, i.e., pseudo-zero order with respect to the substrate (see also Section 3.3), the formation of a dinuclear copper compound is an important contribution to the overall reaction rate, even more so than in the case of monomer DMP, thereby confirming that dinuclear copper species indeed play a key role in the reaction mechanism.

On the basis of these findings the shape of the dioxygen-uptake curves (see Fig. 3) as discussed in Section 2.5 can now be understood. It was observed that at low copper concentrations the slope of the first linear part of the uptake curve was lower than that of the second linear part, whereas at normal copper concentrations the first linear part was steeper than the second. The first linear part of the uptake curve is thought to express the kinetics of the dimer DMP only, whereas the second linear part is ascribed to the kinetics of a mixture of monomer and dimer. The observation that the slope of the first linear part increases more rapidly than the slope of the second part upon increasing the copper concentration, is related to the higher order in copper found with the dimer phenol as compared to the monomer phenol. This higher order in copper with dimer phenol makes the rate of the reaction with dimer phenol more sensitive to the copper concentration.

The amount of DPQ formed during the reaction as a function of the copper concentration is shown in Fig. 5. The percentage of DPQ formed decreases exponentially with increasing copper concentration, as was also found in the experiments with the monomer DMP, although in that
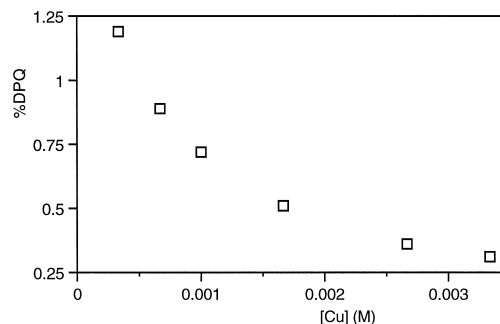

Fig. 5. Formation of DPQ vs. the copper concentration, at N/Cu = 37.5, base/Cu = 1, [dimer]$_0$ = 0.20 M and T = 298 K.

case the formation of higher amounts of DPQ is observed [13]. As already noted in Section 2.5, DPQ can only be formed from monomer DMP, which in turn is formed by redistribution from the dimer. So, the rationalisation given previously in the case of monomer DMP for the higher amounts of DPQ formed at lower concentrations of the copper catalyst [13,23,24], also holds here. This rationalisation implies that the relative amount of mononuclear copper, which is the DPQ-generating species, increases over that of dinuclear copper, which is the PPE-generating species, when decreasing the total concentration of copper.

3.3. Variation of the dimer-to-copper ratio

Viersen et al. found for his system with N, N, N', N'-tetramethylethylenediamine (tmed) ligand, a linear, first-order, relationship between the initial concentration of dimer (or trimer) phenol and the initial reaction rate [20]. However, the phenol concentrations used were rather low ($\sim$ 0.04 M) as compared to those commonly used in the case of the monomer ($\sim$ 0.2 M). According to the Michaelis–Menten kinetic scheme, generally observed with monomer DMP [14,36–38], first-order kinetics in the substrate may be observed at low substrate concentrations. It is quite likely that the concentrations used by Viersen fall in the range where such first-order kinetics are found. Nevertheless, the Michaelis–Menten mechanism may still apply. Therefore, the experiments performed by
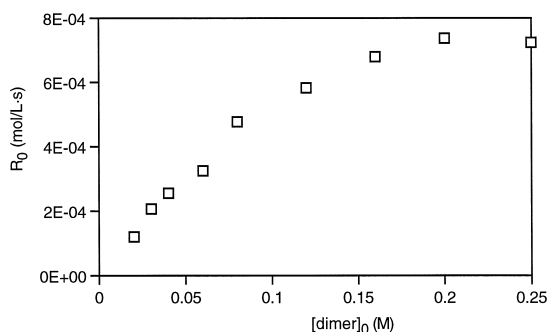
Fig. 6. Initial dioxygen-uptake rate (R_0) as a function of the initial dimer phenol concentration, at N/Cu = 30, base/Cu = 1, [Cu] = 3.33 mM and T = 298 K.

