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OXIDATIONS WITH COPPER-AMINE COMPLEXES—VI[1]*

OXIDATION OF AROMATIC AMINES AND OF ANILINE IN PARTICULAR

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Abstract—Aniline—in alcoholic solutions—was found to undergo *ortho*-oxidation by oxygen under the catalytic influence of (complexes containing) copper ions. The reaction shows analogy, but also some characteristic differences, with the catalytic *ortho*-oxidation reactions of phenols studied previously. The products were 2-amino-5-anilino-quinone-4-anil (70%), azobenzene (19%) and 3-aminophenoxazone (5%). A fourth, as yet unidentified, component was isolated by chromatography over Al_2O_3. The scope of the reaction and the influence of substituents were studied. Possible reaction mechanisms are considered.

In previous investigations on the conversion of phenols into orthoquinone derivatives with oxygen as an oxidant and copper–amine complexes as catalysts, Brackman and Havinga used morpholine for complex formation on account of its stability, its relatively low volatility and its solubility in most media.[2] Extending the research it was found that primary aromatic amines were capable of rapid reaction with oxygen in presence of copper complexes. The results obtained with aniline are described in this paper.

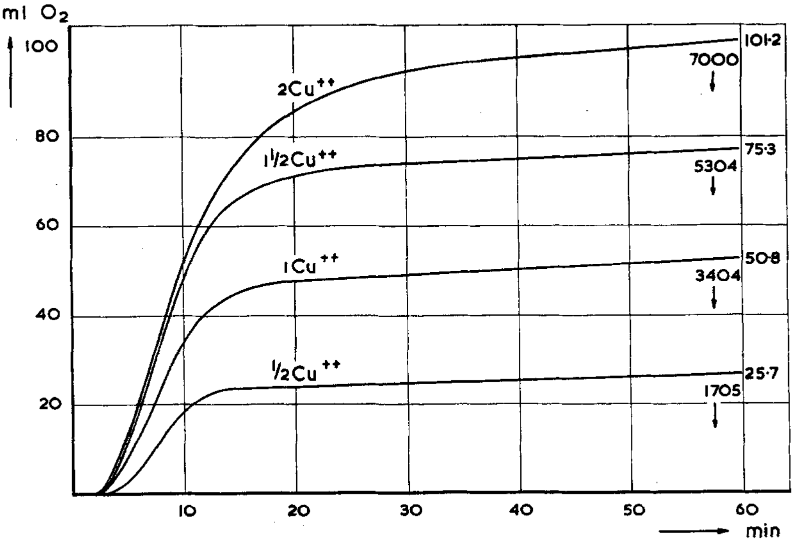

Fig. 1. Oxygen uptake as a function of time for solutions of 0·01 mole of aniline in 20 ml methanol with ½, 1, 1½ and 2 mmoles of cupric acetate. 0·1705, 0·3404, 0·5304 and 0·7000 g of copper complex precipitated in the four experiments enumerated.

The reactions were performed at room temperature under continuous magnetic stirring in the gas/liquid reaction apparatus described previously,[2] using methanol or

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* Preceding paper of this series: W. Brackman and E. Havinga *Rec. Trav. Chim.* **74**, 1107 (1955).

[1] G. Engelsma Thesis, Leiden. To be published.

[2] W. Brackman and E. Havinga *Rec. Trav. Chim.* **74**, 937 (1955).

ethanol as solvent and commercial oxygen as oxidising agent. The copper–amine complex is first allowed to form in the evacuated apparatus, oxygen is then admitted from the gas burette. A precipitate of oxidation products soon forms.

The course of the reaction can be seen from Fig. 1, in which the oxygen uptake is plotted as a function of time for 0·01 mole of aniline in 20 ml of methanol and varying amounts of copper acetate. The oxygen uptake ends rather abruptly, the amount of reaction product (copper complexes) precipitated as well as the amount of oxygen consumed being practically proportional to the amount of copper acetate originally added. Addition of another portion of copper acetate causes the reaction to continue until eventually the aniline has completely been consumed.

The main reaction products were 2-amino-5-anilino-quinone-4-anil, azobenzene and 3-aminophenoxazone-2.* The amount of oxygen consumed corresponds with that calculated on the basis of the reactions leading to these products (cf. Experimental).