Viersen, i.e., varying the dimer phenol concentration at constant base and copper concentrations, were repeated for the catalytic system (with Nmiz ligand) described here, but using higher initial dimer phenol concentrations. The results for the initial reaction rates are shown in Fig. 6. Clearly, the curve in this figure levels off at higher initial dimer concentrations. The phenomenon, that the rates start to decrease above a certain initial phenol concentration (> 0.32 M), observed with the monomer phenol [14], is also observed with the dimer, albeit at lower concentrations (> 0.20 M). This decrease is probably due to too large a change in the reaction medium at high phenol concentration. Measurements above this critical concentration have not been taken into consideration.

If the plot in Fig. 6 is transformed into a double-reciprocal, Lineweaver–Burk plot (not shown), a straight line is obtained. As in the case of the monomer, this linear behaviour can be derived from a simple Michaelis–Menten scheme, indicating that the oxidation of the phenolate is the rate-determining factor. The equation for the straight line, as obtained by linear least-squares analysis of the data-points, can be substituted into the Lineweaver–Burk equation (Eq. (1)):

$$\frac{1}{R_0} = \frac{1}{k_2[C]_0} + \frac{K_m}{k_2[C]_0[\text{dimer}]_0} \qquad (1)$$

Where: $[C]_0$ = initial catalyst concentration (= initial copper concentration) (mol/l); $[\text{dimer}]_0$

= initial dimer phenol concentration (mol/l); k_2 = rate constant for the oxidation of the substrate (s^{-1}); K_m = Michaelis constant (mol/l).

The values found for the rate constant of the oxidation of the phenolate (k_2) and the Michaelis–Menten constant (K_m) are 0.808 s^{-1} and 0.435 M, respectively. The values obtained with the monomer phenol under similar conditions were 0.149 s^{-1} and 0.114 M, respectively [14]. As expected, the oxidation of the dimer phenolate is much more facile than that of the monomer phenolate, which is confirmed by the higher value of k_2 found for the dimer. On the other hand, the formation of a catalyst–substrate complex is more difficult in the case of the dimer than in the case of the monomer, as deduced from the higher value of K_m for the dimer, the reciprocal of which is a measure for the accessibility of the catalytically active site for the substrate.

The amount of DPQ formed during the reaction, expressed as a percentage of the initial amount of dimer phenol, showed a tendency towards lower percentages of DPQ at higher initial dimer phenol concentrations. When the absolute amount of DPQ formed is plotted versus the initial amount of dimer phenol, as shown in Fig. 7, a straight line is obtained. As in the case of the monomer DMP [14], a positive intercept with the y-axis is observed. So, here too, a small amount of DPQ seems to be formed independent of the initial amount of dimer DMP
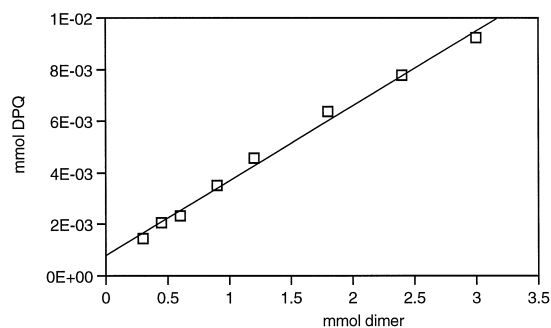

Fig. 7. Amount of DPQ formed vs. the initial amount of dimer phenol. [Cu] = 3.33 mM, N/Cu = 30, base/Cu = 1 and T = 298 K. The drawn line represents the linear least-squares analysis of the experimental data.

present. It is not clear whether this positive intercept is due to a non-zero UV/Vis-absorption at 421 nm because of an experimental factor, or because of some minor side reaction affording DPQ.

The major part of the DPQ formed is a constant percentage (0.29%) of the initial amount of dimer DMP, as a true side product of the actual copper-catalysed oxidative coupling. This percentage is the lowest possible percentage of DPQ that may be found, as expressed in Eq. (2), derived from the line equation obtained from linear least-squares analysis of the data-points in Fig. 7.

$$\%DPQ = 0.291 + 0.0787/x \qquad (2)$$

With: $x =$ initial amount of dimer phenol (mmol).

The amounts of DPQ found with the current catalytic system starting with the dimer phenol under normal conditions ($\sim 0.30\%$), are somewhat higher than those found by Viersen et al. under similar conditions (0.18%) [20]. This is most likely caused by the somewhat different conditions and the different amine ligands used.

3.4. Reactivity and selectivity of mixtures of monomer and dimer

Dioxygen-uptake measurements with mixtures of monomer and dimer phenol were performed to investigate whether or not either one of the phenols is preferred over the other in the oxidative coupling reaction. Our expectation was that, due to the small, but real, difference in acidity the monomer would be somewhat more readily deprotonated than the dimer, the pK_a values of the monomer and the dimer being 11.96 and 12.16, respectively (see Section 2.3). So, equilibrium (3) would lie somewhat at the left side.

$$DMPO^- + DMPODMPOH$$
$$\rightleftharpoons DMPOH + DMPODMPO^- \qquad (3)$$

Since only phenolate anions can coordinate to the copper catalyst and will be oxidised subse-

quently, a preference for the monomer is expected. This hypothesis is supported by the higher value for the Michaelis constant (K_m) found for the dimer phenol (see Section 3.3), which is an indication that complex formation between the catalyst and the substrate is more difficult in the case of the dimer phenol.

The observed reaction rates of the measurements with different mixtures of monomer and dimer at an N/Cu ratio of 30 and a base/Cu ratio of 1 are shown in Fig. 8. A straight line depicting additive behaviour of the reaction rate is added for comparison. The total phenol concentration in the reaction mixture was 0.20 M in all measurements.

It is clear from Fig. 8 that our hypothesis, that monomer DMP would be preferred as a substrate, is not correct. A small but significant preference for the dimer phenol as the substrate is observed. A similar effect was observed by Viersen, albeit at lower initial phenol concentrations [20]. So, apart from the slightly lower acidity of the dimer, there must be another difference with respect to the monomer, to (more than) offset the somewhat retarding effect this lower acidity should have on the reactivity of the dimer. The only other difference between the monomer and the dimer is, apart from the size, the fact that the dimer is more easily oxidised. So, even though the formation of a (dinuclear) copper–phenoxo species may be
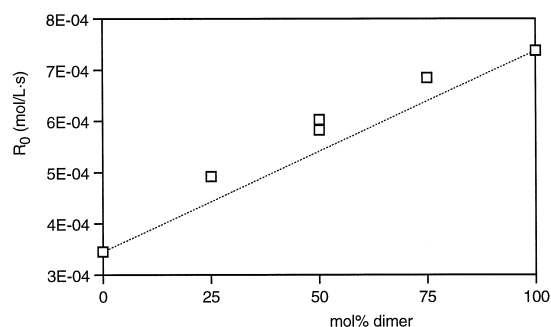

Fig. 8. Initial reaction rate (R_0) vs. the percentage (mol%) of dimer phenol in a mixture of monomer and dimer. [Cu] = 3.33 mM, N/Cu = 30, base/Cu = 1, [ROH]$_{total}$ = 0.20 M and T = 298 K. The dotted line represents the theoretical case of a linear increase in reaction rate from 0 to 100 mol% of dimer phenol.

somewhat more difficult in the case of the dimer, the subsequent oxidation step is faster than in the case of the monomer, as shown by the value for k_2 for the dimer which is about five times higher than for the monomer. Apparently, in the case of the dimer, once the dinuclear copper phenolate intermediate is formed, the subsequent oxidation step occurs rapidly. In the case of the monomer, however, this dinuclear intermediate has a higher chance to dissociate before the, compared to the dimer, slower oxidation step can take place. The overall effect is obviously that the dimer is somewhat preferred as a substrate compared to the monomer.