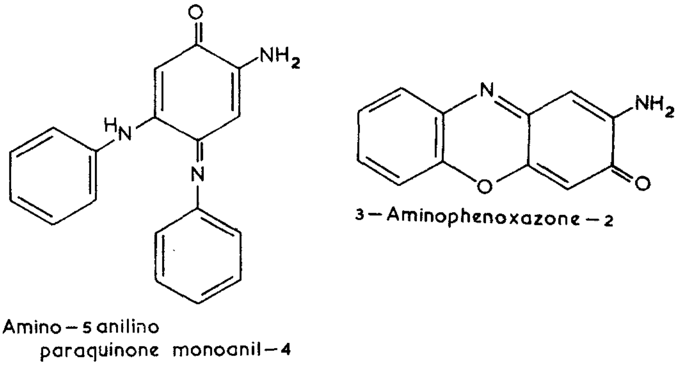

FIG. 2. Products isolated after catalytic autoxidation of aniline.

The reaction mixtures were analysed by separation of the precipitate from the mother liquor and subsequent extraction of the precipitate with ethanol. The liquid and the alcohol extracts contain azobenzene. The copper containing precipitate proved to be rather refractory to the usual methods of analysis but could be worked up by treating with ethanol which had been saturated with oxalic acid (some copper oxalate precipitates) and pouring the solution into ice-chilled dilute ammonia. The solid which separated was washed with water and crystallised from 70% ethanol, yielding a product identical with the substance obtained by oxidation of aniline with $NaBrO_3$ according to Majima.[3] Its constitution was proved to be 2-amino-5-anilino-quinone-4-anil and not the isomeride 2-anilino-5-amino-quinone-4-anil, a problem still unsolved after the investigation of Majima.

Condensation of both our product and of the compound obtained from bromate oxidation afforded a phenazine that proved to be identical with 2:3-dianilino-phenazine. The latter compound had been prepared from 3,4-dianilino-*o*-quinone and *o*-phenylenediamine according to the directions of Kehrmann and Cordone.[4] Moreover, it proved possible to obtain the 2-amino-5-anilino-quinone-4-anil by oxidation of *o*-aminophenol with silver acetate in the presence of two moles of aniline.

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* A fourth, as yet unidentified, compound could be isolated in minute quantities from the reaction mixtures by chromatography.

[3] R. Majima *Ber. Dtsch. Chem. Ges.* **44,** 231 (1911).

[4] F. Kehrmann and M. Cordone *Ber. Dtsch. Chem. Ges.* **46,** 3011 (1913).

On extraction with ether the filtrate and washing liquids from the treatment of the copper containing precipitate with the ethanolic oxalic acid solution etc. yield the poorly water-soluble 3-amino-phenoxazone-2. This could easily be identified as it is the main product obtained upon oxidation of *o*-aminophenol by HgO [5] or by air.[6]*

Although full details of the mechanism of the catalytic aniline oxidation will be discussed in subsequent papers, we wish to communicate some suggestive data:

(1) Anilines having one or more methyl- or methoxy-substituents, as a rule are subject to rapid oxidation; anilines having a group *ortho*-substituted, however, are very slowly oxidised: it was observed that *m*-and *p*-toluidine, 3,4- and 3,5-dimethylaniline, *m*- and *p*-anisidine and *β*-naphthylamine reacted very rapidly while the rate of oxidation reaction for *o*-toluidine, *o*-anisidine, 2:4-di-methylaniline and α-naphthylamine is very low. Electron withdrawing substituents seem to have an inhibitory effect: *m*-chloro- and *m*-bromo-anilines were found to react very slowly; *o*- and *p*-chloroaniline, *o*- and *p*-bromoaniline and the three nitroanilines were not oxidised.

(2) The products isolated suggest that *o*-aminophenol or the corresponding semiquinone is an intermediate in the copper-catalysed oxidation of aniline.

(3) In addition to the oxidation, in which aniline is the only amine present, a copper-catalysed oxidation of aniline takes place in the presence of an excess of a primary or secondary aliphatic amine to yield other, partly unknown products. Whether this reaction is analogous to the oxidation of phenol catalysed by a copper–amine complex,† is being investigated.

(4) In the presence of cupric acetate, aniline and substituted anilines—even the nitroanilines and N-dimethylaniline—are oxidised very rapidly with H_2O_2. In the case of aniline and *p*-toluidine this reaction gives rise to the same products as the oxidation with oxygen mentioned above. In this connexion it may be mentioned that Mann and Saunders[7] also isolated azobenzene and 2-amino-5-anilino-quinone-4-anil from the oxidation of aniline with H_2O_2 in the presence of $FeSO_4$.

(5) Just as with the phenol oxidation a metal ion that can replace the copper ion in the aniline oxidation, was not found. The rate of the copper-catalysed reaction, however, is considerably increased by addition of Ni^{2+} or Co^{2+}. It may be remarked that both Co^{2+} and Ni^{2+} salts catalyse an oxidation reaction of aniline with H_2O_2, whereas Co^{2+} salts also play the role of catalysts in a reaction of *o*-aminophenol with a primary or secondary amine in the presence of oxygen. These reactions lead to different products, however, the structures of which have not yet been elucidated. The catalysed aniline oxidation is different from the phenol oxidation since the anion also exerts its influence: chloride, bromide and iodide, even in small quantities, are inhibitors. Nitrate, on the other hand, has an accelerating activity. When cupric nitrate instead of cupric acetate is used for the aniline oxidation, the total oxygen uptake increases and the black copper complex arising from this reaction, mainly consists of a still unknown quinonoid compound.

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* The oxidation of *o*-aminophenol by air was found to be strongly catalysed by copper acetate. Normally this reaction is inhibited by the precipitation of a copper complex. This difficulty, however, could be overcome by adding drop-wise a solution of *o*-aminophenol to a solution of copper acetate pyridine complex in ethanol at such a rate that the oxidation was finished before the aminophenol–copper complex starts precipitating.

† See papers I–V of this series.

[5] O. Fischer and O. Jones *Ber. Dtsch. Chem. Ges.* **27**, 2784 (1894).

[6] F. Kehrmann *Ber. Dtsch. Chem. Ges.* **39**, 135 (1906).

[7] P. J. G. Mann and B. C. Saunders *Proc. Roy. Soc.* **B 119**, 58 (1935).

(6) Methanol and ethanol were found to be suitable solvents. In ethyl acetate, dioxane and benzene no reaction was observed.

(7) H_2O_2 reduces the induction time to zero. This is also effected by *o*-aminophenol and analogous compounds, such as *p*-aminophenol, pyrocatechol, hydroquinone, *o*- and *p*-phenylenediamine.

(8) The cuprous ion is probably involved in the reaction mechanism: on addition of cuprous acetate no induction time is observed. The same effect is brought about by addition of a few reducing agents which bear no structural relationships to *o*-aminophenol (phenylhydrazine, semicarbazide, ascorbic acid, $FeSO_4$).

As mentioned above, the *o*- and *p*-halogen-anilines cannot be oxidised under the same conditions as aniline. Addition of small amounts of hydrazine to the system, however, results in oxidation of the aniline component, giving the azobenzene derivative and quinonoid compounds.

For comparison, measurements with O_2–N_2 and O_2–CO mixtures were carried out and with the latter mixtures a considerable increase of the induction time and a lowering of the rate of oxygen uptake occurred which is in contrast with the phenomena observed with the phenol oxidation.

From the nature of the products isolated, the data on the course of the reaction and the effect of compounds added it may be concluded that the following reactions are of primary importance in the aniline oxidation.

(a) The introduction of oxygen at the *ortho*-position of aniline, taking place in an aniline–copper peroxide complex. For this reaction analogy is to be expected with the mechanism of the ortho oxidation of phenol as given in paper V of this series.[1] Some differences, however, seem to exist as evidenced by the sensitivity of the aniline oxidation towards carbon monoxide as well as to the presence of some ions (cf. 5).

(b) A series of oxidation and addition reactions of *o*-aminophenol (or of one of its oxidation products) with two equivalents of aniline, yielding amino-anilino-quinone-anil. Also oxidation and addition reactions of *o*-aminophenol to 3-amino-phenoxazone-2 occur. With these reactions H_2O_2 or a copper peroxide complex may be formed, which affects reaction (a).

(c) Oxidation of aniline to azobenzene. This reaction is catalysed by an aniline–copper–oxygen complex (c.f. Terentiev and Mogilyanskii[8]).