The amount of DPQ formed during the reaction was found to decrease with increasing amount of dimer DMP in the starting mixture, shown in Fig. 9. This behaviour agrees with that reported by Viersen et al. [20].

This decrease is mainly a statistical effect, since with an increasing fraction of dimer phenol in the mixture, the chance of an oxidised monomer being attacked by a monomer phenol, the only combination that can afford DPQ, will decrease. This is clarified by the following statistical analysis. If it is assumed that both monomer and dimer phenol would have the same chance to react, which is a reasonable approximation according to Fig. 8, there is a 25% chance on a monomer–monomer coupling when a 50/50 mixture of monomer and dimer is used. If the amount of DPQ formed with pure

Fig. 9. Experimental ($\square$) and theoretical ($\blacklozenge$) percentages of DPQ formed vs. the amount of dimer phenol in a mixture of monomer and dimer. [Cu] = 3.33 mM, N/Cu = 30, base/Cu = 1, [ROH]$_{total}$ = 0.20 M and T = 298 K.

monomer as the substrate (3.90%) is divided by four, and a correction is applied for the average amount of phenoxy units per phenol molecule, a theoretical percentage of 0.65% DPQ is found. This value is in fair agreement with the experimental value of 0.74% observed with the 50/50 mixture. The other theoretical percentages of DPQ, derived from the value at 0 mol% dimer, are also shown in Fig. 9 (solid diamonds). In this approximation, neither a (small) preference for the dimer phenol to the monomer phenol, nor the formation of (additional) monomer due to a redistribution reaction has been taken into account. However, as a first approximation, this curve is in reasonable agreement with the experimental values. It is noted again that the latter effect, the formation of DMP due to redistribution, is responsible for the non-zero amount of DPQ observed when starting with only dimer phenol as the substrate.

4. Conclusions

Kinetic measurements on the copper-catalysed oxidative phenol coupling with the C–O coupled dimer of DMP, 4-(2',6'-dimethylphenoxy)-2,6-dimethylphenol, have provided more insight into the mechanism of this reaction. Under normal reaction conditions, the rates observed with the dimer phenol are about twice as high compared to the monomer, and an about 13 times lower amount of DPQ is formed. A kinetic order in copper of about 2 is observed, proving that the formation of a dinuclear copper(II)–phenoxo complex is an even more important contribution to the overall reaction rate than in the case of the monomer, thereby confirming the key role such a dinuclear complex has as a catalytic intermediate in this reaction.

As in the case of monomer DMP, a simple Michaelis–Menten scheme can be used to describe the dependence of the reaction rate on the initial amount of dimer phenol, implying that the oxidation of the (dimer) phenol is the rate-determining step. The rate constant of the oxida-
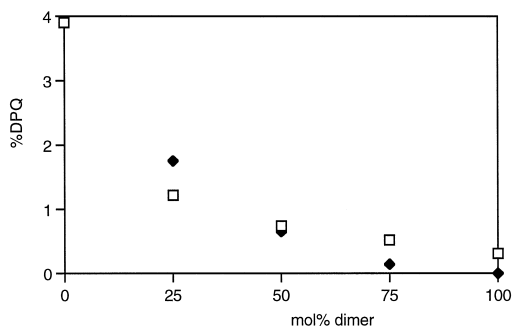
tion of the dimer was found to be about five times higher than in the case of the monomer, showing that the dimer is indeed more easily oxidised than the monomer. The value obtained for the Michaelis constant is also higher than in the case of the monomer, indicating that the formation of a complex between the substrate and the catalyst is more difficult in the case of the dimer, which is confirmed by the higher order in copper. The amount of DPQ formed is linearly proportional to the initial amount of dimer phenol.

Dioxygen-uptake experiments performed with mixtures of monomer and dimer DMP showed a slight, but clear preference for the dimer to the monomer under catalytic conditions. This preference is explained by the faster oxidation of the dimer. The amount of DPQ formed decreased exponentially with an increasing amount of the dimer in the phenol mixture, which has been attributed mainly to a statistical effect.

Acknowledgements

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