EXPERIMENTAL*

Oxidation of aniline. The reaction mixture, consisting of aniline (9·3 g 0·1 mole), cupric acetate. 1 H_2O p.a. (6·0 g 0·03 mole) and methanol (200 ml), is placed in a reaction vessel as described previously[1] and stirred magnetically. The temperature being kept at 20°C, the reaction is finished within 2½ hr. The total of O_2 consumed amounts to 1560 ml (772·5 mm Hg, 20°C). The precipitate formed is filtered off and repeatedly washed with water or dilute ammonia to remove the unreacted cupric acetate. The substance is extracted with ethanol of 40°C till the solvent is colourless. Yield, 10·3 g of a black copper complex.

Azobenzene. The mother liquor and the washings are evaporated to dryness *in vacuo*. The residue consists mainly of azobenzene. On extraction with dilute

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* The micro-analyses are by Mr. Han Kong Wan of our laboratory. Melting points are uncorrected.

[8] A. P. Terentiev and Ya. P. Mogilyanskii *Dokl. Akad. Nauk. SSSR* (*C.R. Acad. Sci., U.R.S.S.*) **103**, 91–3 (1955).

ammonia and crystallisation from 70% ethanol a pure product is obtained. During the oxidation of concentrated solutions of aniline as described above, a small amount of tarry by-products usually forms, from which azobenzene is purified by stream distillation or sublimation. Identification: spectrum and mixed melting point. Yield of crude product, 1·7 g; of pure substance, 1·2 g (13%). Found: C, 78·9; H, 5·8; N, 15·6. Calc. for $C_{12}H_{10}N_2$ C, 79·2; H, 5·5; N, 15·4%.

The black-copper complex. This complex is insoluble in organic solvents. It is sparingly soluble in dilute H_2SO_4 and HCl; the yellow-green colour of the solution turns red-violet via orange-red, indicating a rapid conversion (hydrolysis). The complex is less subject to chemical change when it is dissolved in ethanol to which concentrated H_2SO_4, dry HCl gas or a strong organic acid has been added. From the analysis no definite conclusions as to the composition of the black complex can be drawn. The results suggest that there is a 1:1 ratio of copper atoms to molecules of oxidation products. Found: N, 10·56; Cu, 17·34; N/Cu = 2·77. Calc. for N/Cu: 2·91.

The copper can be removed in the following way. To a solution of oxalic acid·$2H_2O$ (95 g) in ethanol (400 ml) copper complex (10·3 g) is added. A copper oxalate precipitate forms, which may be filtered. As soon as the original complex has disappeared, the solution (with or without precipitate) is poured into water (2·5 l.), to which ice (500 g) and concentrated ammonia (130 ml) have been added. The copper remains in solutionand the organic substance, which precipitates almost quantitatively, forms red-brown cyrstals, mainly consisting of amino-anilino-quinone-anil.

2-*amino*-5-*anilino*-*quinone*-4-*anil*. In order to remove 3-amino-phenoxazone-2 the product is washed with water (20–30°C) until the washings are colourless. A pure product crystallises from 65% ethanol in rosettes of small brown-red needles, m.p. 127–128°. The same crystals form from a solution of the product in petroleum-ether (b.p. 80–100°). At room temperature pink needles, probably containing solvent, are deposited from the latter solution. Yield of the crude product, 6·8 g of pure substance, 6·0 g (63%). Found for the product of m.p. 127–128° N, 14·23. Calc. for $C_{18}H_{15}N_3O$: N, 14·44%.

Freshly prepared amino-anilino-quinone-anil gives a green solution in concentrated H_2SO_4; on standing for 15 min the solution becomes dichroic. The above characteristics, the values of the R_F with paper chromatography and the mixed melting point showed that our product is identical with a compound obtained from aniline by oxidation with $NaBrO_3$ according to the directions of Majima.[3] Starting from both products 2:3-dianilinophenazine was prepared.

2:3-*Dianilinophenazine*. A solution of amino-anilino-quinone-anil (1 g), *o*-phenylene-diamine (0·4 g) and glacial acetic acid (20 g) in ethanol (30 ml) is boiled for 3 hr under reflux. On cooling, the reaction mixture is poured into dilute ammonia (200 ml); an orange-yellow precipitate forms. Crystallisation from 95% ethanol yields shining orange leaflets of 2:3-dianilino-phenazine·1 mole ethanol, m.p. 220–221° (cf. Kehrmann and Cordone, m.p. 218–219°). The violet colour of a solution of the crystals in concentrated H_2SO_4 becomes red-violet on diluting with H_2O. The mixed melting point indicates that the product is identical with the dianilino-phenazine synthesised according to the directions of Kehrmann and Cordone[4] from 4:5-dianilino-*o*-quinoneand *o*-phenylene-diamine. Found: N, 15·33. Calc. for $C_{24}H_{18}N_4$: N, 15·43%

3-*Amino-phenoxazone*-2. On extraction of the filtrate and the washings obtained from the crude amino-anilino-quinone monoanil (see above) with ether, evaporation of the ether and crystallisation of the residue from 80% ethanol, gave 3-amino-phenoxazone-2 (needles or leaves containing 1 mole of alcohol of crystallisation). This compound proved to be identical with the product prepared according to the directions of Fischer and Jonas[5] by oxidation of *o*-aminophenol with HgO as well as with the product obtained from catalytic oxidation of *o*-amino-phenol (identical R_F values with chromatography, spectra, no depression of the mixed melting point). The pure substance melts at 249–250°. The solution in concentrated H_2SO_4 has a violet colour, turning red on addition of water. Found: N, 10·95. Calc. for $C_{12}H_8N_2O_2{\cdot}C_2H_6O$: N, 10·85%. Found: N, 13·13. Calc. for $C_{12}H_8N_2O_2$: N, 13·20%.

Synthesis of 2-amino-5-anilino-quinone-4-anil. The anil was synthesised in a way analogous to the one described for the preparation of 4:5-dianilino-*o*-quinone by Kehrmann and Cordone.[4] With continuous stirring AgO (6·4 g) is added to glacial acetic acid (200 ml) and when all AgO has disappeared, *o*-aminophenol (2·0 g) and aniline (4·0 g) are added simultaneously. The reaction mixture becomes brown-red and Ag deposits. After standing for 15 min the Ag is filtered off and the filtrate is poured into excess of dilute ammonia. The precipitate mainly contains amino-anilino-quinone monoanil and a small amount of 3-amino-phenoxazone-2. The latter is removed by washing with water. The crude amino-anilino-quinone anil is crystallised from 70% ethanol; yield, 4·0 g (75%).

Fourth component. A minute amount of a fourth component is isolated on chromatographic separation of the organic substances forming the copper complex (see below). This compound dissolves in warm ethanol with an orange-yellow colour. On cooling, orange needles, m.p. 158–159°, are deposited. In concentrated H_2SO_4 the compound has a violet colour, turning red on addition of water.

Balance. With the catalytic oxidation of aniline (0·1 mole) described above the following crude products were found: amino-anilino-quinone anil ($0{\cdot}023^5$ mole), azobenzene ($0{\cdot}009^5$ mole) and 3-amino-phenoxazone-2 ($0{\cdot}002^5$ mole). For the formation of these products $0{\cdot}070,^5$ 0·019, 0·005 mole of aniline and 0·047, $0{\cdot}009,^5$ 0·006 mole of O_2 are required. Thus, 94% of the aniline appears to have been converted into the three products enumerated, while the amount of oxygen consumed ($0{\cdot}064^5$ mole) is in agreement with the calculated amount ($0{\cdot}062^5$ mole). Oxidation of methanol to formaldehyde and formic acid occurred since the specific odour of these compounds was observed.

Chromatography. On separation of the copper-free reaction mixture on a column of Al_2O_3 with 80% *cyclo*hexane—20% dioxane as an eluent the following bands appear in order of decreasing mobility:

Band colour	Type	Colour solution in conc. H_2SO_4 Colour solution on addition of H_2O	Compound
1. Yellow	broad	yellow	azobenzene
2. Yellow	narrow	violet/red	unidentified
3. Orange-yellow	narrow	violet/red	3-amino-phenoxazone-2
4. Red	broad	green/red-violet	amino-anilino-quinone anil
5. Brown-black	narrow	—	tarry by-product

With circular paper chromatography the best results were obtained when using 80% methanol—20% water as stationary phase and *cyclo*hexane as eluent. Paper: Whatman no. 1. Colouring of the spots corresponding with the quinonoid compounds was increased by HCl vapour.

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